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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

III. ON THE SIZE AND SHAPE OF THE CEREBRUM IN THE NORWAY RAT (*MUS NORVEGICUS*) AND A COMPARISON OF THESE WITH THE CORRESPONDING CHARACTERS IN THE ALBINO RAT

NAOKI SUGITA

The Wistar Institute of Anatomy and Biology

TWO FIGURES AND TWO CHARTS

In connection with an earlier study on the size and shape of the cerebrum in the albino rat (Sugita, '17), I took up a study of the changes in the size and shape of the cerebrum in the Norway rat during its growth. The method of investigation which was adopted by me for the albino rat, was followed in this case also, so that for these methods it is only necessary to refer to the paper just cited.

Table 1 shows the body and the brain measurements of the Norway rats which were used. The individuals have been grouped according to their brain weights and the average measurements for each group are given in the table. To distinguish these from the like groups for the albino rat, which will often be referred to for comparison, a capital letter N was attached to every Norway rat group number. A large part of this material has been used for further studies on cortical development or for other purposes. In a subsequent paper the individual data will be presented, so that the average values alone are here printed.

The material, consisting of 62 Norway rats (43 males and 19 females) whose brain weights fall between 1.1 grams and 2.4 grams, was collected from time to time in the city and vicinity of Philadelphia from April to November, 1916.

Figures 1 and 2 show the dorsal and lateral views of the Norway rat brain, on which the positions of the five diameters to be

TABLE I

Giving average values of the physical measurements for a series of Norway rats arranged according to brain weight groups. Sexes combined

BRAIN WEIGHT GROUP	NUMBER OF CASES	BODY WEIGHT	BODY LENGTH	TAIL LENGTH	BRAIN WEIGHT
		grams	mm.	mm.	grams
N XI	9	19.7	86	47	1.161
N XII	0				
N XIII	2	35.5	109	87	1.356
N XIV	12	37.0	113	90	1.436
N XV	5	52.6	126	104	1.536
N XVI	8	65.8	136	118	1.644
N XVII	8	93.8	157	129	1.743
N XVIII	4	131.9	166	148	1.836
N XIX	3	193.1	187	164	1.965
N XX	5	250.9	212	179	2.033
N XXI	4	296.1	223	189	2.164
N XXII	1	336.8	223	182	2.266
N XXIII	1	394.0	256	202	2.345

measured are designated. The dimensions of the figures are in accordance with the data given in table 2 and the figures are comparable with figures 1 and 2 given in the study on the albino rat brain (Sugita, '17).

Table 2 shows the average values of the five diameters of the Norway cerebrum, measured at the same locations as in the case

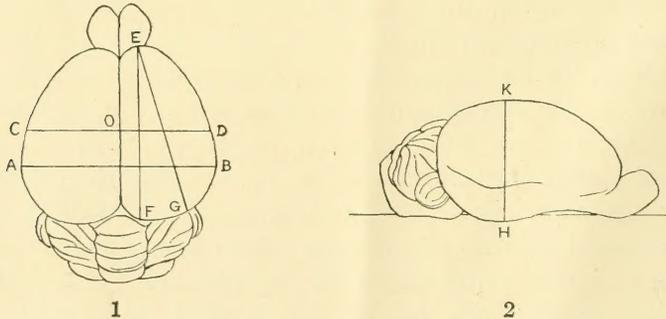


Fig. 1. Dorsal view of the Norway rat brain weighing 1.64 grams—enlarged 1.8 diameters. To show the positions at which the two measurements for the width and the two measurements for the length were taken.

Fig. 2. Lateral view of the Norway rat brain weighing 1.64 grams—enlarged 1.8 diameters. To show the position at which the height was measured.

TABLE 2

Giving the brain weight for each brain weight group, the cube root of the brain weight and the linear measurements for width, length and height of the cerebrum. Norway rat. *W. B* = Width *AB*; *W. D* = Width *CD*, *L. G* = Length *EG*, *L. F* = Length *EF* (see figure 1). *Ht.* = Height *HK* (see figure 2)

BRAIN WEIGHT GROUP	NUMBER OF CASES	BRAIN WEIGHT	CUBE ROOT OF THE BRAIN WEIGHT	<i>W. B</i>	<i>W. D</i>	<i>L. G</i>	<i>L. F</i>	<i>Ht.</i>
		grams		mm.	mm.	mm.	mm.	mm.
N XI	9	1.161	1.051	13.86	12.69	12.63	12.18	8.83
N XII	0							
N XIII	2	1.356	1.107	14.20	12.98	13.60	13.05	9.45
N XIV	12	1.436	1.128	14.45	13.21	13.71	13.24	9.31
N XV	5	1.536	1.154	14.77	13.39	14.18	13.48	9.28
N XVI	8	1.644	1.180	14.91	13.65	14.24	13.62	9.61
N XVII	8	1.743	1.204	15.10	13.92	14.54	13.88	9.97
N XVIII	4	1.836	1.225	15.17	14.20	15.00	14.32	9.98
N XIX	3	1.965	1.252	15.68	14.28	15.23	14.68	10.08
N XX	5	2.033	1.267	15.70	14.34	15.52	14.74	10.02
N XXI	4	2.164	1.293	16.25	14.94	15.92	15.12	10.18
N XXII	1	2.266	1.314	16.60	14.90	16.15	15.70	10.35
N XXIII	1	2.345	1.329	16.55	15.65	16.30	15.50	10.25

of the albino rat and denoted by the same abbreviations (figs. 1 and 2). The data are arranged in groups according to the increasing values of the brain weight at intervals of 0.1 gram.

Chart 1 gives a graphic view of the average measurements of the Norway cerebrum in each brain weight group, plotted on the basis of the data in table 2.

A study of the individual records used for table 2 shows that within any group the individual variability does not amount to more than ± 1.2 per cent, as compared with the average values for the group and each diameter shows a relatively steady increase, generally in close relation with brain weight.

On examining Chart 1, the curves for *W. B* and *W. D* are found to run almost parallel and the same is true for the curves *L. G* and *L. F*, as seen already in the case of the Albino cerebrum. By a comparison of the graphs for the width with the graphs for the length, it is evident that the rapidity of growth along the sagittal diameter is greater than that along the frontal diameter, a relation that was also seen in the Albino cerebrum. *Ht.* increases slowly as compared with the other diameters.

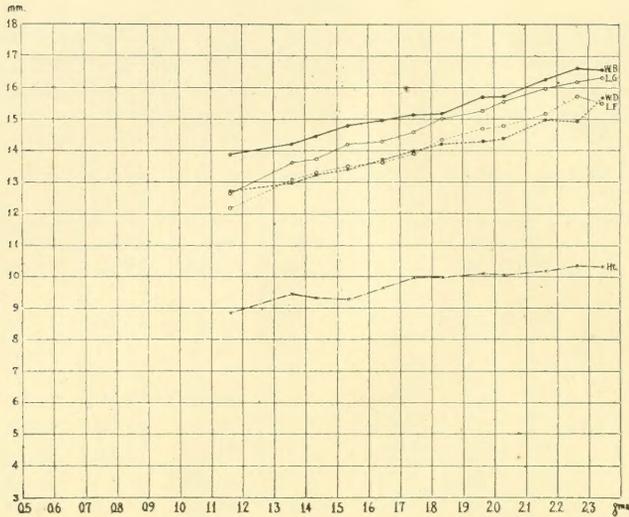


Chart 1 Giving the average values of the five diameters of the Norway rat cerebrum for each brain weight group.

●—● W.B. ○—○ L.F.
 ●—● W.D. ×—× Ht.
 ○—○ L.G.

The approximate value of each diameter can be calculated by the following formulas:

$$W. B. (\text{mm.}) = C_w \times \sqrt[3]{\text{Brain weight (grams)}} \quad (1)$$

where C_w will be 12.8 for a brain weighing 1.3–1.6 grams.
12.5 for a brain weighing 1.6–2.4 grams.

$$W. D. (\text{mm.}) = W. B. (\text{mm.}) - 1.25 \text{ mm.} \quad (2)$$

$$L. G. (\text{mm.}) = C_L \times \sqrt[3]{\text{Brain weight (grams)}} \quad (3)$$

where C_L will be 12.2 for any brain weighing 1.3–2.4 grams.

$$L. F. (\text{mm.}) = L. G. (\text{mm.}) \times 0.955 \quad (4)$$

$$Ht. (\text{mm.}) = C_H \times \sqrt[3]{\text{Brain weight (grams)}} \quad (5)$$

where C_H will be 8.5 for a brain weighing 1.1–1.4 grams.
8.2 for a brain weighing 1.4–1.9 grams.
7.9 for a brain weighing 1.9–2.4 grams.

At the first entry in this study, Group N XI (table 2), the relative volume of the cerebrum ($W. B \times L. G \times Ht.$) is

$$13.86 \times 12.63 \times 8.83 = 1546.92 \text{ (see also table 3 A)}$$

corresponding to a brain weighing 1.161 grams (body weight 19.7 grams, body length 86 mm., tail length 47 mm. and age estimated at about 10 days), while the relative volume of a cerebrum in the last entry, Group N XXIII (table 2), is

$$16.55 \times 16.30 \times 10.25 = 2765.09 \text{ (see also table 3 A)}$$

corresponding to a brain weighing 2.345 grams (body weight 394

TABLE 3

Giving the relative cerebral volumes, obtained by the formula: $W.B \times L.G \times Ht.$, for each brain weight group of the Norway (A) and of the Albino (B). The albino rat brain weight corresponding to the given Norway brain of the same age, obtained by reducing the Norway brain weight by 18 per cent, is also given in (A)

(A) NORWAY RAT				(B) ALBINO RAT		
Brain weight group N XI— N XXIII	Observed brain weight	Calculated weight of the Albino brain of the same age	Relative volume of the Norway cerebrum ob- tained by the formula: $W.B \times L.G \times Ht.$ based on table 2	Brain weight group IX—XX	Observed brain weight	Relative volume of the Albino cere- brum obtained by the formula: $W.B \times L.G \times Ht.$
	Norway rat				Albino rat	
					based on table 3 (Sugita, '17)	
	<i>grams</i>	<i>grams</i>			<i>grams</i>	
N XI	1.161	0.952	1547	IX	0.954	1335
N XIII	1.356	1.112	1825	X	1.047	1356
N XIV	1.436	1.177	1844	XI	1.156	1522
N XV	1.536	1.259	1944	XII	1.253	1606
N XVI	1.644	1.348	2040	XIII	1.334	1663
N XVII	1.743	1.429	2189	XIV	1.449	1788
N XVIII	1.836	1.505	2271	XV	1.558	1956
N XIX	1.965	1.612	2407	XVI	1.662	2014
N XX	2.033	1.667	2442	XVII	1.737	2157
N XXI	2.164	1.774	2634	XVIII	1.832	2228
N XXII	2.266	1.858	2775	XIX	1.924	2285
N XXIII	2.345	1.923	2765	XX	2.037	2568

grams, body length 256 mm. and tail length 202 mm.). According to these determinations, the volume increases by 79 per cent while the weight increases by 102 per cent, showing roughly that the specific gravity of a brain in the fully mature Norway rat is higher than that of younger one.

By an estimate based on the data given by Donaldson and Hatai ('11), it would appear that, if the Albino and the Norway

brains of the same age be compared, the Norway brain weight is 20 to 25 per cent higher than the albino brain weight, when the albino brain weight is taken as the standard. For the purpose of comparison in their developmental stages, I have assumed that the Norway brain would correspond to an Albino brain whose weight is 18 per cent less than the Norway brain weight of like age. Here the Norway brain weight is taken as the standard. The evidence for this conclusion will be given in detail in a later paper which discusses the thickness of the cortex in the brain of the Norway rat.

A comparison of the Norway brain with that of the Albino may be made in two ways; by a comparison of brains of like weight or by a comparison of brains of like ages. In Chart 2, the diameters of the cerebrum in the Norway rat are compared with those in the albino rat. In part A of this chart, the data for the Norway and the albino rats were entered according to the observed brain weights, and in part B of the same chart, the same linear measurements for the Norway as used in part A are entered above brain weights which are 18 per cent below the observed Norway brain weights and which in turn represents the weights for the albino brains of like age with those of the Norway rat. The corresponding brain weights of the Norway and of the albino rats at the same age are given in table 3 A. It is assumed that the albino brain weight is 82 per cent of that for the Norway.

If, as shown in part A of Chart 2, the comparison is made between the brains of the two rats using similar brain weight groups, *W. B* in the Norway cerebrum surpasses *W. B* in the Albino on the average by 0.4 mm. *L. G* is quite equal in both the rats for brains weighing 1.1 to 1.6 gms, after which stage it is clearly greater for the Albino. *Ht.* is on the average slightly in favor of the Norway.

If, on the other hand, as shown in part B of the chart, a Norway cerebrum be compared with an Albino cerebrum of the same age (over 10 days), the Norway cerebrum has a greater *W. B* than the Albino, by about 1.00 mm., and also a greater *L. G*. The excess of *L. G* in the early age is on the average 0.7 mm., but this difference decreases as the age advances, owing to the more rapid growth of the albino cerebrum in this dimension.

Ht. in the Norway cerebrum is greater on the average than that of the Albino of the same age by ca. 0.6 mm. As was to be expected the excess in the dimensions of the Norway brain are greater in part B, Chart 2, where the brains are compared according to age, because at like ages the Norway brain is heavier.

The chief point of interest brought out by this comparison is the similarity in the direction of the corresponding curves for the two forms and the fact that the age at which *L. G.* crosses *W. B.* in the Albino is approximately the age at which these diameters come nearest to crossing in the Norway.

Table 3 A gives the relative volumes of the cerebrum in each brain weight group of the Norway rat, obtained by the formula:

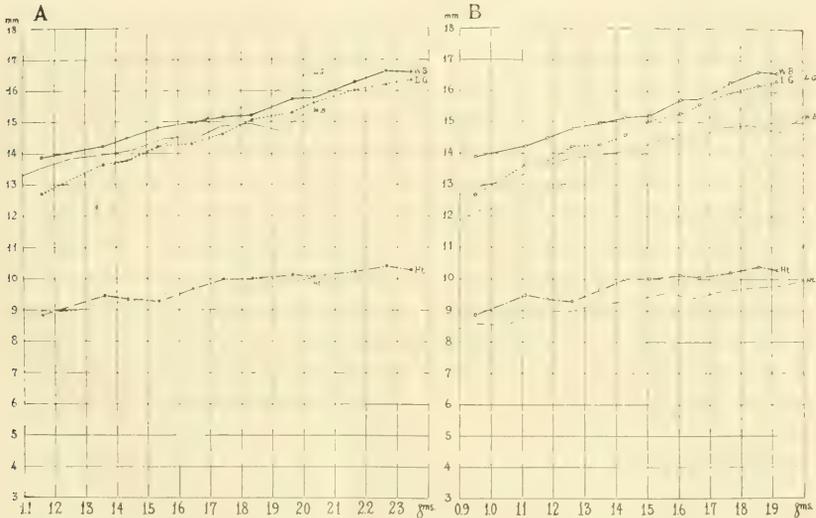


Chart 2 Giving a comparison of the cerebral measurements (*W. B.*, *L. G.* and *Ht.*) of the Norway and the albino rats. Part A was plotted according to the observed weight of the brain for each brain weight group of the Norway rat. Part B was plotted according to the corresponding weight of the brain in the Albino of the same age, the Albino brain weights being obtained by reducing the observed weight of the Norway brain by 18 per cent. The measurements for the Norway cerebrum were based on table 2 of this paper and the measurements for the Albino cerebrum were based on table 3 of the first paper of this series (Sugita '17).

—○—	<i>W. B.</i> (Norway)	—	<i>W. B.</i> (Albino)
●●●	<i>L. G.</i> (")	-----	<i>L. G.</i> (")
- - -○-	<i>Ht.</i> (")	- - - - -	<i>Ht.</i> (")

$W. B \times L. G \times Ht.$, based on the measurements given in table 2. Table 3 B gives the similar calculations for the Albino cerebrum based on the measurements given in table 3 of the first paper in this series (Sugita, '17).

Table 4 gives for both the rats the cerebral volumes (A) according to brain weight, and (B) according to age. In table 4 A,

TABLE 4

Giving the ratios of the cerebral volumes of the Norway to the Albino rats (A) pairing the brains of the same weight and (B) pairing the brains of the same age. Calculated on the basis of the data given in table 3

(A)			(B)		
Pairs of groups in which a comparison of cerebral volume was made. Like brain weights		Ratio of cerebral volume between two groups of the like weight. Albino = 1.000	Pairs of groups in which a comparison of cerebral volume was made. Like ages		Ratio of cerebral volume between two groups of the like age. Albino = 1.000
Norway	Albino		Norway	Albino	
N XI	XI	1.016	N XI	IX	1.159
N XIII	XIII	1.097	N XIII	X ¹	1.271 ¹
N XIV	XIV	1.031	N XIV	XI	1.212
N XV	XV	0.994	N XV	XII	1.210
N XVI	XVI	1.013	N XVI	XIII	1.227
N XVII	XVII	1.015	N XVII	XIV	1.224
N XVIII	XVIII	1.019	N XVIII	XV	1.161
N XIX	XIX	1.053	N XIX		
N XX	XX	0.951	N XX	XVI	1.212
			N XXI	XVII	1.221
			N XXII	XVIII	1.248
			N XXIII	XIX	1.210
Average.....		1.021	Average.....		1.214

¹ As the reduced brain weight of Group N XIII falls between the brain weights of Groups X and XI, the mean value of the cerebral volumes of Groups X and XI was used in comparison.

the brains of like brain weight groups are compared, by pairing the groups which carry the same number. By this comparison, it is seen that, on the average, the values for the Norway rat are somewhat greater, except in Group XV and in the old age group, Group XX, in which the reverse is true. This shows that the Norway brain has, as a rule, a less specific gravity than the brain of the albino which has the same weight. One important

factor in producing this relation is that the Norway brain is younger and less advanced in myelination than the albino brain of the same weight.

In table 4 B the cerebral volume of a Norway rat is compared with the cerebral volume of an Albino of presumptively the same age. Each Norway brain weight group is paired with an albino group which has the average brain weight nearest to the corresponding albino brain weight of the same age with the Norway group. The data were all taken from table 3. Compared in this way, the Norway cerebrum has a volume about 21 per cent above that of the albino cerebrum of the same age, as shown in table 4 B.

The width-length index of the Norway cerebrum, which is obtained according to formula $\frac{W. D \times 100}{L. F}$, is 104 in the youngest Group N XI, and decreases as the brain weight advances, dropping to 97 or less in the last and oldest groups. Compared with the like group of the Albino, the width-length index of the Norway cerebrum is on the average always higher by 2 or more points than that of the albino cerebrum. So, it may be concluded that the Norway cerebrum is becoming somewhat elongated as the age advances, but not to so marked a degree as does the albino cerebrum and that it is always somewhat more rounded in shape as compared with the albino cerebrum of the same weight or age. The method of measurement here used reveals only in part the degree of difference in the shape of the two brains, for direct inspection shows the surface of the Norway cerebrum to be distinctly more rounded than that of the Albino, especially at the frontal poles.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

IV. ON THE THICKNESS OF THE CEREBRAL CORTEX OF THE NOR- WAY RAT (*MUS NORVEGICUS*) AND A COMPARISON OF THE SAME WITH THE CORTICAL THICKNESS IN THE ALBINO RAT

NAOKI SUGITA

From the Wistar Institute of Anatomy and Biology

TEN CHARTS

I. INTRODUCTION

In my second study in this series (Sugita, '17a), I described in detail the postnatal growth of the cortex in thickness in the brain of the albino rat. With the same purpose and by the same technique, I have examined also the growth of the cerebral cortex of the Norway rat, the wild form from which the albino rat has been derived. Donaldson and Hatai ('11) have been interested in a comparison of the wild Norway with the albino rats in respect of their body measurements and the size of the central nervous system. They have concluded that on account of domestication the albino rat grows less well than the wild Norway rat, from which it has been derived, and especially that the relative weight of the brain of the adult albino rat is about 16 per cent less than that of the Norway rat of like body weight. It has been assumed as probable that the greater weight of the brain in the Norway rat is due to an enlargement of the constituent neurons rather than to an increase in their number. The percentage of water appears to be nearly the same in the central nervous system of both forms during the period of active growth, but after this period it remains slightly higher in the Norway rat. From these differences between the two forms as regards the weight and the water content of their brains, it is also inferred that there will be some structural

differences in the cerebral cortex. Consequently, it became desirable for me to compare in these two forms, one wild and aggressive and the other gentle and domesticated, the course of the growth of the cerebral cortex.

Using my previous studies on the Albino (Sugita, '17a) and on the form of the Norway brain (Sugita, '18) as a point of departure, I will present in this paper the data on the cortical thickness of the Norway rat and will compare these with the data for the Albino. In this comparison of the brains of the two forms, the data, other than those on cortical thickness, are all quoted from Donaldson and Hatai ('11, '15).

II. MATERIAL

The Norway rats used in this study, were all supplied through the courtesy of The Wistar Institute and were trapped alive in Philadelphia and its vicinity, between April and November, 1916. There were 36 males and 18 females, representing every stage of growth between 17 and 394 grams in body weight. In the preparation of the material and the arrangement of the data, the same methods as those described in my former study on the Albino (Sugita, '17a) were followed. For the discrimination of a Norway group from an albino group of the same tabular number, the Norway records carry the capital letter N before their group number.

The following tables, tables 1 and 2, give the sex, body and tail lengths, and body and brain weights of the Norway rats used in this study, grouped according to their brain weights and averaged for each group. Table 1 contains the material used for the sagittal and frontal sections and table 2 that for the horizontal sections.

Comparing the body measurements of this series with those given in table 85 in "The Rat" (Donaldson, '15), it is found that the average values for my material by groups correspond fairly well with the table values.

The increase in the body measurements of the Norway rat according to age is imperfectly known, so that we can not infer the age from the body measurements with any exactness.

TABLE 1

Showing the sex, body weight and length, tail length and brain weight of the Norway rats used in this study (sagittal and frontal sections) accompanied by the averages for each brain weight group

NO.	LITTER NO.	SEX	BODY WEIGHT	BODY LENGTH	TAIL LENGTH	BRAIN WEIGHT
			<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>
N XI b	(1)	m	19.8	84	41	1.155
a	(1)	m	20.8	86	44	1.160
i	(2)	m	17.8	85	65	1.175
			19.5	85	50	1.164
N XII						
N XIII a	(3)	m	35.3	110	66	1.369
			35.3	110	86	1.369
N XIV b	(4)	m	33.1	104	84	1.407
g	(3)	m	37.5	112	88	1.429
a	(4)	m	33.8	113	94	1.431
i	(3)	m	36.3	107	86	1.431
e	(5)	m	43.6	124	108	1.437
k	(3)	f	36.1	112	87	1.445
			36.7	112	91	1.430
N XV c		m	42.6	122	102	1.517
e		m	66.7	135	114	1.557
			54.7	129	108	1.537
N XVI a		m	74.8	137		1.619
g		m	54.8	130	107	1.632
e		m	56.3	128	105	1.636
			62.0	132	106	1.629
N XVII e		f	81.0	152	120	1.710
g		m	57.0	137	113	1.721
a		f	118.5	172	136	1.738
c		f	104.0	164	132	1.788
			90.1	156	125	1.739
N XVIII c		f	136.9	157	147	1.825
a		m	128.1	177	142	1.833
			132.5	167	145	1.829
N XIX b		m	160.7	177	158	1.962
a		f	251.0	210	174	1.981
			205.9	194	166	1.972

TABLE I—Continued

NO.	LITTER NO.	SEX	BODY WEIGHT	BODY LENGTH	TAIL LENGTH	BRAIN WEIGHT
			<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>
N XX c a	(1)	f	254.0	215	180	2.015
		f	253.1	213		2.089
			253.6	214	180	2.052
N XXI g d		m	331.0	215	195	2.156
		m	231.8	215	174	2.187
			281.4	215	185	2.172
N XXII						
N XXIII a		m	394.0	256	202	2.345
			394.0	256	202	2.345

TABLE 2

Showing the sex, body weight and length, tail length and brain weight of the Norway rats used in this study (horizontal sections) accompanied by the averages for each brain weight group

NO.	LITTER NO.	SEX	BODY WEIGHT	BODY LENGTH	TAIL LENGTH	BRAIN WEIGHT
			<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>
N XI d h c	(1)	m	20.0	85	42	1.133
	(2)	m	17.0	83	64	1.160
	(1)	m	20.7	87	41	1.199
			19.2	85	49	1.164
N XII						
N XIII b	(3)	m	35.7	108	87	1.343
			35.7	108	87	1.343
N XIV c h j f d	(4)	m	31.7	103	83	1.407
	(3)	m	36.7	111	87	1.428
	(3)	m	38.4	115	88	1.443
	(5)	f	43.8	126	102	1.475
	(4)	m	34.7	108	87	1.481
			37.1	113	89	1.447
N XV b d		m	48.5	121	100	1.511
			54.1	122	101	1.529
			51.3	122	101	1.520

TABLE 2—Continued

NO.	LITTER NO.	SEX	BODY WEIGHT	BODY LENGTH	TAIL LENGTH	BRAIN WEIGHT
			<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>
N XVI f		f	56.7	129	109	1.613
h		f	73.9	148	132	1.666
d		f	66.7	138	112	1.674
b		m	98.3	156	141	1.699
			<i>73.9</i>	<i>143</i>	<i>124</i>	<i>1.663</i>
N XVII f		m	71.8	140	112	1.717
b		m	95.4	155	130	1.718
d		m	125.0	180	150	1.773
h		f	97.7	152	139	1.779
			<i>97.5</i>	<i>157</i>	<i>133</i>	<i>1.747</i>
N XVIII b		f	128.5	168	153	1.815
d		f	134.0	163	148	1.870
			<i>131.3</i>	<i>166</i>	<i>151</i>	<i>1.843</i>
N XIX c		m	167.6	175	160	1.953
			<i>167.6</i>	<i>175</i>	<i>160</i>	<i>1.953</i>
N XX e		f	321.8	230	188	2.008
b	(4)	f	227.0	206	178	2.028
			<i>274.4</i>	<i>218</i>	<i>183</i>	<i>2.018</i>
N XXI f		m	339.4	244	190	2.150
j		f	282.3	216	195	2.162
			<i>310.9</i>	<i>230</i>	<i>193</i>	<i>2.156</i>
N XXII						
N XXIII a		m	394.0	256	202	2.345
			<i>394.0</i>	<i>256</i>	<i>202</i>	<i>2.345</i>

But, according to the authors cited above, the marked difference between the two forms in body size does not appear during the period of rapid growth, but later, so that at maturity the Norway rat has a body weight 25 to 40 per cent above that of the Albino rat of like age. For the same age however, the percentages of water in the central nervous system is just a trifle higher in the case of the Norway. Relative to the body weight, the Norway rat at maturity has a heavier brain than the albino rat, the difference being about 16 per cent in favor of the Norway.

On the basis of these rough data, the approximate age of the individuals in tables 1 and 2 can be inferred.

To my regret, I did not obtain material under 17 grams in body weight. I could, therefore, not make a complete study of the postnatal growth of the cerebral cortex of the Norway rat from birth on and must in consequence be content to present in this paper the data beginning with material probably from 10 to 12 days old. It may, however, be noted here, that, among the rats trapped, the following were evidently members of the same litter and still following the mother.

(1) N XI a, N XI b, N XI c, N XI d, with their mother N XX a, and three other young which were used for another purpose.

(2) N XI i, N XI h, and four others.

(3) N XIII a, N XIII b, N XIV g, N XIV h, N XIV i, N XIV j, N XIV k.

(4) N XIV e, N XIV f, and two others.

(5) N XIV a, N XIV b, N XIV c, N XIV d and two others, with their mother N XX b.

This suggests that the Norway rats whose brain weighs less than 1.5 grams or whose body weighs less than about 40 grams are not yet independent of their mothers.

III. TECHNIQUE

For the technique of fixation and imbedding and the making and staining of the sections, the same procedures which have been already described (Sugita, '17 a) were followed. Thirteen different localities were measured on sections in three planes corresponding to those used in the former study of the Albino cortex (cf. figs. 2, 4 and 6 in the paper cited).

As to the cortical cell-lamination of the Norway rat, two sets of figures with explanations were given in the former paper (Sugita, '17 a) reproduced from Lewis (1881) and Fortuyn ('14) and to those I would like to call attention on this occasion. There does not appear to be any important difference between the Norway and the albino rats in the cell-lamination of the cerebral cortex.

IV. OBSERVED DATA GIVEN IN TABLE AND CHART

As in the case of the albino rat, the measurement of the cortical thickness of the Norway brain was made at the localities I-XIII by the direct measurement of the sections as prepared and was then recorded without correction. The results thus obtained are condensed in table 3.

Table 3 shows for each brain weight group the average thickness of the cerebral cortex of the Norway rat as directly observed in each of the three sections and the general average obtained by averaging the thicknesses of the sagittal, frontal and horizontal sections. The average brain weight corresponding to the average thickness of the cortex is obtained by doubling the weight of the brain, from which the sagittal and frontal sections were taken, adding the weight of the brain from which the horizontal sections were taken, and dividing the sum by three.

Chart 1 is based on table 3 and shows the increase in the general average thickness of the cerebral cortex of the Norway rat,

TABLE 3

Showing the general average thickness of the cerebral cortex of the Norway rat according to brain weight groups, also the average thickness in the sagittal, frontal and horizontal sections. Observations on slide, without correction

BRAIN WEIGHT GROUP	SAGITTAL SECTION			FRONTAL SECTION	HORIZONTAL SECTION			GENERAL AVERAGE	
	Number of cases	Brain weight <i>grams</i>	Thick-ness <i>mm.</i>	Thick-ness <i>mm.</i>	Number of cases	Brain weight <i>grams</i>	Thick-ness <i>mm.</i>	Brain weight <i>grams</i>	Thick-ness <i>mm.</i>
N XI	3	1.164	1.34	1.43	3	1.164	1.44	1.164	1.40
N XII	0				0				
N XIII	1	1.369	1.35	1.50	1	1.343	1.50	1.360	1.45
N XIV	6	1.430	1.43	1.48	5	1.447	1.54	1.436	1.48
N XV	2	1.537	1.40	1.50	2	1.520	1.58	1.532	1.49
N XVI	3	1.629	1.41	1.54	4	1.663	1.63	1.640	1.53
N XVII	4	1.739	1.51	1.56	4	1.747	1.59	1.742	1.55
N XVIII	2	1.829	1.51	1.64	2	1.843	1.63	1.834	1.59
N XIX	2	1.972	1.56	1.58	1	1.953	1.68	1.965	1.61
N XX	2	2.052	1.49	1.48	2	2.018	1.58	2.041	1.52
N XXI	2	2.172	1.53	1.53	2	2.156	1.75	2.166	1.60
N XXII	0				0				
N XXIII	1	2.345	1.60		1	2.345	1.73	2.345	1.67

as directly observed, and without correction and also the average values for the sagittal, frontal and horizontal sections, according to the increase of the brain weight.

V. CORRECTED DATA PRESENTED IN TABLES AND CHARTS

Using the detailed observed values which were all carefully tabulated, although they have not been published, a series of

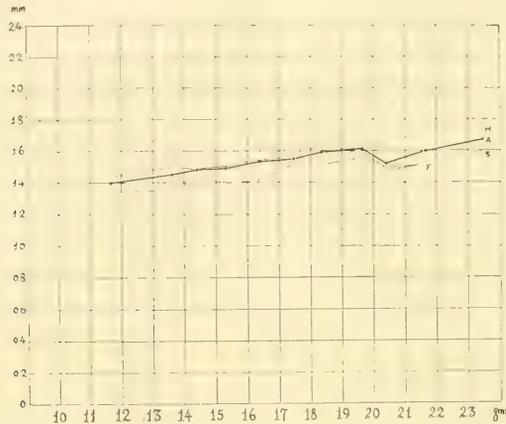


Chart 1 Giving the average thickness of the cortex on slide (not corrected) in the sagittal, frontal and horizontal sections and the general average thickness on brain weight group in the Norway rat. Based on table 3. - - - -S Average thickness of the cortex in sagittal section. Measured on slide. ———F Average thickness of the cortex in frontal section. Measured on slide. - - - -H Average thickness of the cortex in horizontal section. Measured on slide. •—•A General average thickness of the cortex of three kinds of sections. Measured on slide.

correction-coefficients, obtained in exactly the same manner as for the albino rat, were found and applied to the observations on the Norway cortex. The corrected values are those entered in tables 4, 5 and 6. The tables also contain in each case the measurements from which the correction-coefficient was obtained and for each brain weight group the average value of the correction-coefficient for that group.

Table 7 shows the corrected values for the average thickness of the cortex, obtained in the same way as were the uncorrected

TABLE 4

Showing the corrected values of the cortical thickness in the sagittal section for each individual and for each brain weight group. The data for the correction-coefficients are indicated separately for each brain and the coefficient is given with the average for each group

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		THICKNESS OF THE CORTEX (SAGITTAL SECTION)						
		Diam. L. F on fresh brain	Diam. L. F on slide	Loc. I	Loc. II	Loc. III	Loc. IV	Loc. V	Average	
	grams	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.	
N XI	b	1.155	11.75	10.40	2.18	1.73	1.44	1.21	1.05	1.52
	a	1.160	12.10	10.15	2.40	1.83	1.63	1.32	1.07	1.65
	i	1.175	12.55	9.80	2.61	1.83	1.61	1.26	1.04	1.67
		1.164		1.20	2.40	1.80	1.56	1.26	1.05	1.61
N XII										
N XIII	a	1.369	12.95	10.10	2.47	1.87	1.72	1.33	1.27	1.73
		1.369		1.28	2.47	1.87	1.72	1.33	1.27	1.73
N XIV	b	1.407	13.45	10.50	2.76	2.04	1.73	1.59	1.36	1.90
	g	1.429	13.05	10.10	2.56	1.82	1.72	1.40	1.32	1.76
	a	1.431	13.15	10.40	2.64	2.01	1.82	1.56	1.34	1.87
	i	1.431	13.05	10.25	2.56	1.90	1.71	1.48	1.31	1.79
	e	1.437	12.80	10.05	2.47	1.87	1.73	1.40	1.24	1.74
	k	1.445	13.35	10.30	2.83	2.03	1.78	1.64	1.38	1.93
		1.430		1.28	2.64	1.95	1.75	1.51	1.33	1.84
N XV	c	1.517	12.70	10.10	2.56	1.92	1.72	1.38	1.20	1.76
	e	1.557	13.75	10.25	2.83	1.93	1.72	1.49	1.44	1.88
		1.537		1.30	2.70	1.93	1.72	1.44	1.32	1.82
N XVI	a	1.619	13.50	10.25	2.68	2.04	1.77	1.46	1.34	1.86
	g	1.632	13.45	10.00	2.86	2.17	1.84	1.53	1.21	1.92
	e	1.636	13.55	10.10	2.73	1.98	1.77	1.49	1.31	1.86
		1.629		1.33	2.76	2.06	1.79	1.49	1.29	1.88
N XVII	e	1.710	13.70	10.50	2.84	2.09	1.95	1.55	1.42	1.97
	g	1.721	13.40	10.35	2.78	2.13	1.98	1.63	1.38	1.98
	a	1.738	13.60	10.70	2.72	2.00	1.76	1.40	1.21	1.82
	c	1.788	14.20	11.20	2.93	2.15	1.92	1.65	1.33	2.00
		1.739		1.29	2.82	2.09	1.90	1.56	1.34	1.94
N XVIII	c	1.825	14.30	10.85	2.91	2.07	1.88	1.49	1.28	1.93
	a	1.833	14.20	11.50	2.89	2.06	1.69	1.51	1.48	1.93
		1.829		1.27	2.90	2.07	1.79	1.50	1.38	1.93

TABLE 4—Continued

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		THICKNESS OF THE CORTEX (SAGITTAL SECTION)					
		Diam. L. F on fresh brain	Diam. L. F on slide	Loc. I	Loc. II	Loc. III	Loc. IV	Loc. V	Average
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>
N XIX b	1.962	14.70	11.50	2.98	2.12	1.97	1.54	1.46	2.01
a	1.981	14.40	11.50	2.83	2.08	1.75	1.54	1.44	1.93
	<i>1.972</i>	<i>1.26</i>		<i>2.91</i>	<i>2.10</i>	<i>1.86</i>	<i>1.54</i>	<i>1.45</i>	<i>1.97</i>
N XX c	2.015	14.55	11.50	2.86	2.00	1.81	1.55	1.43	1.93
a	2.089	14.95	12.00	2.75	1.93	1.67	1.34	1.30	1.80
	<i>2.052</i>	<i>1.25</i>		<i>2.81</i>	<i>1.97</i>	<i>1.74</i>	<i>1.45</i>	<i>1.37</i>	<i>1.87</i>
N XXI g	2.156	15.15	11.90	3.01	2.15	1.82	1.58	1.40	1.99
d	2.187	15.30	11.50	2.94	2.09	1.85	1.60	1.41	1.98
	<i>2.172</i>	<i>1.30</i>		<i>2.98</i>	<i>2.12</i>	<i>1.84</i>	<i>1.59</i>	<i>1.41</i>	<i>1.99</i>
N XXII									
N XXIII a	2.345	14.50	12.50	2.74	2.07	1.75	1.38	1.33	1.86
	<i>2.345</i>	<i>1.16</i>		<i>2.74</i>	<i>2.07</i>	<i>1.75</i>	<i>1.38</i>	<i>1.33</i>	<i>1.86</i>

values shown in table 3. This table (table 7) serves as a standard for discussing the actual thickness of the fresh cortex of the Norway rat. The average thickness in the adult Norway rat is 2.06 mm., as obtained by averaging the thicknesses of the cortex in Groups N XV–N XXIII, in which stages the cortex may be considered to have reached its full thickness.

Charts 2 to 7 show graphically the data given in tables 4 to 6 respectively, and chart 8, which is based on table 7 giving the average values, presents a general picture of the growth changes in the cortex according to brain weight.

Charts 2, 4 and 6 show the individual determinations for the thickness of the cortex in the sagittal, frontal and horizontal sections, respectively, plotted according to the brain weight. Chart 2 gives the individual records for locality I and locality V with the average for all localities from I to V in the sagittal sections. In a like manner, chart 4 gives the values for localities VII and VIII with the average of localities VI to VIII for the

TABLE 5

Showing the corrected values of the cortical thickness in the frontal section for each individual and for each brain weight group. The data for the correction-coefficients are indicated separately for each brain and the coefficient is given with the average for each group

BRAIN WEIGHT GROUP	BRAIN WEIGHT	COEFFICIENT		THICKNESS OF THE CORTEX (FRONTAL SECTION)				
		Diam. W. D on fresh brain	Diam. W. D on slide	Loc. VI	Loc. VII	Loc. VIII	Average	
	grams	mm.	mm.	mm.	mm.	mm.	mm.	
N XI	b	1.155	13.00	9.90	2.05	2.11	1.68	1.95
	a	1.160	12.70	10.00	1.94	1.92	1.62	1.83
	i	1.175	12.50	9.20	1.96	1.99	1.62	1.86
		1.164		1.31	1.98	2.01	1.64	1.88
N XII								
N XIII	a	1.369	13.00	10.00	2.07	2.21	1.59	1.96
		1.369		1.30	2.07	2.21	1.59	1.96
N XIV	b	1.407	13.05	9.90	2.27	2.13	1.71	2.04
	g	1.429	13.20	9.50	2.18	2.29	1.71	2.06
	a	1.431	12.85	10.70	2.04	2.00	1.73	1.92
	i	1.431	13.40	10.30	1.90	2.06	1.57	1.84
	e	1.437	13.25	9.80	1.89	2.13	1.56	1.86
	k	1.445	13.30	9.90	2.12	2.15	1.65	1.97
		1.430		1.32	2.07	2.13	1.66	1.95
N XV	c	1.517	13.20	10.00	1.98	2.21	1.62	1.94
	e	1.557	13.50	9.60	2.28	2.39	1.76	2.14
		1.537		1.36	2.13	2.30	1.69	2.04
N XVI	a	1.619	13.80	10.80	2.01	2.13	1.72	1.95
	g	1.632	13.70	9.90	2.24	2.57	1.83	2.21
	e	1.636	13.80	10.00	2.14	2.36	1.75	2.08
		1.629		1.35	2.13	2.35	1.77	2.08
N XVII	e	1.710	13.80	10.00	2.15	2.31	1.68	2.05
	g	1.721	13.60	10.40	2.20	2.35	1.75	2.10
	a	1.738	14.10	10.60	2.01	2.17	1.66	1.95
	c	1.788	13.95	10.60	2.35	2.40	1.82	2.19
		1.739		1.33	2.18	2.31	1.73	2.07
N XVIII	c	1.825	14.45	10.70	2.20	2.35	1.73	2.09
	a	1.833	13.95	11.70	2.18	2.22	1.80	2.07
		1.829		1.27	2.19	2.29	1.77	2.08

TABLE 5—Concluded

BRAIN WEIGHT GROUP	BRAIN WEIGHT	COEFFICIENT		THICKNESS OF THE CORTEX (FRONTAL SECTION)			
		Diam.W. <i>D</i> on fresh brain	Diam.W. <i>D</i> on slide	Loc. VI	Loc. VII	Loc. VIII	Average
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>
N XIX b	1.962	14.60	11.60	2.08	2.28	1.68	2.01
a	1.981	13.95	10.80	2.04	2.21	1.72	1.99
	1.972	1.26		2.06	2.25	1.70	2.00
N XX c	2.015	14.30	10.50	2.14	2.32	1.73	2.06
a	2.089	14.50	11.20	1.80	2.08	1.66	1.85
	2.052	1.33		1.97	2.20	1.70	1.96
N XXI g	2.156	14.75	11.10	2.03	2.24	1.69	1.99
d	2.187	15.05	10.80	2.19	2.54	1.77	2.17
	2.172	1.36		2.11	2.39	1.73	2.08
N XXII							
N XXIII							

frontal sections. Chart 6 does the same for localities IX and XIII with the average of localities IX to XIII in the horizontal sections. Charts 3, 5 and 7 show the average values of the cortical thickness in the sagittal, frontal and horizontal sections, for each brain weight group. Further, on each chart is shown the change in thickness at each one of the localities measured in that section.

Chart 8 is based on table 7 and shows the general average (corrected) thickness of the cerebral cortex of the Norway rat according to the brain weight and also the average thickness in each of the sections.

VI. DISCUSSION

The relations existing between each of the several localities measured in this study of the Norway are quite similar to the relations found in the cerebral cortex of the albino rat. Individual variations appear, but these are no higher than ± 6 per cent, compared with the average values of the group. No sex differ-

TABLE 6

Showing the corrected values of the cortical thickness in the horizontal section for each individual and for each brain weight group. The data for the correction-coefficients are indicated separately for each brain and the coefficient is given with the average for each group

BRAIN WEIGHT GROUP	BRAIN WEIGHT	COEFFICIENT		THICKNESS OF THE CORTEX (HORIZONTAL SECTION)						
		Diam. W. B on fresh brain	Diam. W. B on slide	Loc. IX	Loc. X	Loc. XI	Loc. XII	Loc. XIII	Average	
	grams	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.	
N XI	d	1.133	13.80	11.00	2.52	1.91	1.72	1.56	1.31	1.80
	h	1.160	13.80	10.10	2.85	1.99	1.92	1.69	1.50	1.99
	c	1.199	13.90	10.80	2.52	1.84	1.75	1.62	1.33	1.81
		1.164	1.30		2.63	1.91	1.80	1.62	1.38	1.87
N XII										
N XIII	b	1.343	14.20	10.30	2.91	2.02	2.03	1.85	1.57	2.08
		1.343	1.38		2.91	2.02	2.03	1.85	1.57	2.08
N XIV	c	1.407	14.20	10.60	2.57	2.06	1.93	1.72	1.48	1.95
	h	1.428	14.35	10.70	3.19	2.14	2.08	1.82	1.57	2.16
	j	1.443	14.35	10.50	2.96	2.22	2.24	1.95	1.69	2.21
	f	1.475	14.55	10.90	2.92	2.08	2.03	1.81	1.55	2.08
	d	1.481	14.60	10.25	2.91	2.22	1.88	1.74	1.56	2.06
		1.447	1.36		2.91	2.14	2.03	1.81	1.57	2.09
N XV	b	1.511	14.65	10.10	3.19	2.32	2.15	1.97	1.78	2.28
	d	1.529	14.50	10.50	3.11	2.21	2.12	1.91	1.62	2.19
		1.520	1.41		3.15	2.27	2.14	1.94	1.70	2.24
N XVI	f	1.613	14.90	11.00	3.25	2.34	2.10	1.96	1.66	2.26
	h	1.666	15.00	10.95	2.95	2.23	2.22	1.94	1.76	2.22
	d	1.674	15.15	11.30	2.93	2.14	2.12	1.85	1.52	2.12
	b	1.699	14.75	11.05	3.33	2.36	1.92	1.76	1.48	2.17
		1.663	1.35		3.12	2.27	2.09	1.88	1.61	2.19
N XVII	f	1.717	15.45	11.45	2.89	2.18	2.16	1.93	1.62	2.16
	b	1.718	14.60	11.30	2.73	2.17	2.04	1.80	1.41	2.03
	d	1.773	15.10	10.75	2.77	2.23	2.13	1.84	1.51	2.10
	h	1.779	15.40	11.35	3.27	2.31	2.18	2.02	1.72	2.30
		1.747	1.35		2.92	2.22	2.13	1.90	1.57	2.15
N XVIII	b	1.815	15.00	11.00	3.06	2.21	2.08	1.84	1.57	2.15
	d	1.870	15.40	10.85	3.60	2.38	2.14	1.96	1.76	2.37
		1.843	1.39		3.33	2.30	2.11	1.90	1.67	2.26

TABLE 6—Concluded

BRAIN WEIGHT GROUP	BRAIN WEIGHT	COEFFICIENT		THICKNESS OF THE CORTEX (HORIZONTAL SECTION)					Average
		Diam. W. B on fresh brain	Diam. W. B on slide	Loc. IX	Loc. X	Loc. XI	Loc. XII	Loc. XIII	
	grams	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.
N XIX c	1.953	15.65	11.70	3.14	2.17	2.14	2.01	1.81	2.25
	<i>1.953</i>	<i>1.34</i>		<i>3.14</i>	<i>2.17</i>	<i>2.14</i>	<i>2.01</i>	<i>1.81</i>	<i>2.25</i>
N XX e b	2.008	15.55	11.90	3.10	2.28	2.09	1.87	1.52	2.17
	2.028	15.85	12.00	2.78	2.05	1.97	1.71	1.43	1.99
	<i>2.018</i>	<i>1.31</i>		<i>2.94</i>	<i>2.17</i>	<i>2.03</i>	<i>1.79</i>	<i>1.48</i>	<i>2.08</i>
N XXI f j	2.150	16.55	12.10	3.30	2.66	2.22	1.94	1.57	2.34
	2.162	16.25	12.40	3.60	2.38	2.16	1.98	1.57	2.34
	<i>2.156</i>	<i>1.34</i>		<i>3.45</i>	<i>2.52</i>	<i>2.19</i>	<i>1.96</i>	<i>1.57</i>	<i>2.34</i>
N XXII									
N XXIII a	2.345	16.55	12.90	3.14	2.58	2.17	1.69	1.54	2.22
	<i>2.345</i>	<i>1.28</i>		<i>3.14</i>	<i>2.58</i>	<i>2.17</i>	<i>1.69</i>	<i>1.54</i>	<i>2.22</i>

ence in cortical thickness is recognizable when the brain weights are similar.

In the sagittal sections, the cortex attains nearly its full thickness when the brain weighs 1.63 grams (Group N XVI), while in the frontal and horizontal sections, this is attained somewhat earlier, that is, in the brains weighing 1.53 grams (Group N XV) (cf. charts 3, 5, 7, 8). In the general average thickness of the cortex of the Norway rat, the full thickness is attained in the brains weighing about 1.53 grams, at which phase the body weight observed is about 55 grams (tables 1 and 2) (chart 8). In the full grown Norway rat at brain weights between 1.6 and 2.4 grams, the average cortical thickness ranges between 1.97 and 2.14 mm., with a mean value for Groups N XVI–N XXIII (table 7) of 2.06 mm. The average thickness for each locality is given in table 8 for the Norway rat, together with the corresponding values for the Albino, thus making it possible to compare the cortical thickness in the two forms.

TABLE 7

Showing the average corrected thickness of the cerebral cortex in the Norway rat for each brain weight group.

BRAIN WEIGHT GROUP	SAGITTAL SECTION		FRONTAL SECTION	HORIZONTAL SECTION		GENERAL AVERAGE	
	Brain weight	Thickness	Thickness	Brain weight	Thickness	Brain weight	Thickness
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>	<i>mm.</i>	<i>grams</i>	<i>mm.</i>
N XI	1.164	1.61	1.88	1.164	1.87	1.164	1.79
N XII							
N XIII	1.369	1.73	1.96	1.343	2.08	1.360	1.92
N XIV	1.430	1.84	1.95	1.447	2.09	1.436	1.96
N XV	1.537	1.82	2.04	1.520	2.24	1.532	2.03
N XVI	1.629	1.88	2.08	1.663	2.19	1.640	2.05
N XVII	1.739	1.94	2.07	1.747	2.15	1.742	2.05
N XVIII	1.829	1.93	2.08	1.843	2.26	1.834	2.09
N XIX	1.972	1.97	2.00	1.953	2.25	1.965	2.07
N XX	2.052	1.87	1.96	2.018	2.08	2.041	1.97
N XXI	2.172	1.99	2.08	2.156	2.34	2.166	2.14
N XXII							
N XXIII	2.345	1.86		2.345	2.22	2.345	2.04

Within the limits of our material, the course of development of the cortical thickness in every locality seems, in general, similar to that in the corresponding locality of the albino rat, the descriptions of which were given in the former paper (Sugita, '17 a, pp. 574-577).

VII. A COMPARISON OF THE NORWAY RAT WITH THE ALBINO RAT IN RESPECT OF CORTICAL THICKNESS

The main object of the present paper is to compare the data from the Norway with those from the albino rat, in respect of the cortical thickness, a comparison of much interest, since the two forms are so closely related genetically and at the same time show differences in body size and in absolute brain weight which have been already noted.

Comparing the mature brains, which weigh alike, of the both forms (table 8), the Norway cortex, whose thickness on the average in Groups N XVI to N XX (brain weight average 1.844 grams) is 2.05 mm., surpasses by 0.15 mm. or 8 per cent the albino cortex, whose thickness on the average in Groups XVI to XX

(brain weight average 1.815 grams) is 1.90 mm. Here the albino cortex is taken as the standard for the determination of the percentage difference. For the comparison of each locality and the averages of each section, table 8 is to be consulted. It is remarkable that both in the sagittal and horizontal sections the

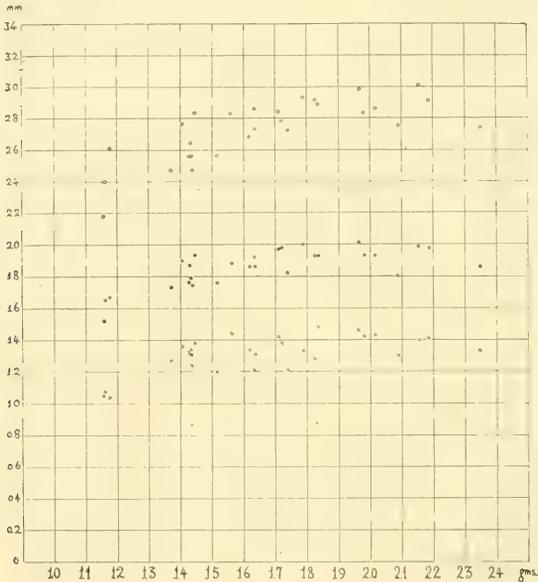


Chart 2 Giving the corrected thickness of the cerebral cortex of the Norway rat in the sagittal section. Individual entries for the cortical thickness at localities I and V, and the average thickness of the sagittal section (localities I, II, III, IV and V) are given. Based on table 4. ° Cortical thickness at locality I. Corrected. × Cortical thickness at locality V. Corrected. • Average thickness of the sagittal section. Corrected.

percentage differences follow in the same order from the frontal to the occipital pole, rising towards the occipital pole. The occipital parts, represented by the pair of localities V and XIII, are the most developed in the Norway, surpassing the corresponding parts of the Albino by 15 and 28 per cent respectively. The pair of localities IV and XII, whose positions are adjoining, show also a marked excess in thickness, that is, 10 and 11 per cent

respectively. The only other large difference is 15 per cent at locality VI.

Accordingly, in the mature rats, the average thicknesses in the sagittal, frontal and horizontal sections are respectively 6.7, 9.1

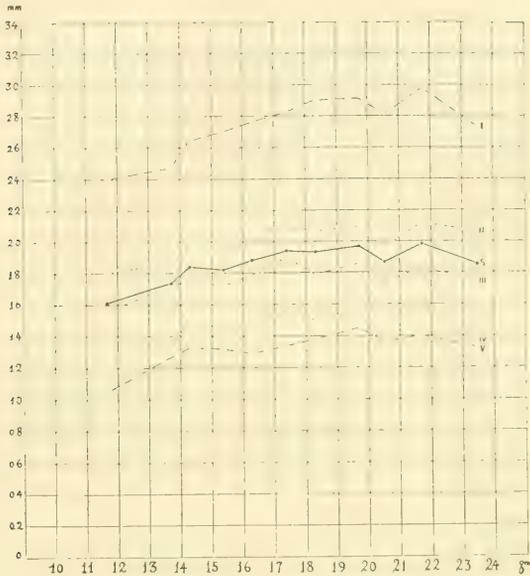


Chart 3 Giving the average thickness of the cortex for each brain weight group at localities I, II, III, IV and V in the sagittal section and the average thickness at five localities in each brain weight group in sagittal section. Based on table 4. — · — · — (above the heavy line) Cortical thickness at locality I. Corrected. — — — — (above the heavy line) Cortical thickness at locality II. Corrected. — · — · — (near the heavy line) Cortical thickness at locality III. Corrected. — — — — (below the heavy line) Cortical thickness at locality IV. Corrected. — — — — (below the heavy line) Cortical thickness at locality V. Corrected. ●—●S Average thickness of the sagittal section by each brain weight group.

and 8.0 per cent greater and the general average thickness is, consequently, 8 per cent greater in the Norway than in the albino rat, while the brain weights are almost the same (about 1.8 grams).

As regards the differences in cortical thickness here found a few comments may be made. Possibly all of the larger differ-

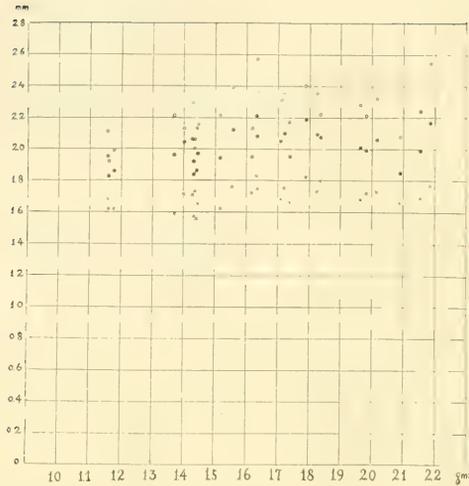


Chart 4 Giving the corrected thickness of the cerebral cortex of the Norway rat in the frontal section. Individual entries for the cortical thickness at localities VII and VIII, and the average thickness of the frontal section (localities VI, VII and VIII) are given. Based on table 5. ° Cortical thickness at locality VII. Corrected. × Cortical thickness at locality VIII. Corrected. • Average thickness of the frontal section. Corrected.

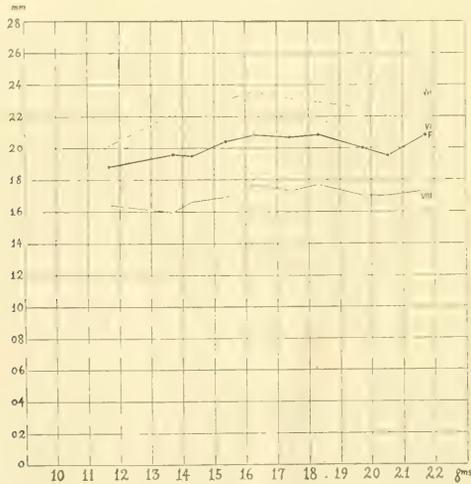


Chart 5 Giving the average thickness of the cortex for each brain weight group at localities VI, VII and VIII in the frontal section and the average thickness at three localities for each brain weight group in frontal section. Based on table 5. ----- Cortical thickness at locality VI. Corrected. - - - - - Cortical thickness at locality VII. Corrected. — Cortical thickness at locality VIII. Corrected. •—•F Average thickness of the frontal section by each brain weight group.

ences noted may be correlated with differences in function, but at present we shall consider only those which appear in the occipital cortex, that is, at localities IV, V, XII, and XIII. There is reason to think that the eye and the visual apparatus in general are less well developed in the Albino than in the Norway rat.

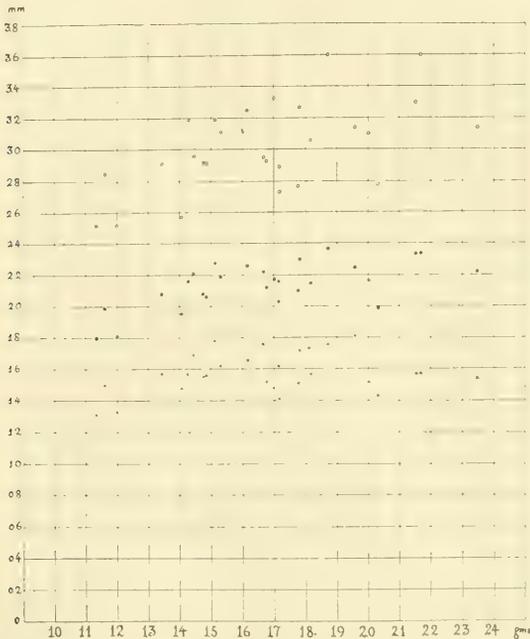


Chart 6 Giving the corrected thickness of the cortex of the Norway rat in the horizontal section. Individual entries for the cortical thickness at localities IX and XIII and the average thickness of the horizontal section (localities IX, X, XI, XII and XIII) are given. Based on table 6. °Cortical thickness at locality IX. Corrected. ×Cortical thickness at locality XIII. Corrected. •Average thickness of the horizontal section. Corrected.

The visual cortex of the rat is at the occipital end of the brain (Ferrier, '86) and would probably be underdeveloped in the Albino in which vision was less perfect. The relatively less thickness of the cortex in the localities IV, V, XII and XIII in the Albino brain would therefore fit with the diminished visual function in this form.

If, during the growing period, a comparison of cortical thickness in brains of like weight is made, the result is somewhat puzzling, as seen in chart 9, which gives the thickness of the cortices of the Norway and the albino rats in brains of the same weight.

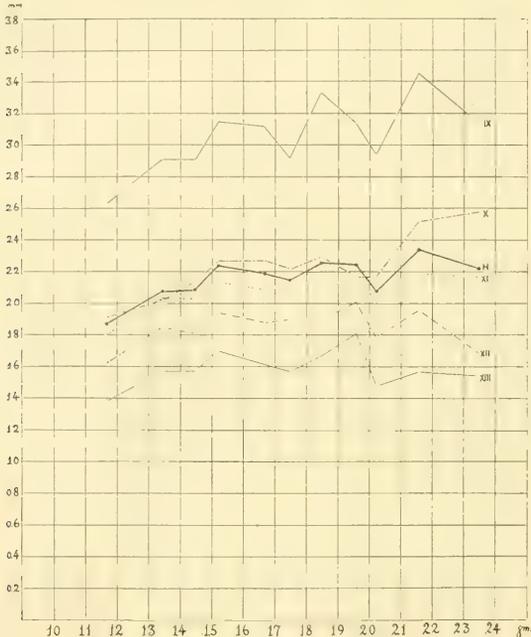


Chart 7 Giving the average thickness of the cortex for each brain weight group at localities IX, X, XI, XII and XIII in the horizontal section and the average thickness at five localities in each brain weight group in horizontal section. Based on table 6. — (above the heavy line) Cortical thickness at locality IX. Corrected. - · - · - (above the heavy line) Cortical thickness at locality X. Corrected. - - - - - Cortical thickness at locality XI. Corrected. - - - - - (below the heavy line) Cortical thickness at locality XII. Corrected. — (below the heavy line) Cortical thickness at locality XIII. Corrected. •—•H Average thickness of the horizontal section for each brain weight group.

Generally the cortical thickness of the Norway rat, whose brain weighs more than 1.3 grams, is clearly higher than that of the albino rat of like brain weight, while in brains weighing less than 1.2 grams the relation is reversed. This seems surprising, but

has its reason. If the data are treated as follows, which seems to me quite a rational treatment, the reason will be disclosed. The brain of the Norway rat at birth weighs usually somewhat more than that of the newborn albino rat, and the final brain weight in the full grown Norway is ca. 2.5 grams or 25 per cent higher than that in the mature albino rat of like age, which weighs about 2.0 grams. As already shown by Donaldson and

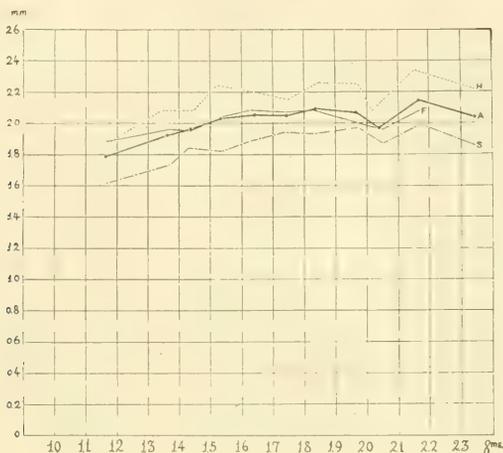


Chart 8 Giving the corrected thickness of the cortex in the sagittal, frontal and horizontal sections and the general average thickness for each brain weight group. Based on table 7. Norway rat. —•—•—S Average thickness of the cortex in sagittal section. Corrected. —F— Average thickness of the cortex in frontal section. Corrected. - - - - -H Average thickness of the cortex in horizontal section. Corrected. •—•—A General average thickness of the cortex of three kinds of sections. Corrected.

Hatai ('11), the span of life is probably the same in both the forms, extending to about three years. So, if throughout this span of life the developmental course of the brains was quite similar for both forms, the brains which have like weights would not represent the same stage of the development, but on the contrary, a brain of the Norway rat would be under these conditions, in a younger stage.

Table 9 gives the percentage of water in the brains of the Norway and of the albino rats. The comparison of the data of the

TABLE 8

A comparison of the cortical thicknesses at each locality and on the average, in the adult Norway and the albino brains of the same absolute weight. The measurements used here are average values of Groups N XVI-N XX and Groups XVI-XX respectively, taken from tables 4 to 6 of this paper and tables 6 to 8 (Sugita, '17a). The corresponding brain weights are 1.844 grams in the Norway and 1.815 grams in the Albino. The thickness of the Albino cortex is always taken as the standard for computing the percentage differences

SECTIONS	LOCALITIES	THICKNESS OF THE CORTEX		CORTEX OF THE NORWAY RAT EX- CEEDS BY
		Norway rat	Albino rat	
		<i>mm.</i>	<i>mm.</i>	<i>per cent</i>
Sagittal	Locality I	2.84	2.80	1.4
	II	2.06	1.92	7.3
	III	1.82	1.74	4.6
	IV	1.51	1.36	10.0
	V	1.37	1.19	15.1
	Average.....	1.92	1.80	6.7
Frontal	Locality VI	2.11	1.84	14.8
	VII	2.28	2.18	4.6
	VIII	1.73	1.59	8.9
	Average.....	2.04	1.87	9.1
Horizontal	Locality IX	3.09	3.08	0.3
	X	2.23	2.06	8.2
	XI	2.10	2.04	3.0
	XII	1.90	1.71	11.1
	XIII	1.63	1.27	28.3
	Average.....	2.19	2.03	8.0
General average		2.05	1.90	8.0

two forms is made so as to bring those of approximately the same age on the same line of the table. It will be seen by these comparisons that the Norway rat brain, if paired with the albino rat brain of like age, shows almost the same value of the percentage of water, while the brain weight differs by 16 to 20 per cent in favor of the Norway rat brain, the weight of the Norway brain being taken as the standard.

So, from the point of view of age, a Norway rat brain should be in the same phase of development with an albino brain,

TABLE 9

Giving the percentage of water in the brain of the Norway and of the albino rats of the same age. The comparison of the data of the two forms is made so as to bring those of approximately the same age on the same line of the table. Based principally on tables 10 and 12, given by Donaldson and Hatai ('11) on pp. 439-443, *Jour. of Comp. Neur.*, vol. 21

NORWAY RAT (MALES)			ALBINO RAT (MALES) OF LIKE AGE				
AGE	BODY WEIGHT OBSERVED	BRAIN WEIGHT	PERCENTAGE OF WATER ON BRAIN		BODY WEIGHT CALCULATED	BRAIN WEIGHT CALCULATED	LESS THAN NORWAY BRAIN WEIGHT
			Observed	Calculated			
<i>days</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>	<i>per cent</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>
1	5.1	0.236 ¹	88.2	88.00	4.7	0.217	8
10	12.2	0.859	86.9	87.05	11.8	0.840	2
13	18.1	1.245	85.3	85.39	14.9	1.011	19
15	17.7	1.195	84.5	84.58	16.1	1.057	12
16	26.1	1.368	82.8	84.19	16.7	1.077	21
19	25.5	1.423	81.5	83.12	18.7	1.131	21
25	32.6	1.498	80.9	81.39	23.9	1.237	17
40	35.8 ³	1.525	79.2	79.39	42.5	1.434	6
47	38.5 ³	1.522	79.3	79.24	54.1	1.507	1
106	68.6 ³	1.878	78.4	78.50	174.0	1.830	3
	200.0	2.15 ²	78.7	78.59	160.0	1.807	16
	215.0	2.17	78.8	78.53	170.0	1.824	16
	231.0	2.20	78.6	78.45	180.0	1.838	16
	248.0	2.23	78.7	78.38	190.0	1.854	17
	267.0	2.25	78.2	78.32	200.0	1.866	17
	287.0	2.28	78.2	78.24	210.0	1.879	18
	308.0	2.31	78.9	78.18	220.0	1.890	18
	331.0	2.33	78.2	78.12	230.0	1.903	18
	355.0	2.35	78.3	78.11	240.0	1.913	19
	380.0	2.38	78.2	78.10	250.0	1.923	19
	406.0	2.41	78.0	78.06	260.0	1.933	19
	434.0	2.43	78.2	77.96	270.0	1.944	20
	463.0		77.9	77.50	280.0	1.954	
	494.0		78.0		290.0		
	525.0		78.0		300.0		

¹ The data given in this column below this entry are based on unpublished observations of Donaldson and Hatai, the records of which are kept in the Wistar Institute.

² The data given in this column below this entry were obtained by calculation according to body weight.

³ As the result of confinement, the body growth in the Norway is remarkably retarded.

which weighs 16 to 20 per cent less. With this relation in view, I reduced by 18 per cent—which is the mean value of 16 to 20 per cent (see table 9)—the weight of the Norway rat brains in table 7, and assumed that I thus obtained brain weights which represent the corresponding brain weights of the albino rat in respect to the cortical development. I have plotted the values for the actual cortical thickness on the reduced brain weights by

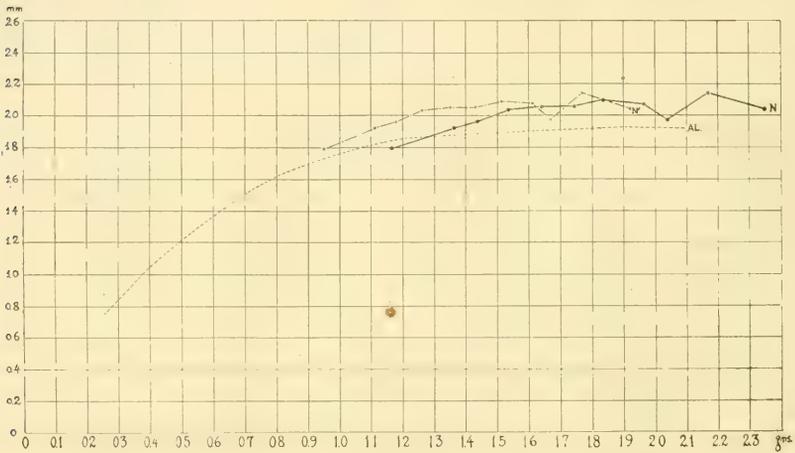


Chart 9 Giving a comparison of the thickness of the Norway cortex with that of the albino cortex, on brain weight. •—•N General average thickness of the Norway cortex according to the actual brain weight group. - - - -AL General average thickness of the Albino cortex according to the brain weight group. Smoothed. Taken from chart 9 of the second paper of this series. •—•—•N' General average thickness of the Norway cortex entered according to the reduced brain weight representing the albino brain weight of the corresponding age.

the dot and dash line in chart 9, in which the smoothed graph for the cortical thickness of the albino rat is represented by a dotted line. Glancing at the chart, my assumption appears to be justified as both the graphs for the reduced Norway and the Albino are found to run a similar course. This relation is acceptable, since, as shown in the tables given by Donaldson and Hatai ('11), and also by Miller ('11), the relative weight of the brain in the mature albino rat is 12 to 16 per cent less than in the Norway rat of like body weight, and, furthermore, the relative weight of the

body in the Albino is about 20 to 40 per cent less than in the Norway rat of like age (table 9). Accordingly, the albino brain should be about 18 per cent or more, less than the Norway brain of like age, and the data for the thickness of the cortex in the two forms show a fairly constant relation, when plotted as in chart 9 in accordance with this assumption (see also table 3, Sugita, '17 a).

As stated, Norway rats under about 10 days of age have not been studied, but a comparison of the graph for the thickness of the cortex in the normal albino rat with the graph for the Norway cortex displaced for age makes it reasonable to assume that a Norway brain which weighs 1.16 grams (Group N XI) corresponds to an albino brain which weighs about 0.95 grams (Group IX), at which stage the cerebral cortices of the both forms have nearly completed their active growth in thickness and are going over to the second phase, during which the cortical area keeps pace with the increase in brain volume. It may be assumed also (see later) that, in the Norway rat, with a brain weight of about 1.4 grams the cortical myelination is beginning to take place.

Thus in the postnatal life of the Norway rat, the first phase of the development of the cerebral cortex covers the period during which the brain weight increases to 1.16 grams from birth, when the brain weight is about 0.25 grams, and the second phase of the cortical development covers the period, during which the brain weight increases from 1.16 grams to about 1.44 (Group N XIV) when the cortex attains within 4 per cent the full thickness. By the middle of the second phase the process of myelination is active, and before the end of this phase the cortex has already attained nearly its full thickness.

This assumption, that the completion of the cortical development in thickness coincides with the period of active myelination, is supported by another set of facts. Table 10 gives the absolute weights of the dry substance in the brain of the Norway rat, arranged according to brain weight. These values were calculated by me from tables originally given by Donaldson and Hatai ('11). The data are plotted in chart 10, which also gives the corresponding data for the albino rat, in a dotted curve.

TABLE 10

Giving the weight of the dry substances in the brain of the Norway rat according to brain weight. Based on the observed data given by Donaldson and Hatai ('11), in p. 448, *Jour. Comp. Neur.*, vol. 21. Both sexes averaged. *Males only.

TOTAL BRAIN WEIGHT	WEIGHT OF THE DRY SUBSTANCES IN THE BRAIN	TOTAL BRAIN WEIGHT	WEIGHT OF THE DRY SUBSTANCES IN THE BRAIN
grams	grams	grams	grams
0.25	0.041	1.55	0.309
0.35		1.65	0.339
0.45		1.75	0.377
0.55		1.85	0.400
0.65	0.067*	1.95	0.407
0.75	0.100	2.05	0.445
0.85	0.100	2.15	0.460
0.95		2.25	0.498
1.05		2.35	0.500
1.15	0.155	2.45	0.540
1.25	0.210	2.55	0.534
1.35	0.229	2.65	0.575
1.45	0.291	2.75	0.600*

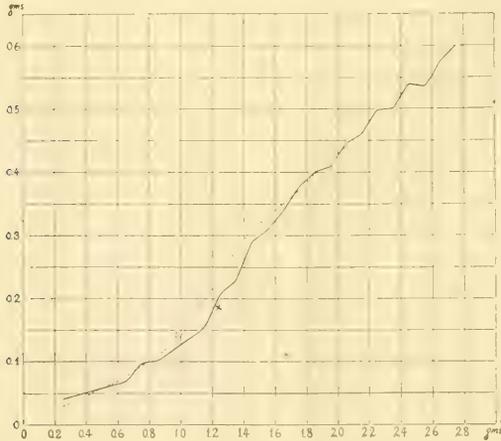


Chart 10 Giving the absolute weights of the dry substance in the Norway brain, arranged according to brain weight, based on the observations of Donaldson and Hatai ('11), accompanied by the corresponding data for the albino rat, in a dotted line. × and * show the turning points of the curves.

This chart shows clearly that the solids in the Norway brain increase rapidly after the brain weight has reached something more than 1.2 grams (see \times). This turning point of the graph corresponds to 0.95 grams of brain weight in the Albino (see *). It was found in the albino rat that, when the brain weight has surpassed 1.15 grams, namely 0.95 plus 0.20 grams, myelination of the cortical fibers is active. Hence, in the Norway brain, the myelination in the cortex should be active when the brain weight has reached 1.44 grams, namely somewhat more than 1.2 plus 0.2 grams. Furthermore, as we have seen that in the albino rat the beginning of myelination in the cortex coincides with the phase when the cortex has nearly attained its full thickness, so we see the same relations in the Norway rat also.

From these facts we conclude that the brains of the both forms pass through the same course of cortical development according to age, as the span of life is the same in the two. The weights of the brains which are in the same stage of development, are however not the same in the both forms, being in the Norway rat about 18 per cent—the Norway brain weight being taken as the standard—heavier than in the albino rat. The statement of Donaldson which was expressed in the paper cited, to wit: "If in the animals compared the brain weights are the same, then the Norway rat has a smaller body weight and a higher percentage of water in the central nervous system," might be rewritten as follows: When ages are the same, the Norway rat has a greater body weight, a heavier brain (18 per cent more in weight), a thicker cortex and nearly the same percentage of water in the central nervous system.

A comparison of the cortical development in the two forms can be made adequately only by first reducing by 18 per cent the actual brain weight of the Norway rat and then comparing the cortex in both forms according to the corrected brain weight. Since mature Norway brains have only a slightly greater volume than the Albino brains of like weight (see table 4 A, Sugita, '18), but at the same time have a cerebral cortex on the average 8 per cent thicker, it follows that in the Norway brain the proportion of gray substance is greater. This difference apparently accounts for the higher percentage of water found in the Norway brain.

VIII. SUMMARY

1. The thickness of the cerebral cortex of the Norway rat has been systematically investigated, employing as material 36 males and 18 females, all over 17 grams in body weight, and using uniformly the methods which were adopted by me for the investigation of the cerebral cortex of the albino rat.

2. The observed data are first given and later are corrected to the values for the fresh condition of the material. The corrected data are given fully in tables and in charts.

3. The relations of the cortical thicknesses at the several localities measured are quite similar among themselves to those found in the albino rat. The average thickness of the cortex in the adult Norway rat is always higher (1 to 28 per cent) than that of the corresponding locality in the adult albino rat. The occipital cortex is better developed (thicker) in the Norway rat. This is to be associated with the more perfect visual apparatus in the Norway rat.

4. As to the phases of development of the cortical thickness, a Norway brain of a given age corresponds to an albino brain, which weighs about 16 to 20 per cent less. The Norway brain weighing 0.25 to 1.16 grams (Groups N II to N XI) is in its first phase of active development which corresponds to an Albino brain weighing 0.25 to 0.95 grams. The Norway brain weighing 1.16 to 1.44 grams (Groups N XI to N XIV) is in its second phase of development of the cortex corresponding to the albino brain weighing 0.95 to 1.15 grams.

5. The cortex of the Norway rat attains nearly its full thickness at the time when the brain weighs somewhat more than 1.44 grams, corresponding to the age of twenty days and to a body weight of something more than 36 grams. At this phase probably the rapid myelination of the fibers in the cerebral cortex is taking place.

6. The general average thickness of the cortex in the mature Norway rat is 2.06 mm., exceeding by about 8 per cent that of the albino rat brain of the same weight.

7. Owing to the greater thickness of the cerebral cortex the mature Norway brain contains more gray matter than does the albino brain of like weight and this excess of gray matter explains the somewhat higher percentage of water found in the Norway brain.

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METABOLIC ACTIVITY OF THE NERVOUS SYSTEM

II. THE PARTITION OF NON-PROTEIN NITROGEN IN THE BRAIN OF THE GRAY SNAPPER (*NEOMAENIS GRISEUS*) AND ALSO THE BRAIN WEIGHT IN RELATION TO THE BODY LENGTH OF THIS FISH

SHINKISHI HATAI

*The Wistar Institute of Anatomy and Biology, and Department of Marine Biology,
Carnegie Institution of Washington*

ONE CHART

The prime object of the present investigation was to extend some observations made recently concerning the metabolic activity of the central nervous system of the albino rat (Hatai, '17) to the nervous system of lower vertebrates. It was my hope that such a comparative study might yield valuable data for an understanding of the complex phenomena of metabolism in this important organ.

In the course of the present investigation I was able to accumulate a considerable amount of data on the weight of the brain together with its water content, a study which has revealed several interesting facts which have not been yet fully appreciated, so that I have decided to present these data also in the following pages. In connection with this work, it is a pleasure to acknowledge my indebtedness to Dr. A. G. Mayer, Director of the Department of Marine Biology of the Carnegie Institution of Washington. Dr. Mayer not only granted me the privileges of the laboratory at the Dry Tortugas, but gave me encouragement and many helpful suggestions throughout the course of this work.

MATERIAL USED

The gray snapper, *Neomaenis griseus*, was chosen for this investigation not only because these fish are abundant in sub-tropical seas, but also because they possess numerous virtues for experimental purposes. The snapper may be kept in the laboratory for a long period, and in captivity as well as when free, takes almost any kind of food, cooked or raw, animal or vegetable. The fish is well known for sagacity and boldness and is suited for various kinds of experimentation. Indeed the snapper has already been carefully studied by Reighard ('08) as to its behavior. Thus, with the hope that the gray snapper may in future prove to be a suitable form for certain lines of experimental work, I have utilized all the brains which have been used for chemical investigation, together with some others, for studying the growth of the brain in weight with respect to body length. Most of the fish were secured by netting them, but on account of the difficulty of getting the larger fish by this method, I have also used dynamite as well as the hook and line. I have noted in table 1 the method adopted for catching each individual.

TECHNIQUE EMPLOYED

The fish were examined as soon as they were brought into the laboratory. However, as in the case of netting them, when too many were caught at once some were kept in a live box for not more than two days, except in a few cases in which they were kept for special purposes for several days. When the fish were kept in a live box for more than two days it is so stated in table 1.

In every instance the length of body was recorded in the following way. The fish was laid on its side and the length was determined by means of calipers from the tip of the snout to the middle of the caudal edge of the tail. The body weights of the fish were also taken in a few instances. Although I realized the desirability of recording the body weight in all cases, yet it was not always possible to make this measurement.

TABLE I

Showing the brain weights according to various body lengths, together with the percentage of water in the brain, of the gray snapper. Arranged according to increasing body length

BODY		BRAIN WEIGHT	WATER IN BRAIN	REMARKS
Length	Weight			
<i>mm.</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>	
88	12	0.122	78.85	Net
137	43	0.234	78.63	Net
155	59	0.284	79.33	Net
215		0.622	79.52	Net
216	140	0.628	81.12	Dynamited
217		0.483	78.34	Net
225		0.670	79.05	Net
227	173	0.627	80.43	Dynamited
237		0.575	78.19	Net
238	197	0.660	79.91	Hook
240		0.711	79.92	Net
245	220	0.732	81.48	Dynamited
249	218	0.723	80.69	Dynamited
252		0.748	79.55	Net
252		0.762	78.64	Net
253	229	0.897	80.65	Dynamited
256		0.748	77.51	Net
258		0.828	79.47	Net
259		0.844	78.32	Net
262		0.833	78.75	Net
262		0.882	77.85	Net
263		0.864	77.29 ♀	Net
263	269	0.803	80.08	Hook
263	261	0.816	79.68	Hook
268		0.859	79.74	Net
269		0.781*	77.49	Net
271		0.921	78.78 ♂	Net
277		0.816	78.57	Net
278		0.843	78.32	Net
278	311	0.871	82.91	Hook
285		0.985	79.17 ♀	Net
293		1.006	77.28 ♂	Net
294		0.861	78.86 ♂	Net
295		0.925	77.56 ♂	Dynamited
296		0.900	78.07	Net
298		0.982	78.49 ♂	Kept in live box 4 days
300		0.907	79.21 ♂	Dynamited
300		0.971	78.17 ♀	Net
301		0.952	77.10 ♂	Net

TABLE 1—Continued

BODY		BRAIN WEIGHT	WATER IN BRAIN	REMARKS
Length	Weight			
<i>mm.</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>	
302		1.042	77.87 ♀	Net
302		1.042	77.06 ♂	Net
303		0.776	75.40 ♀	Dynamited
306		1.079	79.17 ♀	Kept in live box
317		0.974	78.03 ♂	Net
318		1.072	79.57 ♀	Net
330		1.124	76.51 ♂	Net
335	681	1.164	80.07 ♀	Kept several days in box
336		1.124	77.67 ♀	Kept several days in box
340	908	1.126	76.16 ♀	Net
345		1.061	79.15 ♀	Net
348	1½ lbs.	1.141	77.46 ♀	Net
353	2 lbs.	1.117	76.63 ♀	Net
353	2 lbs.	1.169	77.81 ♀	Net
360		1.178	77.88 ♂	Net
362		1.257	78.65 ♂	Net
367	781	1.262	76.67 ♂	Hook
369		1.286	77.08 ♀	Net
374	2 lbs.	1.249	76.24 ♂	Net
380	3 lbs.	1.281	75.33 ♂	Net
385		1.418	♂	Net
390		1.336	77.59 ♂	Net
392		1.353	79.67 ♂	Net
392		1.644	♀	Dynamited
401		1.584	♀	Dynamited
408		1.618	♀	Dynamited
416		1.632	♂	Dynamited
424		1.369	78.54 ♀	Dynamited
430		1.400	♀	Dynamited
432		1.424	79.97 ♂	Dynamited
438		1.530	♂	Dynamited
439		1.400	♀	Dynamited
439		1.499	80.00 ♀	Dynamited
441		1.601	♀	Dynamited
448		1.591	♀	Dynamited

As soon as the brain was exposed by means of a small bone forceps, it was separated from the spinal cord between the first vertebra and the base of the skull. It was not practicable to find the first spinal nerve or to determine the caudal end of the fourth ventricle, methods which are usually adopted in separat-

ing the brain from the spinal cord in the mammalian nervous system. Anteriorly the olfactory nerves were cut close to the olfactory bulbs. The saccus vasculosus was not included with the brain. The brain which was thus removed was placed in a small bottle which had been previously weighed, and this was weighed again to a milligram. After the fresh weight of the brain was determined, the bottle with its contents was placed in a steam oven at a temperature of 80°-90°C. for several days (Tortugas laboratory) and then later dried at the Wistar Institute under better laboratory conditions at 96°C. The various other methods used for the analysis of the brain will be described later.

THE BRAIN WEIGHT IN RELATION TO BODY LENGTH

Altogether observations on 74 brains of the gray snapper have been made.

From table 1 the average brain weight of the sanpper for several values of the body length has been calculated and the results are given in table 2.

In order to show the general distribution of the brain weights in relation to the body length, I have prepared a chart based on the data given in tables 1 and 2.

In the chart males and females are not distinguished. As will be seen from chart 1, the distribution of brain weight in respect

TABLE 2

Showing the average brain weight of the gray snapper for the several values of the body length

BODY LENGTH RANGE	BODY LENGTH OBSERVED	BRAIN WEIGHT		NUMBER OF SNAPPERS
		Observed	Calculated by formula	
<i>mm.</i> 200-250	<i>mm.</i> 231	0.643	0.667	10
250-300	271	0.860	0.840	23
300-350	319	1.037	1.048	15
350-400	373	1.296	1.282	12
400-450	428	1.513	1.520	11
Average.....		1.070	1.071	

to the increasing body length from 150 mm. upward is practically linear. This linear relation between these two characters is better shown by the positions of the averaged values, which are also plotted. It is well known that in the adult stage the relation between brain weight and body length or body weight is practically linear, even in the case of some mammals (see for instance growth of brain in weight in the albino rat in respect to body length or body weight, Donaldson, '09) but it is remarkable to find the linear relation in fish when they are so small. This linearity during the period of early growth probably means that in the gray snapper the brain reaches its struc-

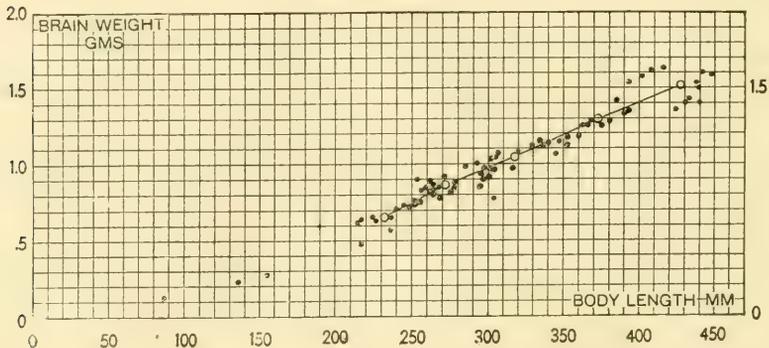


Chart 1 Showing the weight of the brain of the gray snapper according to body length. The observed weights are represented by 74 fish. • = observed weight — o — o — = average observed weight (table 2).

tural maturity early, and that the subsequent increase in weight indicates merely a uniform swelling of the nervous system as a whole. The maturity of the brain at a relatively early stage of growth may be inferred also from practical constancy of the percentage of water in the brain from the very small to the very large fish in this series (page 48).

It is to be regretted that it was not possible to obtain data on smaller specimens, though every effort was made to obtain such specimens while I was at the Tortugas Laboratory. We were even unable to find any of the gray snapper fry, though the fry of the school master (*Neomaenis apodus*) which is most closely

related to the gray snapper, was abundant everywhere. Possibly the months of June and July were not a proper season to find them, or the fry of the gray snapper may not live in the open seas or along the beach, but may be in hiding under the intricate roots of mangroves, a tree not found on the Tortugas Islands.

On account of the scantiness of the data on the gray snapper less than 200 mm. in body length, I am unable to present a complete record of the growth of the brain. However it appears from the general trend of the growth curve that, with the possible exception of the very early period, the relation between the brain weight and body length does not deviate much from linearity.

Kellicott ('08) who studied the growth of the brain in the smooth dogfish (*Mustelus canis*, Mitchill) in respect to the body weight, found the graph to resemble that for the mammalian brain; that is the graph shows a rapid rise at the early period which is followed by a slower rate of growth. The form of the curve suggests a logarithmic formula such as was used to represent the growth of the brain in the albino rat (Hatai, '09). In other words the form of the graph for the gray snapper is strikingly different from that for the dogfish. This difference may be due to the fact that in the dogfish the brain possesses a voluminous cerebellum, as well as olfactory bulbs, and the combined weights of these two structures may be greater than that of the rest of the brain, while these two structures in the gray snapper are very small and the latter was not included. It appears that these two parts, olfactory bulbs and cerebellum, of the dogfish brain grow very rapidly during the earlier period, thus giving the form of the graph similar to that for the mammal.

Since the brain weight of the gray snapper shows a linear relation to the body length through a wide range, and since the fish which are usually caught fall within this range, I have devised the following formula for brain weight on body length, in hopes that it may prove useful for some future investigation.

Brain weight (gms.) = 0.00433 Body length (mm.) - 0.333 .

The results of the calculation are given in table 2 and there

contrasted with the observed values. The agreement is highly satisfactory, and thus the formula may be employed when the probable brain weight of the gray snapper in which body length is known, is desired. I may point out that the absolute amount of increment of the weight of the brain following every millimeter increase of the body length is slightly over four milligrams (4.33 milligrams).

PERCENTAGE OF WATER IN THE BRAIN

Altogether 64 snappers were examined to determine the water content in the brain, and the results have been already given in table 1. An examination of the table reveals several striking relations in regard to the percentage of water. The percentage of water given by the smallest fish is 78.85 per cent while that of the larger fish, having a body length of 424 mm. and ranking in length third from the largest in which the water determination was made, gives 78.54 per cent. The frequency distribution of the percentage of water gives the following results.

TABLE 3

Showing the frequency distribution of the percentage of water in the brain of the gray snapper

PER CENT OF WATER	NUMBER OF CASES
75-76	2
76-77	5
77-78	15
78-79	17
79-80	16
80-81	6
81-82	2
82-83	1
Total number.....	64

Despite the fact of a wide range in the percentage of water, the distribution of the frequencies is practically normal, and furthermore the high and low values are well mingled, when these

values are arranged according to the body length of the snapper (table 1) and there is no noticeable tendency for the lower values of the percentage of water to occur more frequently among larger fish, or vice versâ. From this we infer that so far as the present data are concerned, the percentage of water in the small and large fish is nearly identical within a wide range of body length, and therefore the percentage of water does not vary regularly with the length or size of the fish. The average of 64 determinations gives the percentage of water as 78.61 per cent.

This wide variation in the percentage of water I am unable to explain at the present moment. It was thought at first that the method of capture, particularly the use of dynamite, might be responsible for it. Careful examination however (see remarks in table 1) of the table shows at once that such is not the case, and these wide variations are not correlated with the method of capture. It is true that the cranial cavity of the fish contains liquid as well as a jellylike substance, and the adhesion of particles of this substance may alter to some extent the percentage of water, but this factor is too insignificant to cause the wide variations shown in the table.

One other factor, though it appears to be important, cannot be readily tested, namely, masked age; that is a failure of the size and weight of the fish to indicate the age. We have no way to determine the age of the gray snapper. It may be that the size of the fish shows a wide range of variation for any given age. If size was positively correlated with age, then the low percentage of water would be given by the older fish, and vice versâ. Therefore should we be able to arrange the data according to the ages of the fish, not the size of the fish as has been done, the values for the water should arrange themselves in a regular descending order with increasing age. This is, however, a mere speculation and must wait the test of future investigation.

Still another possible factor is the low grade of organization of the fish brain compared with that of the higher vertebrates. It is conceivable that owing to this low grade of organization, the structural maturity, or especially the process of myelination, may not progress regularly, and that within the same size or at

the same age, a wide range of variation might exist in respect to the degree of myelination, according to the environment of the fish or to the general nutritional conditions. Whether or not this suggestion has a value, only further investigation can determine.

Scott ('12) found that the percentage of water in the brain of the smooth dogfish differs very little between small and large specimens, and gives on the average 78.5 per cent. Donaldson ('05) who examined the brains of the summer flounder (*Paralichthys dentatus*) noted also but slight variation in the percentage of water in the brains of large and small individuals. The average from sixteen flounders in which the body weight ranges from 539 grams to 1290 grams, is 78.45 per cent. Thus the average percentages of water obtained by Donaldson, Scott and by myself are 78.45 per cent (flounder), 78.5 per cent (dogfish) and 78.61 per cent (gray snapper) respectively. For the purpose of comparison I gave the percentages of water in the brain of several fish, as determined by various investigators.

As will be seen from table 4 despite the widely different sizes and probably wide differences in the age of fish, the percentages of water in the brains are very close to one another, and further interest lies in the fact that the values given by the fish brains are not much different from the percentage of water in the adult mammalian brain.

Since the reduction in the water in the brain is induced by the deposition of the so called 'myelin substance' (Donaldson, '16) we may infer that the process of myelination in the fish brain attains its mature form at a very early period¹ thus permitting but very slight variation from small to large individuals. Scott ('12) also concludes from his observations on the water content

¹ In a private communication Dr. G. W. Bartelmez informs me that in *Ameiurus melas*, larvae 10 to 12 mm. long show already well advanced myelination of the roots of all the cranial nerves, as well as of the fasciculus longitudinalis medialis. The age of the larvae, according to Dr. Bartelmez's estimate, is about ten to twelve days after fertilization. The largest adults measure as much as 120 mm. or nearly ten times the length of the larvae in which the myelination is already well advanced. From the above we may safely assume that myelination takes place in the fish at an early stage of development.

of the dogfish that the differences in the reduction of water in the two cases is that "the nervous (and body) changes which occur in the mammal are post-embryonic and extra-utero. In the

TABLE 4

Showing the percentage of water in the brain of several fish. Data compiled from various sources

SPECIES	BODY WEIGHT	BODY LENGTH	BRAIN WEIGHT	PER CENT OF WATER	ALCOHOL-ETHER EXTRACT	SEX	OBSERVER
Cyprinus carpio.....				77.50	8.33		Von Bibra (1854)
Cyprinus barbus.....				78.00	9.37		Von Bibra (1854)
Salmo farco.....				78.92	8.42		Von Bibra (1854)
				-80.00			
Lucius esox.....				81.93	7.25		Von Bibra (1854)
Fish.....					9.10		Schlossberger (1856)
Cyprinus auratus.....				77.80			Bezold (1857)
Summer flounder.....	539	393	0.253	78.05			Donaldson (1905)
Summer flounder.....	540	397	0.305	79.06		♂	Donaldson (1905)
Summer flounder.....	540	386	0.351	78.00		♂	Donaldson (1905)
Summer flounder.....	560	411	0.338	78.70			Donaldson (1905)
Summer flounder.....	630	409	0.279	78.06		♂	Donaldson (1905)
Summer flounder.....	640	404	0.293	78.43		♀	Donaldson (1905)
Summer flounder.....	682	405	0.288	79.56			Donaldson (1905)
Summer flounder.....	834	440	0.311	78.60		♀	Donaldson (1905)
Summer flounder.....	840	462	0.358	78.98		♀	Donaldson (1905)
Summer flounder.....	860	453	0.406	78.37		♀	Donaldson (1905)
Summer flounder.....	880	459	0.381	77.11		♂	Donaldson (1905)
Summer flounder.....	890	459	0.417	77.98		♀	Donaldson (1905)
Summer flounder.....	1010	460	0.355	78.22		♀	Donaldson (1905)
Summer flounder.....	1010	447	0.369	78.72		♂	Donaldson (1905)
Summer flounder.....	1080	478	0.412	79.06		♀	Donaldson (1905)
Summer flounder.....	1290	505	0.391	78.27		♀	Donaldson (1905)
Average.....				78.45			
Mustelus canis ¹				78.5			Scott (1912)
Barracuda.....	12 lbs.	1047	1.554	79.39		♂	Hatai (1917)
Neomaenis griseus ²				78.61			Hatai (1917)
Cherna americana:							
Red Grouper.....	14½ lbs.	807	1.230	78.80			Hatai (1917)
Shark Sp?.....	160 lbs.		32.593	80.07		♂	Hatai (1917)

¹ Average of 97 determinations from very small to very large. Percentage of water shows very slight variation.

² Average of 51 gray snappers. Range of variation is shown in table (1).

dogfish they take place in utero." He, however, has not determined the water content in the brain of the dogfish in utero.

From the foregoing it is clearly important to determine the water content in the brain of the fish at very early stages in order to discover the period of rapid reduction which must take place in consequence of the appearance of myelin in the brain. It is the hope of the writer to do this in the near future.

CHEMICAL ANALYSIS OF THE BRAIN (GRAY SNAPPER)

Utilizing the materials which were employed for the determination of the percentage of water, I have determined the nitrogen in the total solids, as well as the amount in the ether-alcohol soluble fraction extracted from the total solids. The results of these determinations are shown in table 5.

TABLE 5

Showing the amount of the ether-alcohol soluble and insoluble fractions in the brain of the gray snapper; also the amount of nitrogen in the total solids, as well as the nitrogen in the ether alcohol fraction

SERIES	BRAINS		SOLIDS	WATER	TOTAL NITROGEN	WEIGHT OF		NITROGEN IN	
	NUMBER	FRESH				Residue	Alcohol-ether Extract	Residue	Alcohol-ether Extract
		<i>weight</i>		<i>per cent</i>	<i>mgms.</i>	<i>gms.</i>	<i>gms.</i>	<i>mgms.</i>	<i>mgms.</i>
1	28	27.303	5.665	79.14	462	2.707	2.958	364	98
					8.15%	47.79%	52.21%	78.79%	21.21%
2	19	20.013	4.588	77.07	334	1.938	2.650	269	65
					7.28%	42.24%	57.75%	80.54%	19.46%
Average				78.11	7.72%	45.02%	54.98%	79.67%	20.33%

To carry out the determinations presented in table 5, I have divided the entire materials into two groups in which group 1 gives for the brain a percentage of water which ranges between 78 per cent and 80 per cent, while in group 2 the percentage of water ranges between 76 per cent and 77 per cent. All the other brains which gave percentages of water beyond these limits were excluded. Since all these data for the fish may be discussed conveniently by comparing them with similar data obtained

from the rat brain, I may state simply that the values for the alcohol-ether soluble fraction obtained in this series of fish are similar to those obtained by Von Bibra ('54) and by Schlossberger ('56) in other forms of fish (table 3).

CONTENT OF 'NON-PROTEIN NITROGEN' IN THE BRAIN

Altogether 44 snappers of medium size were used for the purpose of determining the various extractive nitrogenous substances in the brain. These brains were divided into three samples, each giving nearly the same amount of moist brain weight. One additional sample was obtained from the brains of the schoolmaster (*Neomaenis apodus*) which is a species most closely related to the gray snapper.

The fresh brains of each sample were ground finely and then preserved in 150 cc. of 2.5 per cent solution of trichloroacetic acid in water. The ground brains were transferred to a bottle by means of 50 cc. water, thus making altogether 200 cc. of solution. The filtrates from this mixture were brought back to the Wistar Institute for analysis. The methods used for the determination of various nitrogen fractions were as follows:

1. Total non-protein nitrogen. Micro method of Folin and Farmer as modified by Benedict and Bock.
2. Amino-acid nitrogen. Van Slyke's nitrous acid method. Also the same author's micro apparatus.
3. Urea nitrogen. Urease method.
4. Ammonia nitrogen. By the usual aeration method.

In all cases, except the case of the amino acid, the nitrogen content was determined by means of the DuBoseq colorimeter. The results obtained from these determinations are given in table 6.

Since it is my intention to discuss this subject later in comparison with the similar data recently obtained from the brain of the albino rat, I shall merely direct attention to the fact that these three samples give results very close to each other. Furthermore the results obtained from the sample of the schoolmaster also agree with those found in the case of the gray snapper.

TABLE 6

Showing nitrogen content in terms of the non-proteins, the amino acids, the urea and the ammonia, in the brains of the gray snapper and of the 'schoolmaster.'

SERIES	BRAINS		MILLIGRAMS NITROGEN PER 100 GRAMS OF FRESH BRAIN				
	Number	Weight	Non-Protein	Amino acids	Urea	Ammonia	Undetermined nitrogen
<i>Neomaenis griseus</i>							
		<i>gms.</i>					
1	16	13.166	204	101.8	13.2	17.7	71.3
2	13	10.713	224	125.0	17.8	18.9	62.3
3	15	12.048	203	121.2	15.8	17.4	48.6
Average		11.976	210	116.0	15.6	18.0	60.7
<i>Neomaenis apodus</i>							
1	10	11.195	225	126.0	17.3	17.2	64.5

This agreement in the various substances might also be taken to support the belief of the systematists that these two species are closely related.

COMPARISON BETWEEN THE GRAY SNAPPER AND THE ALBINO RAT IN REGARD TO THE CHEMICAL COMPOSITION OF THE BRAIN

In order to compare the data on the chemical composition of the brain in the gray snapper with those for the brain of the albino rat, table 7 was prepared. The entries for the fish are based on tables 5 and 6, while the data on the albino rat were obtained from an earlier paper (Hatai, '17).

When comparison is made between the fish brain and the entire brain of the albino rat, we find a distinct difference in regard to the content of the total nitrogen and of the nitrogen in the lipoids, as well as in the total amount of the ether-alcohol extractive materials. These differences must undoubtedly be correlated with anatomical differences in the two forms of the brains. In the rat we find a well developed cerebrum and cerebellum in which the myelinated nerve fibers are relatively less than in the stem, while the cell bodies are more abundant. On the other hand in these fish brains we find a mere trace of the

TABLE 7

Showing the comparison of the gray snapper with the albino rat in regard to the chemical composition of their brains

	GRAY SNAPPER ENTIRE BRAIN	ALBINO RAT STEM OF ENCEPHA- LON	ALBINO RAT ENTIRE BRAIN
Water in brain, per cent.....	78.11	75.16	77.96
Total nitrogen in fresh tissue, per cent.....	1.69	1.89	1.95
Total nitrogen in solids, per cent.....	7.72	7.75	8.98
Alcohol-ether extract in solids, per cent.....	54.98	55.03	47.14
Nitrogen in alcohol-ether soluble fraction, per cent	20.60	19.90	18.20
Percentage of water in lipid-free tissue, per cent...	88.80	87.06	87.00
Milligrams of non-protein nitrogen per 100 grams of fresh tissue, milligrams.....	225	150	159
Partition of nitrogen in milligrams of nitrogen per gram of solids			
Non-protein-N.....	9.6	6.0	7.6
Amino-acids-N.....	5.3	2.9	3.5
Urea-N.....	0.7	0.7	0.7
Ammonia-N.....	0.8	0.6	0.7
Partition of non-protein nitrogen in percent of pro- tein nitrogen			
Non-proteins.....	13.04	9.72	10.37
Amino acids.....	7.20	4.68	4.60
Urea.....	0.97	1.05	0.95
Ammonia.....	1.11	1.04	1.01

cerebrum and cerebellum compared with the size of the stem in which the myelinated nerve fibers are abundant. Consequently we should expect a higher value of the total nitrogen in the rat brain than in the fish brain, since the former possesses relatively a much greater number of cell bodies in those two well developed parts, the cerebrum and cerebellum. At the same time the rat brain ought to give relatively a less amount of lipoids, owing to the greater abundance of the gray matter in the predominant parts. In the fish brain the insignificant growth of the cerebrum and cerebellum makes the stem of the brain relatively predominant in the quantitative relations, and since the stem is the portion of the brain in which the myelinated fibers are mostly found, we should expect the percentage value of the lipid fraction in the fish brain to be relatively higher than in the rat.

If we compare now the entire brain of the snapper with the stem of the albino rat brain (table 7) we notice a surprisingly close similarity. This we should expect since as was already stated the fish brain is practically represented by the stem, since the cerebral and cerebellar portions are relatively insignificant. Thus we notice the practical identity in the percentage values of the total nitrogen, lipoid nitrogen, and the amount of the lipoids. The percentage of water in the stem of the rat is however far less than in the entire brain of the fish which may be accounted for by the fact that in the brain of the fish the cerebrum and the cerebellum, though small in relative quantity; nevertheless are composed of structures rich in water, and thus bring the value of the water higher in the fish than in the stem alone of the albino rat brain.

The nitrogen content of the lipoid is slightly higher in the fish brain than in the albino rat brain, though almost identical with that in the stem. This difference may be due to the quantitative difference in the proportion of various lipoids in which the nitrogen content is not the same.

I now wish to consider the partition of the non-protein nitrogen in the fish brain compared with the brain of the albino rat. As will be seen from table 7 the content of the non-protein nitrogen is considerably greater in the fish than in the rat brain. We also notice that the greater part of the non-protein nitrogen is represented by the nitrogen of the amino acids. The nitrogen values given by both the urea and ammonia are small and are practically identical both in the fish and rat. The greater amount of non-protein nitrogen found in the fish brain in comparison to the rat is interesting, though I am unable to explain this difference satisfactorily. I wish however to call attention to two factors which may have some bearing on the difference just noted.

1. It seems probable that on account of the low grade of organization of the fish brain the physical consistence of the nervous system may not be as stable as that of the more highly organized mammalian nervous system, and thus the wear and tear process may be greater and produce a correspondingly greater amount of waste products in the fish brain.

2. According to Folin and Denis ('14) the normal human blood contains, on the average of four cases, 32 milligrams of non-protein nitrogen per 100 cc. of blood, while Wilson and Adolph ('17) found in the blood of various fresh water fish much higher values for the non-protein nitrogen (42 mgms. per 100 cc.) than in the human blood, and furthermore these investigators found a greater fraction of the non-protein nitrogen was represented by the nitrogen of amino acids (23 mgms. per 100 cc. or about 55 per cent of the total non-protein nitrogen). Thus my own observations on the fish brain closely agree with those of Wilson and Adolph on the fish blood, so far as the relative abundance of the non-protein nitrogen is concerned, as well as in the relation of the amino acid nitrogen to the total non-protein nitrogen.

Denis ('13-'14) found also a considerably greater amount of non-protein nitrogen in the blood of marine fishes when contrasted with human blood. Denis found 62 mgms. of non-protein nitrogen per 100 cc. of blood (average of 10 species of teleosts) and as high as 1087 mgms. in the case of the elasmobranchs (average of three species). Thus the greater abundance of the non-protein nitrogen in the fish blood, accompanied by a slow circulation, might be largely responsible for a greater accumulation of the non-protein nitrogenous extractive substances in the fish brain.

SUMMARY

The gray snapper, *Neomaenis griseus*, was mainly used for the present investigation. The following are the more important facts brought out.

1. The relation between brain weight and body length is practically linear. This linear relation appears in the fish as small as 150 mm. in length. The fish smaller than 150 mm. were not studied because they could not be obtained.

2. The percentage of water in the brain varies very little from small to large (body length : 88 mm. to 448 mm.). A similar relation was observed by Donaldson ('05) in the brain of the summer flounder and by Scott ('12) in the brain of the smooth dogfish. The probable explanation is that the process of mye-

lination is completed in the fish brain relatively earlier than in the mammalian brain.

3. With respect to the total nitrogen, nitrogen in ether-alcohol extract, and the lipid content, the fish brain closely resembles the stem of the rat brain, but significantly differs from the entire rat brain. This is explained by the fact that the mature fish brain resembles essentially the stem of the mammalian brain owing to the small growth of cerebrum and cerebellum.

4. The non-protein nitrogen is considerably greater (42 per cent) in amount in the fish brain than in the rat brain. The suggestions were made that probably on account of unstable physical consistence of the fish nervous system, the wear and tear of the neurons may be greater than in the more highly organized mammalian nervous system, thus producing a larger quantity of the waste products, and also that on account of higher non-protein nitrogen content of the fish blood, accompanied by a slow circulation, the deposition of the waste products might become greater, and at the same time a less vigorous removal further tends to increase the accumulation.

5. The greater fraction of the non-protein nitrogen is represented by the amino acid nitrogen in both the fish and the rat.

6. The amounts of urea nitrogen and of ammonia nitrogen are closely similar to those found in the rat brain.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

V. PART I. ON THE AREA OF THE CORTEX AND ON THE NUMBER OF CELLS IN A UNIT VOLUME, MEASURED ON THE FRONTAL AND SAGITTAL SECTIONS OF THE ALBINO RAT BRAIN, TOGETHER WITH THE CHANGES IN THESE CHARACTERS ACCORDING TO THE GROWTH OF THE BRAIN

V. PART II. ON THE AREA OF THE CORTEX AND ON THE NUMBER OF CELLS IN A UNIT VOLUME, MEASURED ON THE FRONTAL AND SAGITTAL SECTIONS OF THE BRAIN OF THE NORWAY RAT (*MUS NORVEGICUS*), COMPARED WITH THE CORRESPONDING DATA FOR THE ALBINO RAT

NAOKI SUGITA

From the Wistar Institute of Anatomy and Biology

THREE FIGURES AND FOUR CHARTS

PART I

I. INTRODUCTION

The present study is an extension of an earlier one on the thickness of the cerebral cortex in the albino rat (Sugita, '17 a) and aims to present the extent of the actual area occupied by the cortical cells, as seen in sections which were taken from the fixed levels of the albino brain, and also to follow the changes in this area during the postnatal growth of the brain. In the course of this investigation, the number of nerve cells contained in a unit volume of a fixed locality in the frontal section was counted and the changes in this number with advancing age were ascertained. Furthermore the relation between the cell number and the cortical area was critically examined.

For this study, the sections, which had been previously used for the investigation of the thickness of the cortex of the albino rat brain, were again utilized. The material, amounting to 78

albino rats, sexes combined, which was used in the present study, is identical with that listed in table 1 of the former paper (Sugita, '17 a), to which the reference should be made for this study also.

These studies were made during the winter semester of 1916-1917.

II. MEASUREMENTS AND ENUMERATIONS

A. *Area of the cortex in the sagittal section*

As previously described (Sugita, '17 a), the sagittal section (fig. 1) was taken in a plane passing through the frontal pole and parallel to the mesial surface of the hemisphere. This section from each individual brain was projected on a sheet of paper by the Leitz-Edinger Projection apparatus, at a magnification of exactly twenty diameters, and the outline of the image then accurately traced on the sheet. At the transitional part of the cortex at the frontal pole to the olfactory bulb and at the subiculum, where the cortex goes over into the structure of the cornu Ammonis, the borderlines were drawn along the radiation of the cells in those parts (fig. 1). The anterior borderline (a-a') is formed by a prolongation of the line bounding the dorsal surface of the olfactory bulb. The posterior borderline (p-p') is clearly located, because this was drawn at the point where the thickness of the ganglionic layer abruptly diminishes at the beginning of the ganglion cell band characteristic for the cornu Ammonis. The area of the cortex, including the lamina zonalis, which contains no proper nerve cells, was then repeatedly measured to a square millimeter on the drawing, using the Ott Compensating Planimeter. The values obtained were then averaged, and 1/400 of the value, which corresponds to the cortical area on the slide, was recorded. This value was then converted into that for the fresh condition of the material, by the following procedure.

On the outline, which was taken from the section on the slide, the diameter from frontal pole to the occipital pole (*L. F*) was measured and reduced, and, according to the formula given in the former paper (Sugita, '17 a), which reads

Correction-coefficient = $\frac{\text{The diameter } L. F \text{ in fresh cerebrum}}{\text{The diameter } L. F \text{ on the slide}}$,

the correction-coefficient was determined. The value for the area obtained by the (first) direct measurement from the slide was then corrected to the corresponding value for the fresh condition of the material, by multiplying by the square of the correction-coefficient. The corrected values thus obtained are given in the last column of table 1.

The values for the cortical areas in the respective sagittal sections of each individual were then grouped according to the

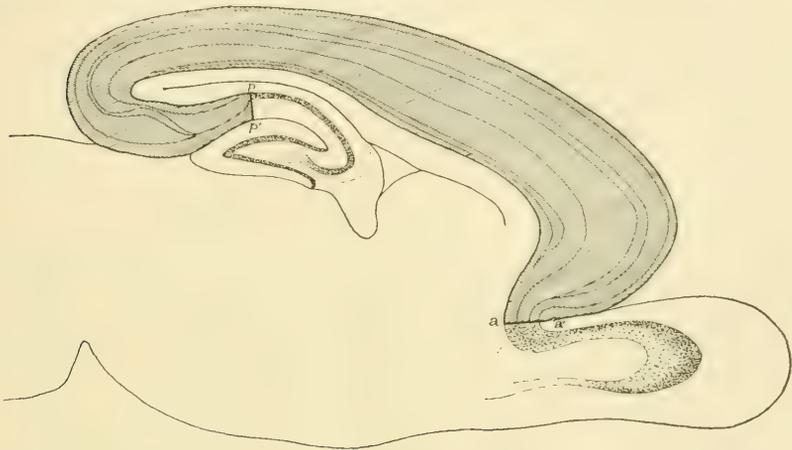


Fig. 1 Showing, by shading, the cortical area measured on the sagittal section of the albino rat brain. The anterior borderline ((*a-a'*) is formed by a prolongation of the line bounding the dorsal surface of the olfactory bulb. The posterior borderline (*p-p'*) is drawn at the point where the ganglionic layer goes over abruptly to the ganglion cell band in the cornu Ammonis.

brain weight, into twenty groups, as in the other studies of this series, and the average value for each group was found. The average areas of the cortex in the sagittal section for each group (table 1) were plotted in chart 1 (graph s), which shows the increase in area according to the increase in brain weight.

B. Area of the cortex in the frontal section

The frontal section (fig. 2) was cut in the plane passing through approximately the middle point of the mesial surface of the

TABLE 1

Showing the observed and corrected values of the area of the cerebral cortex in the sagittal section of the albino rat brain, accompanied by the data for the correction-coefficient in the individual cases and the correction-coefficient for the group. *L. F* is the longitudinal diameter of the cerebrum

GROUP	BRAIN WEIGHT	OBSERVED AREA OF CORTEX	CORRECTION-COEFFICIENT		CORRECTED AREA OF CORTEX
			<i>L. F</i> in fresh brain	The same on slide	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²
I a	0.153	3.2	5.50	4.97	4.1
c	0.154	3.0	5.60	4.80	4.1
b	0.177	4.0	5.70	5.13	4.9
	0.161	3.4	1.13^2		4.4
II a	0.213	4.0	5.80	5.13	5.1
b	0.221	3.9	6.00	5.43	4.8
c	0.261	4.8	6.60	5.60	6.7
d	0.271	4.8	6.75	5.80	6.5
e	0.288	4.5	6.70	5.75	6.1
(Birth)	0.251	4.4	1.15^2		5.8
III a	0.311	6.1	7.35	6.45	7.9
b	0.322	6.3	7.20	6.40	8.0
g	0.374	8.1	7.40	7.40	8.1
c	0.390	6.7	7.50	6.70	8.4
i	0.395	7.4	7.95	7.20	9.0
	0.358	6.9	1.10^2		8.3
IV b	0.400	6.7	7.70	6.65	9.0
a	0.402	8.4	7.75	7.30	9.4
c	0.420	8.2	7.95	7.20	10.0
i	0.443	10.6	8.30	8.10	11.1
d	0.459	8.8	8.05	7.60	9.9
e	0.466	9.6	8.40	7.80	11.1
	0.432	8.6	1.08^2		10.1
V i	0.501	10.2	8.35	7.90	11.4
a	0.525	12.7	8.55	8.45	12.9
b	0.528	11.1	8.50	8.05	12.4
c	0.534	9.0	8.65	7.60	11.6
d	0.537	10.1	8.30	7.70	11.7
e	0.555	12.3	9.25	8.65	14.0
f	0.558	11.0	9.20	8.50	12.9
g	0.564	11.4	8.85	8.40	12.7
h	0.579	11.5	9.10	8.35	13.6
	0.542	11.0	1.07^2		12.6

TABLE 1—Continued

GROUP	BRAIN WEIGHT	OBSERVED AREA OF CORTEX	CORRECTION-COEFFICIENT		CORRECTED AREA OF CORTEX	
			<i>L. F</i> in fresh brain	The same on slide		
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²	
VI c	0.610	12.0	9.35	8.35	14.9	
	a	0.617	10.7	9.25	14.4	
	e	0.690	15.0	9.60	17.1	
		0.639	12.6	1.11 ²		15.5
VII a	0.740	15.7	10.50	9.80	18.1	
	b	0.760	11.5	10.65	8.50	18.1
		0.750	13.6	1.15 ²		18.1
VIII a	0.800	14.4	10.50	9.25	18.5	
	h	0.805	13.8	10.90	9.20	19.4
	b	0.822	16.2	10.45	9.60	19.2
	c	0.849	18.0	10.50	9.70	21.1
	k	0.870	15.1	10.95	9.40	20.5
	d	0.898	17.0	11.45	10.15	21.6
		0.841	15.8	1.13 ²		20.1
IX d	0.959	17.9	11.60	10.50	21.8	
	e	0.960	16.9	11.40	9.85	22.5
	a	0.972	15.4	11.30	9.70	20.9
	(10 days)	0.964	16.7	1.14 ²		21.7
X a	1.033	13.9	11.90	9.40	22.3	
	b	1.036	15.9	11.85	9.85	23.1
	e	1.051	17.5	12.05	10.05	25.0
		1.040	15.8	1.22 ²		23.5
XI a	1.107	17.3	12.00	10.00	25.2	
	b	1.189	18.8	12.50	10.25	28.0
	c	1.193	19.1	12.65	10.50	27.8
	d	1.195	16.0	12.60	10.00	25.4
	(20 days)	1.171	17.8	1.22 ²		26.6
XII c	1.234	18.4	12.30	10.35	26.0	
	a	1.273	15.7	12.45	9.65	26.2
		1.253	17.1	1.24 ²		26.1
XIII a	1.301	18.7	13.00	11.10	25.7	
	g	1.307	15.6	12.95	10.00	26.2
	b	1.327	17.2	13.20	10.50	27.2
	c	1.346	17.8	13.00	10.10	29.5
	h	1.392	21.9	13.45	11.60	29.5
		1.335	18.2	1.23 ²		27.6

TABLE 1—*Concluded*

GROUP	BRAIN WEIGHT	OBSERVED AREA CORTEX	CORRECTION-COEFFICIENT		CORRECTED AREA OF CORTEX
			<i>L. F</i> in fresh brain	The same on slide	
	<i>grams.</i>	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²
XIV a	1.412	17.5	13.40	10.40	29.1
e	1.441	15.2	13.25	10.10	26.2
b	1.483	21.1	13.30	11.30	29.3
	<i>1.445</i>	<i>17.9</i>		<i>1.26²</i>	<i>28.2</i>
XV a	1.530	17.4	13.70	10.80	28.1
b	1.542	19.6	13.50	11.40	27.5
c	1.552	17.2	13.70	10.65	28.6
d	1.573	20.0	13.70	11.15	30.1
e	1.574	18.9	13.75	11.05	29.3
	<i>1.554</i>	<i>18.6</i>		<i>1.24²</i>	<i>28.7</i>
XVI a	1.642	18.9	14.10	11.30	29.4
g	1.643	18.7	14.65	11.60	29.7
c	1.647	18.7	13.75	11.05	29.0
e	1.690	17.5	13.65	10.70	28.6
	<i>1.656</i>	<i>18.4</i>		<i>1.26²</i>	<i>29.2</i>
XVII f	1.720	18.3	14.90	11.60	30.2
a	1.721	18.4	13.90	10.90	29.8
b	1.730	23.5	13.85	11.70	32.8
c	1.731	20.8	14.30	11.60	31.7
	<i>1.726</i>	<i>20.2</i>		<i>1.24²</i>	<i>31.1</i>
XVIII c	1.817	18.5	15.20	11.50	32.4
a	1.844	24.7	14.00	12.10	33.0
e	1.855	21.6	15.05	12.15	33.1
	<i>1.839</i>	<i>21.6</i>		<i>1.24²</i>	<i>32.8</i>
XIX a	1.924	20.6	15.40	12.30	32.3
	<i>1.924</i>	<i>20.6</i>		<i>1.25²</i>	<i>32.3</i>
XX a	2.039	22.6	15.10	12.60	32.5
b	2.069	25.1	15.55	13.20	34.8
	<i>2.054</i>	<i>23.9</i>		<i>1.19²</i>	<i>33.7</i>

hemisphere and cutting the corpus callosum, the commissura anterior and the chiasma opticum (Sugita, '17 a). On the drawing of the outline of the frontal section (fig. 2), which was traced

in the same manner as that for the sagittal section, the dorsal and the ventral borderlines of the cortical area were drawn. The dorsal border (*d*) was determined by the ectal borderline of the corpus callosum, which lies under the tip of the cortex at the bottom of the fissura sagittalis, and the ventral border (*v-v'*) was drawn perpendicular to the surface at the basal end of the cell group which is found under the cortex proper just below the region of the fissura rhinalis, latero-basal to the cap-

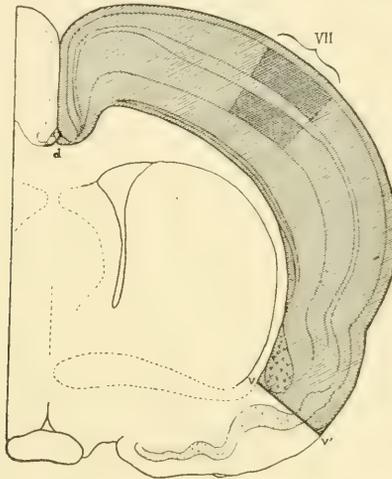


Fig. 2 Showing, by shading, the cortical area measured on the frontal section of the albino rat brain. The dorsal border (*d*) is chosen at the borderline of the corpus callosum. The ventral border (*v-v'*) was drawn perpendicular to the surface at the basal end of the cell group found near the fissura rhinalis, latero-basal to the capsula externa. The double shaded part, locality VII, indicates the area where the cell number and cell size were determined.

sula externa. This latter border is not so sharply defined, but we could not find any better marking point than this cell group. The area of the cortex, thus bounded, was then measured and recorded. In making the measurement, the area of the cortex was at first measured and then the total area of the frontal section,—of one hemicerebrum—excluding the cavity of the lateral ventricle and the tractus opticus, was measured. The ratio of the cortical area to the total area of the section was then computed. Correction of the observed values to those for the

fresh condition of the material was made in the same manner as for the sagittal cortex, by multiplying by the square of the value of the correction-coefficient. This latter was obtained by the formula given in a former paper (Sugita, '17 a), as follows:

$$\text{Correction-coefficient} = \frac{\text{The diameter } W. D \text{ in fresh cerebrum}}{\text{The diameter } W. D \text{ on the slide}}$$

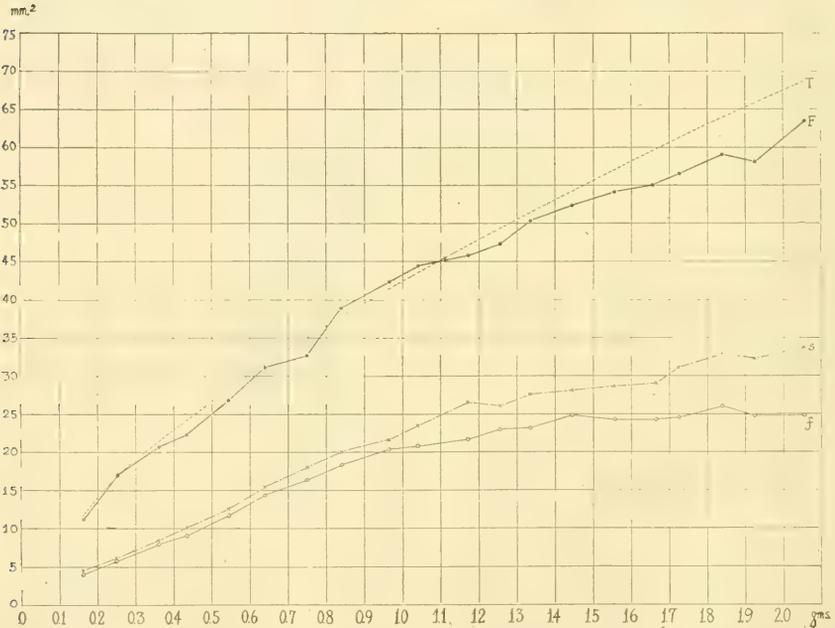


Chart 1 Showing the corrected areas of the cerebral cortex in the sagittal and the frontal sections and the area of the whole frontal section, all according to the brain weight, accompanied by the theoretical value of the last which is assumed to be proportional to the square of the cube root of the brain weight. Albino rat. \times —.—.— \times , Cortical area in the sagittal section. \circ — \circ of Cortical area in the frontal section. \bullet — \bullet F, Area of the whole frontal section. -----T, Theoretical area of the frontal section, i.e., the square of the cube root of the brain weight. All graphs are based on the data in tables 1 and 2.

These data are all entered in table 2, in which the average measurements for each brain weight group are also given. The graphs for the total area of the frontal section (graph F) and for the area of the frontal cortex (graph f) in chart 1 are based on the corrected data given in table 2.

TABLE 2

Showing the observed and corrected values of the area of the cerebral cortex and of the total frontal section and the percentage of the cortical area to the total frontal section of the albino rat brain, accompanied by the data for the correction-coefficient in the individual cases and the correction-coefficient for the group. *W. D* is the frontal diameter of the cerebrum

GROUP	BRAIN WEIGHT	OBSERVED		CORRECTION-COEFFICIENT		CORRECTED		PERCENTAGE OF CORTICAL AREA IN TOTAL SECTION
		Area of cortex	Area of total section	<i>W. D</i> in fresh brain	The same on slide	Area of cortex	Area of total section	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>per cent</i>
I a	0.153	2.8	9.2	6.45	5.65	3.7	12.0	34
c	0.154	2.6	8.2	6.35	5.40	3.6	11.4	34
b	0.177	3.5	9.9	6.95	6.26	4.3	12.2	35
	0.161	3.0	9.1	1.14 ²		3.9	11.9	35
II a	0.213	4.4	13.0	8.40	7.35	5.7	17.0	34
b	0.221	3.6	11.9	7.95	6.50	5.4	17.8	30
c	0.261	4.6	13.0	7.80	7.10	5.6	15.7	36
d	0.271	4.4	13.1	7.75	6.80	5.7	16.9	34
e	0.288	4.1	11.8	8.55	7.05	6.0	17.4	35
(Birth)	0.251	4.2	12.6	1.16 ²		5.7	17.0	34
III a	0.311	5.1	15.3	8.50	7.65	6.3	18.9	33
b	0.322	5.1	13.0	8.70	6.80	8.3	21.2	39
g	0.374	7.2	19.0	8.95	8.40	8.2	21.6	38
c	0.390	6.5	15.9	8.85	7.60	8.8	21.5	39
i	0.395	7.5	17.8	9.10	8.60	8.4	20.0	42
	0.358	6.3	16.2	1.13 ²		8.0	20.6	39
IV b	0.400	7.6	19.4	9.00	8.50	8.5	21.7	39
a	0.402	6.8	16.7	9.10	7.90	9.0	22.2	41
c	0.420	6.7	17.9	9.00	8.15	8.2	21.8	38
i	0.443	8.0	19.0	9.15	8.40	9.4	22.3	42
d	0.459	6.9	17.2	9.50	7.95	9.8	24.5	40
e	0.466	9.4	21.8	9.30	9.25	9.5	22.1	43
	0.432	7.6	18.7	1.10 ²		9.1	22.4	41
V i	0.501	9.0	22.3	9.80	9.20	10.2	25.3	40
a	0.525	9.8	22.4	9.65	9.10	11.0	25.2	44
b	0.528	8.7	19.6	9.90	8.60	11.5	26.0	44
c	0.534	7.6	18.6	10.30	8.25	11.4	29.0	39
d	0.537	8.8	20.1	10.00	8.80	11.4	26.0	44
e	0.555	9.9	22.5	9.90	9.00	12.0	27.2	44
f	0.558	9.2	20.0	10.00	8.55	12.6	27.4	46
g	0.564	10.2	22.9	10.10	9.15	12.4	28.0	44
h	0.579	10.1	22.1	10.10	9.05	12.8	27.6	46
	0.542	9.3	21.2	1.13 ²		11.7	26.9	44

TABLE 2--Continued

GROUP	BRAIN WEIGHT	OBSERVED		CORRECTION-COEFFICIENT		CORRECTED		PERCENTAGE OF CORTICAL AREA IN TOTAL SECTION
		Area of cortex	Area of total section	W. D in fresh brain	The same on slide	Area of cortex	Area of total section	
	<i>grams</i>	<i>mm.²</i>	<i>mm.²</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.²</i>	<i>mm.²</i>	<i>per cent</i>
VI c	0.610	9.9	21.7	10.15	8.50	14.1	31.0	46
a	0.617	9.6	21.6	10.55	8.65	14.3	32.2	44
e	0.690	11.6	23.7	10.60	9.40	14.8	30.2	49
	0.639	10.4	22.3	1.19 ²		14.4	31.1	46
VII a	0.740	11.1	22.1	11.00	9.20	15.9	31.6	50
b	0.760	10.2	20.3	11.20	8.70	16.9	33.6	50
	0.750	10.7	21.2	1.24 ²		16.4	32.6	50
VIII a	0.800	10.6	21.8	11.15	8.60	18.8	36.7	51
h	0.805	11.3	23.6	10.60	8.30	18.5	38.6	48
b	0.822	13.6	28.5	11.85	10.20	18.4	38.5	48
c	0.849	13.7	28.8	11.40	9.90	18.2	38.3	48
k	0.870	13.4	27.7	11.45	9.60	19.1	39.5	48
d	0.898	13.1	31.2	11.75	10.20	17.4	41.5	42
	0.841	12.6	26.9	1.20 ²		18.4	38.9	48
IX d	0.959	13.5	28.4	11.80	9.70	20.0	42.0	48
e	0.960	13.8	29.4	12.15	10.10	20.0	42.6	47
a	0.972	14.3	28.4	11.95	9.80	21.3	42.4	50
(10 days)	0.964	13.9	28.7	1.21 ²		20.4	42.3	48
X a	1.033	14.1	30.3	12.40	10.30	20.4	44.0	46
b	1.036	13.4	30.5	12.40	10.15	20.0	45.5	44
e	1.051	13.2	25.9	12.10	9.40	21.8	43.0	51
	1.040	13.6	28.9	1.23 ²		20.7	44.2	47
XI a	1.107	13.7	28.7	12.90	10.20	21.8	45.7	48
b	1.189	13.3	27.8	13.15	10.30	21.7	45.4	48
c	1.193	14.6	30.8	12.70	10.30	22.2	47.0	47
d	1.195	12.8	27.2	12.50	9.80	21.0	44.5	47
(20 days)	1.171	13.6	28.6	1.26 ²		21.7	45.7	48
XII c	1.234	15.0	31.9	12.95	10.70	22.0	46.8	47
a	1.273	11.9	23.6	12.90	9.10	24.0	47.5	50
	1.253	13.5	27.8	1.31 ²		23.0	47.2	49
XIII a	1.301	13.9	28.3	13.20	10.25	23.0	47.1	49
g	1.307	13.9	29.9	12.70	10.00	22.5	48.3	47
b	1.327	12.2	28.2	13.35	9.70	23.2	53.3	43
c	1.346	13.3	29.0	13.15	9.85	23.7	51.8	46
h	1.392	16.3	34.8	13.10	10.90	23.6	50.3	47
	1.335	13.9	30.0	1.29 ²		23.2	50.2	46

TABLE 2—*Concluded*

GROUP	BRAIN WEIGHT	OBSERVED		CORRECTION-COEFFICIENT		CORRECTED		PERCENTAGE OF CORTICAL AREA IN TOTAL SECTION
		Area of cortex	Area of total section	W. D. in fresh brain	The same on slide	Area of cortex	Area of total section	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>per cent</i>
XIV a	1.412	13.9	29.4	13.65	10.30	24.4	51.6	47
	1.441	12.4	25.7	13.10	9.20	25.2	51.0	49
	1.483	15.2	33.3	13.80	10.80	24.8	54.4	46
	1.445	13.8	29.5	1.34 ²		24.8	52.3	47
XV a	1.530	14.4	33.6	13.80	10.80	23.5	54.8	43
	1.542	13.9	30.5	13.70	10.40	24.2	53.0	46
	1.552	14.2	31.7	13.50	10.30	24.4	54.4	45
	1.573	14.2	30.8	13.90	10.60	24.4	53.1	46
	1.574	14.8	32.2	13.70	10.50	25.2	54.8	46
	1.554	14.3	31.8	1.30 ²		24.3	54.0	45
XVI a	1.642	16.4	37.0	13.80	11.20	24.9	56.2	44
	1.643	11.6	27.4	13.40	9.50	23.2	54.7	42
	1.647	14.3	29.8	14.00	10.50	25.5	53.2	48
	1.690	13.0	30.7	13.45	10.00	23.5	55.3	42
	1.656	13.8	31.2	1.33 ²		24.3	54.9	44
XVII f	1.720	12.5	28.7	13.50	9.60	24.8	56.8	44
	1.721	14.8	34.5	14.00	11.00	24.0	56.0	43
	1.730	17.5	40.4	14.70	12.35	24.8	57.2	43
	1.731	17.5	39.2	14.40	12.10	24.8	55.6	45
	1.726	15.6	35.7	1.26 ²		24.6	56.4	44
XVIII e	1.817	13.3	31.1	14.00	10.10	25.6	59.8	43
	1.844	17.4	38.1	15.00	12.10	26.7	58.5	46
	1.855	14.2	32.0	14.30	10.60	25.8	58.3	44
	1.839	15.0	33.7	1.32 ²		26.0	58.9	44
XIX a	1.924	14.8	33.9	14.10	10.90	24.8	57.0	44
	1.924	14.8	33.9	1.29 ²		24.8	57.0	44
XX a	2.039	16.8	42.7	14.80	12.10	25.2	63.9	39
	2.069	15.7	40.3	14.60	11.70	24.5	62.8	39
	2.054	16.3	41.5	1.23 ²		24.9	63.4	39

C. Number of nerve cells

On the frontal sections used for the measurement of the cortical area, the number of nerve cells contained in a unit volume at a fixed locality in the cortex was counted. The locality selected was at the middle part of the cortical band (fig. 2, VII), designated as locality VII in figure 4 in a former paper (Sugita,

'17 a). To represent the cortex, the lamina pyramidalis and the lamina ganglionaris were selected. By the use of the ocular net-micrometer (with Zeiss Comp. Ocular 6 and Zeiss objectives 2 mm. and 4 mm.), the number of nerve cells in five adjoining squares along the cortical band, each square 100 micra on a side, was counted in a given location. The numbers obtained were added together and then, by multiplying by two, was converted to the number in a unit area of 0.1 mm.² on the section. This value, the number of nerve cells in a slice of cortex, 0.1 mm.³ in area and 10 micra thick (the thickness of the section) or 0.001 mm.³ in volume, was then reduced to the number in this volume in the fresh condition of the brain. To make this reduction, I used as the correction-coefficient the cube of the reciprocal of the correction-coefficient obtained by the for-

mula: $\frac{\text{The diameter } W. D \text{ in fresh cerebrum}}{\text{The diameter } W. D \text{ on the slide}}$, which had been

previously employed, because the section on the slide was assumed to have shrunk in all three dimensions equally at the rate of the correction-coefficient and therefore a unit volume in the fresh condition would correspond to the volume of the unit on the slide multiplied by the cube of the reciprocal of the correction-coefficient.

In the lamina pyramidalis, the pyramids are more densely crowded at the ectal than at the ental part of the layer, which adjoins the lamina granularis interna. I adjusted the upper line of the net-micrometer squarely on the border between the lamina zonalis and the lamina pyramidalis and counted the cell number included in a square, 100 micra on each side, at the ectal part of the layer, where the cells are crowded densely. If large blood vessels appeared in the microscopic field, I gave up such a field and counted an adjoining one where no large vessels were present.

In the lamina ganglionaris the large ganglion cells are mixed with a number of small pyramids, almost equal in size to, or somewhat smaller than, the pyramids in the lamina pyramidalis. At first, the number of all the nerve cells, the large and small combined, was counted. Then the large ganglion cells, which

surely represent a group distinct from the small pyramids, were counted alone. So, by subtraction, the number of small pyramids only in the lamina ganglionaris was obtained. In counting the ganglion cells, I adjusted the lower line on the net-micrometer accurately on the border between the lamina ganglionaris and the lamina multiformis, because between the lamina ganglionaris and the lamina granularis interna there is found a pale band poor in cells and therefore it was not convenient to adjust the upper line of the net-micrometer at this border. The number of cells observed, in a slice of 0.1 mm.² in area and 10 micra thick on the slide, were in the similar manner recorded and by the use of the same correction-coefficients, as were used in the case of the pyramidal cells, were reduced to the number for the fresh condition of the brain.

Out of the total number of cells, which came in view in the microscopic field, about one-third does not contain the nucleoli in the cell nuclei. This means that the nucleoli in question lie outside of the section. Nevertheless I counted the cells having nuclei without nucleoli together with those in which nucleoli were to be seen, because my object was to ascertain the cell density in the locality chosen and not to determine the total number of nerve cells in a series of sections. In the latter case, the double counting of one and the same cell must be necessarily avoided. On the other hand, the cells which were represented in the section by only fractions of the cell bodies without nuclei were omitted from the counting. The number of such cells was small. Neuroglia nuclei, which were to be easily distinguished by their smaller size, and the intima cells of the capillaries, if they came in view, were not counted.

Table 3 shows the results of these enumerations.

III. DISCUSSION

D. The area of the cortex in the sagittal section

Examining table 1 and chart 1 (graph s), which give the area of the cortex in the sagittal sections of the albino rat brain, it is seen that the area increases steadily with increasing brain weight.

TABLE 3

Giving for each individual and for each brain weight group the number of nerve cells in 0.001 mm.^3 in volume of the cortex, in the lamina pyramidalis and in the lamina ganglionaris, and also the number of the ganglion cells in the lamina ganglionaris, all counted at the middle part of the cortex in the frontal section, as shown in figure 2. Albino rat

GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		NUMBER OF CELLS IN A VOLUME OF CORTEX, 0.001 MM.^3					
		W. D in fresh brain	W. D on slide	Lam. pyramid.		Lam. ganglion.		Ganglion cells in lam. gangl.	
				Ob- served	Cor- rected	Ob- served	Cor- rected	Ob- served	Cor- rected
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>						
I a	0.153	6.45	5.65	1150	775				
c	0.154	6.35	5.40	1130	695				
b	0.177	6.95	6.26	945	690				
	0.161	$(1/1.14)^3$		1075	720				
II a	0.213	8.40	7.35	830	556	370	248	91	61
b	0.221	7.95	6.50	930	509	393	215	114	62
c	0.261	7.80	7.10	735	554	322	242	104	78
d	0.271	7.75	6.80	726	490	358	242	114	77
e	0.288	8.55	7.05	715	402	424	238	120	67
(Birth)	0.251	$(1/1.16)^3$		787	502	373	237	109	69
III a	0.311	8.50	7.65	625	456	330	241	112	82
b	0.322	8.70	6.80	730	348	415	198	122	58
g	0.374	8.95	8.40	504	417	270	223	98	82
c	0.390	8.85	7.60	493	312	312	197	104	66
i	0.395	9.10	8.60	401	337	262	220	90	76
	0.358	$(1/1.13)^3$		551	374	318	216	105	73
IV b	0.400	9.00	8.50	410	345	258	217	94	79
a	0.402	9.10	7.90	473	309	267	175	95	62
e	0.420	9.00	8.15	451	334	240	178	74	55
i	0.443	9.15	8.40	424	327	227	176	73	56
d	0.459	9.50	7.95	440	258	250	146	77	45
e	0.466	9.30	9.25	355	348	186	182	59	58
	0.432	$(1/1.10)^3$		426	320	238	179	79	59
V i	0.501	9.80	9.20	371	307	199	165	69	57
a	0.525	9.65	9.10	362	303	183	154	67	56
b	0.528	9.90	8.60	365	240	205	134	77	51
c	0.534	10.30	8.25	432	222	228	117	78	40
d	0.537	10.00	8.80	412	281	210	143	71	48
e	0.555	9.90	9.00	368	277	164	123	62	47

TABLE 3—Continued

GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		NUMBER OF CELLS IN A VOLUME OF CORTEX, 0.001 MM. ³					
		W. D in fresh brain	W. D on slide	Lam. pyramid.		Lam. ganglion.		Ganglion cells in lam. gangl.	
				Ob- served	Cor- rected	Ob- served	Cor- rected	Ob- served	Cor- rected
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>						
V f	0.558	10.00	8.55	357	223	182	114	79	49
g	0.564	10.10	9.15	326	242	178	132	62	46
h	0.579	10.10	9.05	318	229	194	140	64	46
	0.542	(1/1.13) ³		368	258	194	136	70	49
VI e	0.610	10.15	8.50	325	190	182	106	65	38
a	0.617	10.55	8.65	322	177	200	110	60	33
e	0.690	10.60	9.40	286	199	191	133	58	40
	0.639	(1/1.19) ³		311	189	191	116	61	37
VII a	0.740	11.00	9.20	277	186	149	100	48	32
b	0.760	11.20	8.70	300	140	188	88	47	22
	0.750	(1/1.24) ³		289	163	169	94	48	27
VIII a	0.800	11.15	8.60	302	138	170	78	43	20
h	0.805	10.60	8.30	293	140	168	80	48	23
b	0.822	11.85	10.20	266	170	138	88	38	24
c	0.849	11.40	9.90	242	158	140	92	37	24
k	0.870	11.45	9.60	257	151	152	90	45	26
d	0.898	11.75	10.20	255	167	138	90	38	25
	0.841	(1/1.20) ³		269	154	151	86	42	24
IX d	0.959	11.80	9.70	241	133	156	86	40	22
e	0.960	12.15	10.10	224	130	147	85	39	23
a	0.972	11.95	9.80	220	122	150	83	41	23
(10 days)	0.964	(1/1.21) ³		228	128	151	85	40	23
X a	1.033	12.40	10.30	223	128	153	88	45	26
b	1.036	12.40	10.15	212	116	136	75	41	23
e	1.051	12.10	9.40	244	115	149	70	43	20
	1.040	(1/1.23) ³		226	120	142	78	43	23
XI a	1.107	12.90	10.20	234	116	150	74	44	22
b	1.189	13.15	10.30	229	110	148	71	49	24
c	1.193	12.70	10.30	220	118	144	77	42	23
d	1.195	12.50	9.80	222	107	142	68	44	21
(20 days)	1.171	(1/1.26) ³		226	113	146	73	45	23
XII c	1.234	12.95	10.70	210	118	136	76	48	27
a	1.273	12.90	9.10	248	87	171	60	55	19
	1.253	(1/1.31) ³		229	103	154	68	52	23

TABLE 3—Concluded

GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		NUMBER OF CELLS IN A VOLUME OF CORTEX, 0.001 MM. ³					
		W. D in fresh brain	H. D on slide	Lam. pyramid.		Lam. ganglion.		Ganglion cells in lam. gangl.	
				Ob- served	Cor- rected	Ob- served	Cor- rected	Ob- served	Cor- rected
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>						
XIII a	1.301	13.20	10.25	212	99	177	83	56	26
g	1.307	12.70	10.00	205	100	163	80	52	25
b	1.327	13.35	9.70	243	94	180	69	60	23
c	1.346	13.15	9.85	218	92	174	73	57	24
h	1.392	13.10	10.90	190	110	140	81	50	29
	1.335	(1/1.29) ³		214	99	167	77	55	25
XIV a	1.412	13.65	10.30	212	91	164	71	58	25
e	1.441	13.10	9.20	248	86	176	61	63	22
b	1.483	13.80	10.80	218	105	172	82	60	29
	1.445	(1/1.34) ³		226	94	171	71	60	25
XV a	1.530	13.80	10.80	185	88	134	64	47	23
b	1.542	13.70	10.40	207	90	144	63	49	22
c	1.552	13.50	10.30	183	81	152	67	52	23
d	1.573	13.90	10.60	184	82	130	58	53	24
e	1.574	13.70	10.50	204	93	134	60	52	23
	1.554	(1/1.30) ³		193	87	139	62	51	23
XVI a	1.642	13.80	11.20	170	91	127	68	50	27
g	1.643	13.40	9.50	225	81	148	53	56	20
c	1.647	14.00	10.50	186	79	134	57	55	23
e	1.690	13.45	10.00	207	84	148	61	63	26
	1.656	(1/1.33) ³		197	84	139	60	56	24
XVII f	1.720	13.50	9.60	208	75	151	54	60	22
a	1.721	14.00	11.00	178	86	132	64	55	27
b	1.730	14.70	12.35	142	84	118	70	44	26
c	1.731	14.40	12.10	144	85	106	63	42	25
	1.726	(1/1.26) ³		168	83	127	63	50	25
XVIII c	1.817	14.00	10.10	188	71	142	53	54	20
a	1.844	15.00	12.10	170	89	126	66	48	25
e	1.855	14.30	10.60	192	78	139	57	60	24
	1.839	(1/1.32) ³		183	79	136	59	54	23
XIX a	1.924	14.10	10.90	174	81	110	51	52	24
	1.924	(1/1.29) ³		174	81	110	51	52	24
XX a	2.039	14.80	12.10	150	82	95	52	38	27
b	2.069	14.60	11.70	151	78	96	49	37	19
	2.054	(1/1.23) ³		151	80	96	51	38	20

As already shown (Sugita, '17, '17 a), the longitudinal diameter of the sagittal section (from the frontal pole to the occipital pole), that is $L. F$, as well as the cortical thickness, are both steadily increasing as the brain weight increases. The thickness of the cortex is one component of its area in the section, the other being obtained by dividing the area by the thickness, and the length thus found is correlated with the longitudinal diameter of the section ($L. F$) as defined above. The increase of the cortical area will therefore depend on the increase in cortical thickness and the increase in the longitudinal diameter of the section ($L. F$). Table 4 shows these relations. Column B gives the average brain weight by groups, column C the average corrected area of the cortex (taken from table 1), column D the cortical thickness (T_s) and column F the diameter $L. F$, all in the fresh condition of the brain and the last two quoted from the data already published (Sugita, '17, '17 a). In column E is given the ratio C/D or the computed length of the long side, when the cortical area is reduced to a rectangle with the short side equal to the cortical thickness. If these computed lengths are compared with the actual longitudinal diameters of the cerebrum ($L. F$), given in column F, it is of interest to note that, in brains weighing more than 0.5 gram, the ratios, given in column G as E/F , are quite similar, ranging between 1.16 and 1.25 (average 1.22).¹ In the newborn or before birth (Group I), the ratio is somewhat higher. So, if necessary, the cortical area in the sagittal sections may be obtained by the following formula

$$L. F \times T_s \times 1.22 \quad (L. F \text{ and } T_s, \text{ in millimeters})$$

As the sagittal cortical thickness in brains weighing more than 1.17 grams increases only slowly, the cortical area in the sagittal section in brains older than twenty days is approximately proportional to the longitudinal diameter of the cerebrum ($L. F$).

E. The area of the cortex in the frontal section

Reviewing table 2 and chart 1 (graph f), we see that the cortical area in the frontal section increases in the same manner

¹ In making comparisons with the Norway rat in part II of this paper, the average ratio given by Groups XIII to XX will be that used. This average is 1.21.

TABLE 4

Showing the relations of the cortical area in the sagittal section to the longitudinal diameter ($L. F$) of the cerebrum and the cortical thickness. All values for the fresh condition. Albino rat.

A	B	C	D	E	F	G
GROUP	BRAIN WEIGHT	CORTICAL AREA IN SAGITTAL SECTION	CORTICAL THICKNESS IN SAGITTAL SECTION	$\frac{C}{D}$	$\frac{L. F}{\text{IN FRESH BRAIN}}$	$\frac{E}{F}$
	grams	mm. ²	mm.	mm.	mm.	
I	0.161	4.4	0.52	8.5	5.6	1.52
II (birth)	0.251	5.8	0.67	8.7	6.4	1.36
III	0.358	8.3	0.90	9.2	7.4	1.24
IV	0.432	10.1	0.99	10.2	8.0	1.27
V	0.542	12.6	1.14	11.0	8.9	1.24
VI	0.639	15.5	1.29	12.0	9.6	1.25
VII	0.750	18.1	1.43	12.7	10.4	1.22
VIII	0.841	20.1	1.48	13.6	11.0	1.24
IX (10 days)	0.964	21.7	1.55	14.0	11.6	1.21
X	1.040	23.5	1.59	14.8	12.0	1.23
XI (20 days)	1.171	26.6	1.72	15.5	12.5	1.24
XII	1.253	26.1	1.75	14.9	12.8	1.16
XIII	1.335	27.6	1.72	16.0	13.0	1.23
XIV	1.445	28.2	1.70	16.6	13.3	1.25
XV	1.554	28.7	1.76	16.3	13.7	1.19
XVI	1.656	29.2	1.77	16.5	14.1	1.17
XVII	1.726	31.1	1.79	17.4	14.3	1.22
XVIII	1.839	32.8	1.86	17.6	14.7	1.20
XIX	1.924	32.3	1.80	17.9	15.0	1.19
XX	2.054	33.7	1.80	18.7	15.3	1.22
Average (Groups V-XX)						1.22
Average (Groups XIII-XX)						1.21

as in the sagittal section though more slowly. The cortical area in the frontal section is a product of the cortical thickness (T_F) and the length of the cortex along the cerebral surface. This surface line of the cortex in the frontal section may be regarded as a part of a circle and its length may be taken as proportional to the length of the radius or the measurement $W. D$ (the frontal diameter of the cerebrum), which was measured across the section horizontally (Sugita, '17). As shown in table 5,

which is comparable with table 4, the relative value C/D or $\frac{\text{Cortical area}}{\text{Cortical thickness}}$ and the ratio of this value to $W. D$ were calculated. The ratio, given in column G, table 5, falls between 0.85 and 0.99 (average 0.91)² in brains weighing more than 0.5 gram, but shows a tendency to gradually increase as the brain weight increases. In the newborn or before birth (Group I) it is somewhat higher. If the average ratio be taken as usable for all groups, as in the case of the sagittal section, the cortical area in the frontal section may be approximately obtained by the following formula:

$$W. D \times T_f \times 0.91 \quad (W. D \text{ and } T_f, \text{ in millimeters})$$

As, in brains weighing more than 0.95 gram, the cortical thickness in the frontal section (T_f) varies only slightly, the cortical area in the frontal section in these brains will be practically proportional to the frontal diameter of the cerebrum ($W. D$). The agreement of the calculated with the observed values is however not so good as in the case of the sagittal section.

F. The area of the entire frontal section

In chart 1, the graph F, representing the total area of the frontal section, is accompanied by a dotted line T , which represents the value of the square of the cube root of the brain weight (in grams). Theoretically, under the assumption that the specific gravity of the brain remains the same throughout the life, the latter should run a similar course to the former, if the brain enlarges proportionally in all dimensions as it grows. Between Groups II to XIV, both curves take nearly the same course, if some slight discrepancies in the observed values are neglected. But in brains weighing more than 1.4 grams, the differences become so distinct, that they can no longer be regarded as due to errors in measurement. This is probably due to the fact that the brain is not enlarging proportionally in all diameters,

² In making comparisons with the Norway rat in part II of this paper, the average ratio given by Groups XIII to XX will be that used. This average is 0.93.

TABLE 5

Showing, in columns A to E, the relations of the cortical area in the frontal section to the frontal diameter of the cerebrum ($W. D$) and the cortical thickness, and, in columns H to J, the relations of the total area of the frontal section and the frontal diameter of the cerebrum. All values for the fresh condition. Albino rat.

A	B	C	D	E	F	G	H	I	J
GROUP	BRAIN WEIGHT	CORTICAL AREA IN FRONTAL SECTION	CORTICAL THICKNESS IN FRONTAL SECTION	$\frac{C}{D}$	$W. D$ IN FRESH BRAIN	$\frac{E}{F}$	TOTAL AREA OF FRONTAL SECTION	SQUARE OF $W. D$	$\frac{H}{I}$
	grams	mm. ²	mm.	mm.	mm.		mm. ²	mm. ²	
I	0.161	3.9	0.56	7.0	6.6	1.06	11.9	43.6	0.27
II(birth)	0.251	5.7	0.78	7.3	7.7	0.95	17.0	59.3	0.29
III	0.358	8.0	1.02	7.9	8.7	0.91	20.6	75.7	0.27
IV	0.432	9.1	1.11	8.2	9.3	0.88	22.4	86.5	0.26
V	0.542	11.7	1.33	8.7	10.1	0.86	26.9	102.0	0.26
VI	0.639	14.4	1.55	9.3	10.6	0.88	31.1	112.4	0.28
VII	0.750	16.4	1.74	9.5	11.2	0.85	32.6	125.4	0.26
VIII	0.841	18.4	1.82	10.1	11.6	0.87	38.9	134.6	0.29
IX(10 days)	0.964	20.4	1.86	11.0	12.1	0.91	42.3	146.4	0.28
X	1.040	20.8	1.82	11.4	12.4	0.92	44.2	153.8	0.29
XI (20 days)	1.171	21.7	1.91	11.4	12.7	0.90	45.7	161.3	0.28
XII	1.253	23.0	1.91	12.0	13.0	0.92	47.2	169.0	0.28
XIII	1.335	23.2	1.94	12.0	13.2	0.91	50.2	174.2	0.29
XIV	1.445	24.8	1.99	12.5	13.4	0.93	52.3	179.6	0.29
XV	1.554	24.3	1.97	12.3	13.5	0.91	54.0	182.3	0.30
XVI	1.656	24.3	1.94	12.5	13.7	0.91	54.9	187.7	0.29
XVII	1.726	24.6	1.90	12.9	13.8	0.94	56.4	190.4	0.30
XVIII	1.839	26.0	1.97	13.2	14.1	0.94	58.9	198.8	0.30
XIX	1.924	24.8	1.83	13.5	14.3	0.94	57.0	204.5	0.28
XX	2.054	24.9	1.72	14.5	14.6	0.99	63.4	213.2	0.30
Average (Groups V-XX)						0.91			0.28
Average (Groups XIII-XX)						0.93			

the increase in the frontal diameter being retarded relative to the sagittal diameter in brains weighing more than 1.4 grams (Sugita, '17).

If, as given in columns H and I, table 5, the area of the total frontal section is compared with the square of $W. D$ of the corresponding brain group, the above inference will be supported by the fact that the ratio, given in column J of the same table,

is almost equal throughout all brain weight groups, swinging within the narrow limits of 0.26 to 0.30.

G. Percentage of the area of cortex in the total area of the frontal section (one hemisphere)

Figure 2 shows the outline of the frontal section. In the section we see as the principal divisions the cortex, the striatum, the thalamus, the capsula externa and the lateral ventricle, and, among these, the cortex and the striatum stand in marked contrast. In the young brains, the lateral ventricle is wide. This cavity was not included in the measurement of the area. In the wall of it, especially at the dorso-lateral corner, there are seen masses of dividing cells and of neuroblasts, which are due to migrate into the cortex. But in the older brains weighing more than 1.1 grams, the ventricular wall is almost free from dividing cells and the cortex is no longer receiving new cells. By determining the percentage of the cortical area to the total area of the frontal section, we may obtain some clue as to mass relation of the cortex to the other structures seen in the frontal section.

As previously given in table 2, the cortical area in the frontal section amounts to 34 per cent of the total area at birth. It increases from birth up to brains weighing 0.7 to 1.2 grams, when the percentage reaches its highest figure, that is, 50 or sometimes 51, on the average 48 per cent. After this stage, the percentage slowly diminishes as the brain weight increases, and, at full maturity, it reaches 44 per cent or less; even 39 per cent in an old brain weighing more than 2.0 grams. This means clearly that the cortical area increases rapidly by receiving new cells from the matrix and at the same time by the enlargement and separation of the cell bodies, during the first phase, covering the first ten days after birth.

In this phase, as a matter of fact, the remainder of the section is for the most part composed of the matrix and migrating cells, the central nuclei being not yet so largely developed. The transitional layers, or the areas previously occupied by the

transitional layers, which will be replaced by the capsula externa, are relatively wide during this phase.

After twenty days, when the brain has attained nearly the weight of 1.17 grams, the remainder of the section (the central nuclei and the white substance) increases more rapidly than the cortical area and the group of proliferating cells in the ventricular wall disappears. The percentage of the cortical area to that of the whole section consequently decreases under these conditions, though the absolute value of the cortical area is steadily increasing.

From the mode of the changes in the percentage value of the cortical area, we may conclude that, in the albino rat, at least, the period during which the brain weight increases from 0.25 gram (birth) to 1.2 grams (about 20 days), is the period when the cortical elements are principally produced, matured and arranged, and that the cortex is precocious in its construction. The growth or construction of the remaining parts in the frontal section, so far at least as this is expressed by increase in volume, is relatively retarded or delayed until the cortex has acquired all its characteristic elements.

H. The volume of the entire cortex

The true volume of the entire cerebral cortex can not be measured by the methods here used. It will require a special study for that purpose. My present object is to obtain relative values for the cortical volume and a record of the change in these relative values according to brain growth. If the data for the area of the cerebral cortex as measured by me in the two typical sections be reduced to a simple geometrical form, it will be very easy to compare the changes in the computed volume in successive brain weight groups. As already mentioned, the cortical area in the sagittal and the frontal sections, which sections cross one another at right angles, may be reduced to rectangles which have as the long side the lengths proportional respectively to the sagittal and the frontal diameters of the cerebrum ($L.F$ and $W.D$), and as the short side the cortical

thicknesses (T_s and T_f). For the present purpose, the mean cortical thickness (T) may be substituted for both the foregoing values of the cortical thickness, when the brain weight is the same, because T falls at the mean of the T_s and T_f , so that the gain in T_s would be compensated by the loss in T_f (fig. 3). As a consequence the volume of the cortex may be represented by an index value, the formula for which follows.³

$$L. F \times W. D \times T \quad (\text{all in millimeters})$$

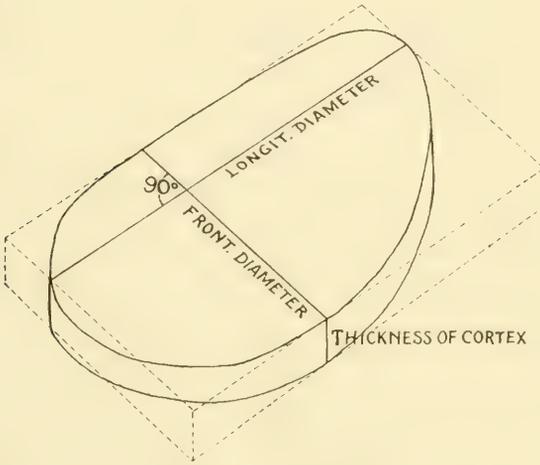


Fig. 3 The solid lines show the simplified geometrical form used to indicate the volume of the entire cortex, which is assumed to be proportional to the rectangular form designated by dotted lines in the figure. The volume of the rectangular figure, which was obtained by the value: $L. F \times W. V \times T$, has been tabulated in column F, table 6, and plotted as graph LWT in chart 2.

The values thus obtained—which mean the actual volume of the rectangle denoted by dotted lines in figure 3—stand in a fixed relation to the true cortical volume which is denoted by solid lines in the same figure, as far as the latter retains a similar form during growth.

³ In this formula, the coefficients 1.22 and 0.91, which were empirically determined, were eliminated, because these coefficients are fixed throughout all the groups to be compared. For Groups XIII to XX, the coefficients are respectively 1.21 and 0.93, and these will be taken into consideration when comparison is made between the Albino and the Norway rats.

TABLE 6

Giving for each brain weight group the average brain weight, ratio in cerebral volume, computed cortical volume and the data used to obtain the computed cortical volume, and ratio in cortical volume

BRAIN WEIGHT GROUP	A	B	C	D	E	F	G
	BRAIN WEIGHT	RATIO OF VOLUME OF CEREBRUM	L, F IN FRESH BRAIN	W, D IN FRESH BRAIN	T_1 AVERAGE (CORTICAL THICKNESS	$\frac{L, F \times T}{W, D \times T}$ COMPUTED VOLUME OF CORTEX	RATIO OF COMPUTED VOLUME OF CORTEX
	grams		mm.	mm.	mm.	mm. ³	
I	0.161		5.6	6.6	0.54	19.96	
II (birth)	0.251	1.00	6.4	7.7	0.73	35.97	1.00
III	0.358	1.34	7.4	8.7	0.96	61.81	1.72
IV	0.432	1.66	8.0	9.3	1.10	81.84	2.28
V	0.542	2.12	8.9	10.1	1.24	111.46	3.10
VI	0.639	2.53	9.6	10.6	1.42	144.50	4.02
VII	0.750	3.12	10.4	11.2	1.58	184.04	5.12
VIII	0.841	3.50	11.0	11.6	1.65	210.54	5.85
IX (10 days)	0.964	4.04	11.6	12.1	1.71	240.02	6.67
X	1.040	4.10	12.0	12.4	1.72	255.94	7.12
XI (20 days)	1.171	4.61	12.5	12.7	1.82	288.93	8.03
XII	1.253	4.80	12.8	13.0	1.83	304.51	8.47
XIII	1.335	5.17	13.0	13.2	1.83	314.03	8.73
XIV	1.445	5.40	13.3	13.4	1.85	329.71	9.17
XV	1.554	5.89	13.7	13.5	1.87	345.86	9.62
XVI	1.656	6.05	14.1	13.7	1.86	359.30	9.99
XVII	1.726	6.44	14.3	13.8	1.85	365.08	10.15
XVIII	1.839	6.72	14.7	14.1	1.92	397.96	11.06
XIX	1.924	6.91	15.0	14.3	1.82	390.39	10.85
XX	2.054	7.85	15.3	14.6	1.76	393.15	10.93

¹ T_1 , here entered, is the mean value of T_s and T_f , previously given in tables 4 and 5 and is not the general average thickness of the cortex of the sagittal, frontal and horizontal sections formerly presented in my second paper in this series (Sugita, '17 a).

Table 6 shows the values for the cortical volume computed by the above method and the ratios, the cortical volume at birth being taken as the unit of the comparison.

Chart 2 (graph LWT) shows graphically the ratios obtained (table 6, column G), accompanied by the graph (graph LWH) which shows the increase in volume of the cerebrum (table 6, column B). The volume of the cerebrum was computed according to my previous procedure (Sugita, '17). From this

chart we see that the cortical volume increases more rapidly than the entire cerebral volume, until the brain attains the weight of 1.17 grams (20 days) (see crosses in chart 2). If we take these marks as the starting points, then the cerebral volume increases to about 1.7 times at full maturity and in the same way the cortical volume increases to about 1.4 times compared with the value at twenty days (table 6). So, it may be stated that after twenty days the increase in cortical volume becomes

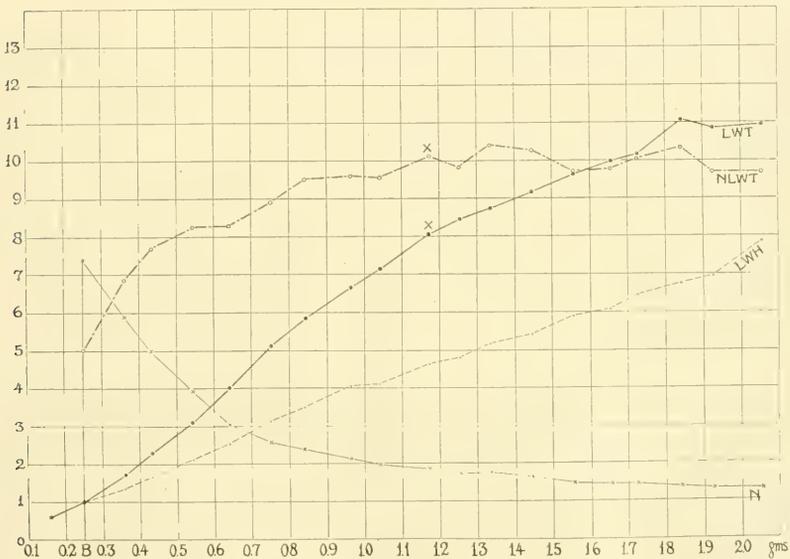


Chart 2 Showing the ratios of the values for the cortical volume, the volume of the cerebrum, the cell density in two unit volumes and the computed number of nerve cells in the entire cerebral cortex of the albino rat, according to the brain weight. •—• *LWT*, The ratios of the computed volume of the cerebral cortex, the volume at birth being taken as the unit. Based on the data in table 6. —•—•—• *LWH*, The ratios of the volume of the entire cerebrum, the volume at birth being taken as the unit. Based on the data presented in a former paper (Sugita, '17) and given also in table 6. ×—× *N*, The cell density in two unit volumes of the cortex. Based on the data given in column C, table 7, as *N*, and plotted here according to the values corresponding to one one-hundredth of the number given in column C, table 7. •—•—• *NLWT*, The ratios of the computed number of nerve cells in the entire cortex, the value at birth being taken as the unit. Here the unit chosen on the ordinate is 5. The data are given in column E, table 7.

slower and is somewhat less in rate than the increase in cerebral volume or brain weight, as is also seen in the graphs given in chart 2.

I. Number of cells in a unit volume of the cortex

In the lamina pyramidalis of the newborn Albino brain, at a dorso-lateral part of the pallium, where, in the frontal section, the cell count was made (fig. 2, VII), there were in the fresh condition about 500 pyramids crowded in a unit volume of 0.001 mm.³ This number decreases, as the brain grows, and falls to 110 in a brain weighing about 1.2 grams (20 days) (table 3). In a brain weighing about 1.5 grams (50 days), the number has dropped nearly to 90, from which it is only slightly reduced in the heavier brains. In an old rat, whose brain weighs more than 2.0 grams, the number is about 80, or less than one-sixth the number at birth. According to another study, which will be published later, the size of the cell body and of the nucleus of the pyramids in the lamina pyramidalis, measured at this same locality, increases very rapidly during the first ten days after birth, till the brain has attained 0.9 gram in weight, when these structures reach their maximum size (Cell body $16\mu \times 20\mu$; Nucleus $14\mu \times 15\mu$). After this stage the cell body and the nucleus are mature in their nucleus-plasma relation, but still changing their chemical composition, as revealed by the stains, while the neuron as a whole is still growing as shown by the developing axon and the dendrites. This fact is in accord with the observation that the number of pyramidal cells in the lamina pyramidalis decreases rapidly after birth, until the brain weight reaches about 0.9 gram (10 days), after which the rate of decrease becomes slow.

The change in cell number in a given volume of the cortex during the growth of the brain is determined by two main factors: (1) the enlargement of the cell body proper and the growth of the cell branches and (2) the development of the intercellular structures (that is, incoming nerve fibers, neuroglia, blood vessels) and myelin formation, separating the cells more and more from each other.

As to the cells in the lamina ganglionaris, the relation is somewhat different from that just described. The total number of cells, including both the small and large pyramids, decreases relatively rapidly after birth, until the brain weight reaches 1.25 grams (25 days). It then shows a slight increase (table 3, Groups XIII and XIV), but decreases again by slow steps and remains almost fixed after 35 days (brain weight 1.4 grams) at 60. Finally, in old rats, only 50 cells were counted in a unit volume of 0.001 mm.,³ or about one-fifth the number at birth.

If the number of the large pyramids alone is considered, then the number decreases rapidly from birth to a brain weight of 0.8 gram (9 days). After this, it decreases slightly and remains almost fixed at 23 up to a brain weighing 1.2 grams. In brains weighing 1.3 to 1.5 grams it shows a tendency to increase slightly for a time—corresponding to the increase in total number of cells in this layer (above mentioned)—but finally becomes fixed again at 23 to 24 throughout maturity. In old age, it has diminished to 20 or about two-sevenths the number at birth. The large ganglion cells attain nearly their full size (Cell body $21\mu \times 28\mu$; Nucleus $18\mu \times 19\mu$) at 0.9 gram in brain weight (10 days), almost at the same time as the small pyramids.

I can not, from the data at hand, satisfactorily explain the increase in cell number in the lamina ganglionaris in the period during which the brain grows from 1.2 grams to 1.4 grams in weight. This fact might however have some connection with the chemical structure of the cells and consequently be related to a change in reaction to the reagents used, so that the size of the large pyramids, after having attained a maximum ($21\mu \times 28\mu$) at a brain weight of 0.9 gram, diminishes slightly, at the same time that their response to the stain changes somewhat, measuring only $20\mu \times 27\mu$ at a brain weight of 1.3 to 1.4 grams, after which they again enlarge to a full size of the cell body (sometimes over $23\mu \times 30\mu$). In the carbol-thionine staining the sections from brains weighing less than 1.0 gram show a violet tone, those from brains weighing more than 1.2 grams a blue tone while those from brains weighing 1.0 to 1.2 grams are intermediate in tone. We shall pass over this question now,

as a detailed description of the size of each cell type and its mode of enlargement according to age will be the theme of a later paper.

To represent the relative cell density in the cerebral cortex for each brain weight group, the sum of the cell numbers in the lamina pyramidalis and the lamina ganglionaris, given in table 3, was used, in order to balance, in some measure, the inequality of the cell distribution. These values are given in table 7, column C, and in chart 2 (graph N). Both table and chart show that the number of nerve cells in a unit volume of the cortex decreases very rapidly during the first ten days after birth (up to the brain weight of 0.95 gram) and after that time it decreases slowly but steadily as the age advances. The cell number at maturity is nearly one-fifth the value at birth.

J. Values for the computed number of nerve cells in the entire cerebral cortex, according to brain weight

The number of nerve cells given in table 3 does not mean the actual volume of complete cells contained in a unit volume, because the parts of cells which showed a nucleus but no nucleolus in the section were also counted. In spite of this, the number in the table indicates fairly the relative number of cells or the relative cell density at different ages in the localities examined, and from this we may be able to get some indication as to the number of nerve cells in the entire cerebral cortex.

If the actual number of cells in a unit volume be proportional to the number of cells counted, the number of cells in the entire cerebral cortex may be indicated (theoretically) by this number multiplied by the number obtained by dividing the volume of the entire cerebral cortex by the unit volume.

The actual volume of the cortex was not measured, but the computed volume is indicated by the following formula, as explained already.

$$L \cdot F \times W \cdot D \times T \quad (\text{all in millimeters})$$

So, if N means the cell number in a unit volume (for example,

N is 240 for Group VIII, as shown in table 7, column C), the relative value of the number of nerve cells in the entire cortex may be computed by the following formula.⁴

$$N \times L. F \times W. D \times T \quad (L. F, W. D \text{ and } T, \text{ in millimeters})$$

The results of this computation are shown in table 7 and in chart 2 (graph NLWT), where the necessary data were all taken from the present or former papers and the relative value of $N \times L. F \times W. D \times T$ is calculated. For N , the corrected sum of the cell numbers in the lamina pyramidalis and in the lamina ganglionaris, given in table 3, was used (table 7, column C). The results are quite interesting. As seen from table 7, columns D and E, and chart 2 (graph NLWT based on column E), the relative value of the computed number of cells in the entire cortex increases rapidly from birth to a brain weighing 0.9 gram (about 10 days), and then for a while the increase becomes slow up to a brain weight of 1.17 grams (20 days), attaining at this time nearly the complete number of nerve cells (see graph NLWT, mark X in chart 2). After having passed this phase, the value for the number of cells remains almost constant throughout the life. The average of the values for Groups XI-XX in table 7 is 530, so that between birth and maturity the number of cells counted has increased two times, but nearly all of this increase has taken place during the first ten days of life. These results coincide very well with the conclusions of Allen ('12), that in the cerebrum mitosis continues with diminishing activity to the 20th day after birth.

⁴ By this computation the number of cells in the entire cortex will be equal to the number of times the unit of volume, 0.001 mm.³ in which the cells were counted, is contained in the entire volume of the cortex, multiplied by the number of cells in a unit volume. The number of cells designated by N is however the sum of the numbers in two unit volumes, that is, the number in one unit volume of the lamina pyramidalis plus the number in one unit volume of the lamina ganglionaris.

Since the numbers of cells used, N , is that in two unit volumes, the foregoing product must be divided by two. As dividing the volume of the cortex by 0.001 is equivalent to multiplying it by 1000, and as the product must be divided by two, the operation may be expressed as follows:

$$N \times L. F \times W. D \times T \times 500 = \text{Number of cells}$$

TABLE 7

Giving the computed number of nerve cells in the entire cerebral cortex, obtained on the basis of the measurements given in this series of studies. The ratio of the number of cells of each later group to that of Group II (birth) is also given

BRAIN WEIGHT GROUP	A	B	C	D	E
	BRAIN WEIGHT	COMPUTED VOLUME OF CORTEX $L. F \times W. D \times T$	SUM OF NOS. OF CELLS IN LAM. PTR. AND LAM. GANG. IN TWO UNIT VOLUMES, K	COMPUTED NUMBER OF CELLS IN CORTEX, ¹ $N \times L. F \times W. D \times T \times \frac{1}{100}$	RATIO OF NUMBER OF CELLS
	<i>grams</i>	<i>mm.³</i>			
II (birth)	0.251	35.97	739	265.8	1.00
III	0.358	61.81	590	364.7	1.37
IV	0.432	81.84	499	408.4	1.54
V	0.542	111.46	394	439.2	1.65
VI	0.639	144.50	305	440.8	1.66
VII	0.750	184.04	257	473.0	1.78
VIII	0.841	210.54	240	505.3	1.90
IX (10 days)	0.964	240.02	213	511.2	1.92
X	1.040	255.94	198	506.8	1.91
XI (20 days)	1.171	288.93	186	537.4	2.02
XII	1.253	304.51	171	520.7	1.96
XIII	1.335	314.03	176	552.7	2.08
XIV	1.445	329.71	165	544.0	2.05
XV	1.554	345.86	149	515.3	1.94
XVI	1.656	359.30	144	517.4	1.95
XVII	1.726	365.08	146	533.0	2.01
XVIII	1.839	397.96	138	549.2	2.07
XIX	1.924	390.39	132	515.3	1.94
XX	2.054	393.15	131	515.0	1.94
Average (Groups XI-XX)				530.0	2.00
Average (Groups XIII-XX)				530.2	2.00

¹ As explained in a footnote (footnote 4), the actual number of cells contained in the computed volume of the cortex should be $N \times L. F \times W. D \times T \times 500$, but, for the convenience, $1/100$ of $N \times L. F \times W. D \times T$, or $1/50,000$ of the actual number of cells contained in the computed volume, was given here as the computed number of cells in the cortex.

The above statement that between birth and maturity the number of nerve cells in the entire cortex has increased two-fold, does not necessarily mean that the additional cells have been all newly formed after birth. As a matter of fact, we see,

in the sections of the newborn brains, many immature cells, the indifferent cells and the neuroblasts, crowded densely together in the ventricular wall and in the transitional layers and these are all migrating to the cortex. The number of cells in the cortex is increased after birth by receiving these cells already formed but lying at birth still outside of the cortex proper, besides by receiving the cells which are newly formed after birth. So the nerve cells, destined for the cortex, are largely present in immature form in the cerebrum at birth, but lie outside of the cortex proper, while the actual number of cells formed after birth may amount only to a small fraction of the total number of nerve cells in the cortex at maturity, though there is active mitosis during the first days after birth.

I have previously recognized three developmental phases in the growth of the cortex in thickness (Sugita, '17 a), as follows:

First phase, from birth to the 10th day.

Second phase, from the 10th to the 20th day.

Third phase, from the 20th to the 90th day.

The first and the second phases here given may also be applied, without any modification, to the changes in cell number in the cerebral cortex, while the third phase does not appear in this connection.

IV. CONCLUSIONS

In an earlier study on the cerebral cortex of the albino rat (Sugita, '17 a), I stated that the cerebral cortex attains nearly its full thickness at the age of twenty days, before myelination in the cortex had begun, and that the organization of the cerebral cortex might be considered as precocious, having been provided with all its mechanisms at the time of weaning. At this age, the brain weight is only a little more than one-half the weight at maturity. Size, volume and weight of the entire brain are all midway in their growth, but there have appeared no striking changes by which we might guess from the gross appearance of the brain anything about the numerical completeness of its cortical elements. Just at this stage, however, cell division in the cerebrum has almost ceased (Allen, '12).

From the data now available, I conclude that, in the albino rat, the cerebral cortex exhibits the complete number of nerve cells at about the 20th day after birth, at which age some of the cells have attained their full size. The area of the cortex in the sagittal and in the frontal sections has shown a continuous increase throughout life and no radical change in rate occurs at this time. But, if the thickness of the cortex be taken into consideration and the volume of the entire cortex be calculated, it becomes clear that the entire volume of the cerebral cortex has stopped the more active increase, which it made earlier, at about the 20th day, and after that the increase becomes slow, and lower in rate than the increase in the volume of the cerebrum. If, further, the cell density in the cortex be considered, it is found that the number of cells as computed for the cerebral cortex (table 7, column E) increases rapidly, especially during the first ten days after birth, but exhibits nearly its complete number at the age of twenty days, after which it shows no significant change.

We may conclude therefore that the cerebral cortex has been completely organized at the age of about twenty days, and that the further development of the cortex does not involve an increase in cell number, but involves mainly the maturing of elements already provided. The education of the cerebral cortex as a whole might properly be said to begin after this age, the preceding period having been largely one of preparation or construction. It is of interest to note that this epoch corresponds to the weaning time of the rat.

According to the study of Donaldson ('08) on the comparison of the albino rat and man, the rat grows thirty times as fast as man. When however the brain of the rat is to be compared with that of man, it must be remembered that at birth the human brain is somewhat more mature and corresponds in organization not with the rat brain at birth but at five days of age (Donaldson MS.). This being the case, the rat cortex at the 20th day of postnatal life probably corresponds with the human cortex at the 15th month (20 less 5). This conclusion has not yet been tested.

V. SUMMARY

1. Employing the sagittal and the frontal sections of 78 albino rats, which were formerly used for the investigation on the thickness of the cerebral cortex (Sugita, '17 a), I made further measurements on the area of the cortex in these sections and counted at a fixed locality the number of nerve cells contained in a unit volume of 0.001 mm.³ in brains from birth to maturity.

2. The observed data were all corrected to the values for the fresh condition of the material, by the use of the correction-coefficients based on the observations. The results were grouped and averaged according to the brain weight groups and the postnatal growth changes systematically analysed.

3. The area of the cortex shown in the sagittal section is found to be proportional to the value $L. F \times T_s$, where $L. F$ is the longitudinal diameter of the cerebrum and T_s is the average thickness of the cerebral cortex in the sagittal section. The actual area (after five days of age) may be calculated by the formula: $L. F \times T_s \times 1.22$ ($L. F$ and T_s , in millimeters), where 1.22 is a constant coefficient which was empirically determined (see table 4, column G).

4. The area of the cortex shown in the frontal section (of one hemicerebrum) is found to be proportional to the value $W. D \times T_f$, where $W. D$ is the frontal diameter of the cerebrum and T_f is the average thickness of the cortex in the frontal section. The actual area (after five days of age) may be calculated by the formula: $W. D \times T_f \times 0.91$ ($W. D$ and T_f , in millimeters), where 0.91 is a constant coefficient which was empirically determined (table 5, column G).

5. The percentage of the total area of that frontal section which is represented by the cortical area is least at birth (34 per cent) and increases as the age advances till it reaches the maximum (50 per cent) at the period of 7 to 20 days (brain weight 0.75 to 1.25 grams). It then decreases slowly and at maturity is less than 44 per cent (table 2). This means that during the first 7 days the cortex is increasing in area more rapidly than the remainder of the section, while during the

following 13 days its rate of increase is similar to that of the remainder. After 20 days the rate of increase for the remainder surpasses that for the cortex.

6. The actual volume of the cortex could not be obtained by the use of the data now available, but the computed volumes of the cerebral cortex at different ages (comparable among themselves), may be found by the use of the formula: $L.F \times W.D \times T$ (all in millimeters), where $L.F$ is the longitudinal diameter of the cerebrum, $W.D$ is the frontal diameter of the cerebrum and T is the average thickness of the cortex. The volume increases most rapidly during the first ten days after birth and the rate of increase in the cortical volume continues to surpass the rate of increase in the entire cerebral volume, during the first twenty days. After twenty days the cortex increases at a somewhat lower rate than the increase of the entire cerebrum in volume (chart 2).

7. The number of cells contained in a unit volume of 0.001 mm.³ of the cortex indicates the cell density of the locality where the count was made. In the lamina pyramidalis the pyramids are most crowded at birth and the number in the unit volume decreases rapidly during the first ten days after birth. After twenty days it decreases slowly but steadily, the number at maturity being about one-sixth the number at birth. As for the lamina ganglionaris, the total cell number in the unit volume (the small and the large pyramids taken together), is at its highest value at birth. It decreases relatively rapidly during the first twenty-five days after birth, then is slightly increased for a time, after which it decreases again slowly and at full maturity it shows about one-fifth the number present at birth. Taking the large ganglion cells alone, we find that the number decreases rapidly during the first eight to ten days, then remains the same up to twenty days, after which it decreases again, showing two-sevenths the initial number at full maturity. The decrease in cell density according to brain growth is due to the enlargement of cell bodies, the development of cell attachments, the separation of cells from each other through myelination, ingrowing fibers and other changes. The average cell density.

represented by the sum of the numbers in the lamina pyramidalis and the lamina ganglionaris, given as N in table 7, decreases rapidly during the first ten days and after that the decrease becomes very slow and steady, showing at maturity a density of about one-fifth of that at birth.

8. The computed value for the number of cells in the entire cerebral cortex may be determined by the formula: $N \times L \cdot F \times W \cdot D \times T$ ($L \cdot F$, $W \cdot D$ and T , all in millimeters), where $L \cdot F$ is the longitudinal diameter of the cerebrum, $W \cdot D$ the frontal diameter of the cerebrum, T the average thickness of the sagittal and frontal cortex and N the average number of the nerve cells in two unit volumes of the cortex, at the particular locality (locality VII) where the counts were made. This computed value for the number of nerve cells in the entire cerebral cortex increases rapidly during the first ten days, at the end of which period it attains nearly 1.9 times the value at birth. During the following ten days, it increases slowly but steadily, and it attains its complete number at the age of twenty days (brain weight 1.17 grams). After this age the number of nerve cells is almost constant. The number of cells at maturity is twice the number at birth.

It is recognized that this conclusion concerning the number of nerve cells in the cortex at various ages is based on enumerations in only two cortical layers at but one locality, and that on this ground its general value might be questioned. When it is recalled however that table 11 in a preceding study on the growth of the cortex in thickness (Sugita, '17 a) shows all the localities measured in the cortex to undergo the same relative increase in thickness between birth and maturity, and always to stand in the same relation to one another, the doubts with regard to the general value of these particular results are largely removed.

9. Considered all together, the data on the development of the cerebral cortex indicate that it has been completely organized in the albino rat at the age of twenty days. The further development after this age represents a maturing of the elements. The completion of the cerebral organization corresponds to the

weaning time of the rat.. If the cerebral organization of the rat brain at five days of age is similar to that of the man at birth, and the growth processes in the rat are thirty times as rapid as in man, then the completion of the cortex which occurs in the rat brain at twenty days should occur in the human brain at about fifteenth month of age.

PART II

ON THE AREA OF THE CORTEX AND ON THE NUMBER OF CELLS
IN A UNIT VOLUME, MEASURED ON THE FRONTAL AND SAGITTAL
SECTIONS OF THE BRAIN OF THE NORWAY RAT (*MUS NOR-
VEGICUS*), AND COMPARED WITH THE CORRESPONDING DATA FOR
THE ALBINO RAT

VI. INTRODUCTION

In the Part I of this paper, I have presented the data on the area of the cerebral cortex measured on the sagittal and the frontal sections of the Albino rat brain and on the number of nerve cells in a unit volume of the cerebral cortex, and, by calculations based on these data, I have come to the conclusion that the entire volume of the cerebral cortex is increasing most rapidly during the first ten days after birth, while from twenty days onwards it increases at a lower rate than the entire cerebral volume. Further, the computed number of nerve cells in the entire cerebral cortex also increases very rapidly during the first ten days after birth and attains nearly its complete number at the age of twenty days.

I now wish to compare these relations in the Albino with those in the Norway rat, in the same manner as I have already done in the matter of the growth of the brain in size (Sugita, '18) and of the thickness of the cortex (Sugita, '18 a).

Employing for the Norway brains the sections on which the cortical thickness was measured earlier and for which the individual body measurements have been already given in table 1 in my fourth paper (Sugita, '18 a), I have measured the area

of the cortex in the sagittal and the frontal section, following methods of measurement just described (part I) in the case of the Albino rat. Correction of the observed values to the values in the fresh condition of the material was also made by the use of the correction-coefficients obtained in the same way as those used for the Albino.

This study was made between March and May, 1917, at the Wistar Institute of Anatomy and Biology.

VII. MEASUREMENTS AND ENUMERATIONS

K. Area of the cortex in the sagittal section (Norway rat)

Table 8 shows the observed and corrected areas of the cerebral cortex in the sagittal section of the Norway brain, also the data for the correction-coefficient for each individual, and the correction-coefficient for each brain weight group. The method of measurement and the positions of the borderlines of the measured area have been already described in part I of this paper, so that the explanations need not be repeated here (fig. 1). Chart 3 (graph s) has been plotted on the basis of table 8.

L. Area of the cortex in the frontal section (Norway rat)

Table 9 gives the observed and corrected areas of the cortex and the total area of the frontal section (one hemicerebrum) of the Norway brain with the data for the correction-coefficient for each individual and the correction-coefficient for each brain weight group. It gives also the percentage of the cortical area to the total area of the section. Chart 3 shows also in graphs (graphs F and f) the corrected data given in table 9.

M. Number of nerve cells (Norway rat)

Table 10 gives the observed and corrected number of nerve cells in a unit volume of 0.001 mm.^3 (0.1 mm.^2 in area and 0.01 mm. in thickness) at a fixed locality (locality VII) of the cortex in the frontal section, for each individual and for each brain weight group. The locality was chosen at a middle part of the cortical band in the frontal section as shown in figure 2, VII,

for the Albino rat. The numbers of cells in the lamina pyramidalis and in the lamina ganglionaris respectively and the number of ganglion cells only in the lamina ganglionaris in five adjoining squares, each 100 micra on each side, were counted and the numbers in the unit volume of 0.001 mm.³ computed (see part I) and recorded in table 10. The relative cell density

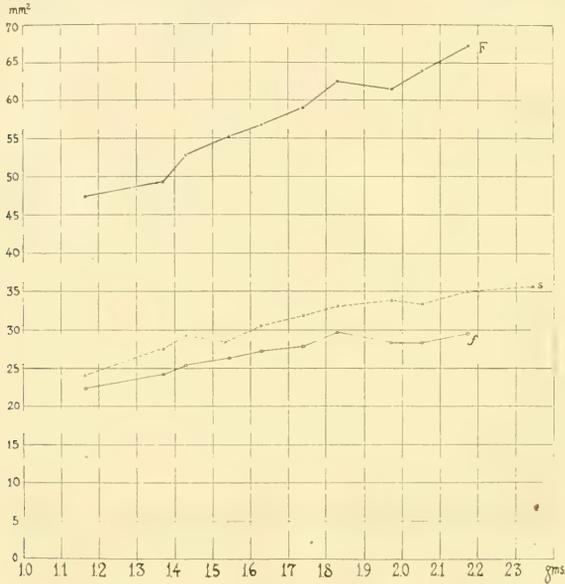


Chart 3 Showing the areas of the cerebral cortex in the sagittal and the frontal sections and the areas of the whole frontal section according to the brain weight. Norway rat. This chart is comparable with chart 1, which gives the corresponding graphs for the albino rat. \times — . . — \times s Cortical area in the sagittal section. \bullet — \bullet f, Cortical area in the frontal section. \bullet — \bullet F, Area of the whole frontal section. All graphs were based on the data in tables 8 and 9.

represented by the sum of the numbers of nerve cells in the lamina pyramidalis and the lamina ganglionaris is tabulated in table 16, column D, and plotted in chart 4 as graph *N'*.

VIII. DISCUSSION AND COMPARISON

The foregoing data, treated in a manner similar to that adopted in the case of the Albino (part I), may now be used for discussion and comparison.

TABLE 8

Showing the observed and corrected values of the area of the cerebral cortex in the sagittal section of the Norway rat brain, accompanied by the data for the correction-coefficient in the individual cases and the correction-coefficient for each brain weight group. *L. F* is the longitudinal diameter of the cerebrum

GROUP	BRAIN WEIGHT	OBSERVED AREA OF CORTEX	CORRECTION-COEFFICIENT		CORRECTED AREA OF CORTEX
			<i>L. F</i> on fresh brain	The same on slide	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²
N XI b	1.155	18.4	11.75	10.40	23.5
a	1.160	17.0	12.10	10.15	24.2
i	1.175	14.2	12.55	9.60	24.3
	1.163	16.5	1.21 ²		24.0
N XII					
N XIII a	1.369	16.7	12.95	10.10	27.5
	1.369	16.7	1.28 ²		27.5
N XIV b	1.407	18.2	13.45	10.50	29.8
g	1.429	16.3	13.05	10.10	27.2
a	1.431	19.1	13.15	10.40	30.6
i	1.431	18.1	13.05	10.25	29.4
e	1.437	15.8	12.80	10.05	25.7
k	1.445	19.2	13.35	10.30	32.3
	1.430	17.8	1.28 ²		29.2
N XV c	1.517	16.4	12.70	10.10	26.0
e	1.557	17.3	13.75	10.30	30.8
	1.537	16.9	1.30 ²		28.4
N XVI a	1.619	17.2	13.50	10.20	30.2
g	1.632	16.8	13.45	9.75	32.0
e	1.636	15.9	13.55	10.00	29.2
	1.629	16.6	1.35 ²		30.5
N XVII e	1.710	18.8	13.70	10.40	32.6
g	1.721	18.7	13.40	10.20	32.3
a	1.738	16.8	13.60	10.40	28.8
c	1.788	20.1	14.20	11.00	33.5
	1.739	18.6	1.31 ²		31.8
N XVIII c	1.825	18.1	14.30	10.70	32.4
a	1.833	22.0	14.20	11.50	33.5
	1.829	20.1	1.28 ²		33.0

TABLE 8—Continued

GROUP	BRAIN WEIGHT	OBSERVED AREA OF CORTEX	CORRECTION-COEFFICIENT		CORRECTED AREA OF CORTEX
			<i>L. F.</i> on fresh brain	The same on slide	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²
N XIX b	1.962	19.9	14.70	11.25	34.1
a	1.981	19.5	14.40	11.00	33.5
	1.972	19.7	1.31 ²		33.8
N XX c	2.015	20.6	14.55	11.30	34.2
a	2.089	20.7	14.95	11.80	33.3
	2.052	20.7	1.28 ²		33.8
N XXI g	2.156	21.1	15.15	11.90	34.2
d	2.187	20.2	15.30	11.50	35.7
	2.172	20.7	1.30 ²		35.0
N XXII					
N XXIII a	2.345	22.4	14.50	11.50	35.7
	2.345	22.4	1.26 ²		35.7

N. The area of the cortex in the sagittal section. Norway rat compared with the Albino

Table 11 shows the relations between the cortical area in the sagittal section and the longitudinal diameter of the cerebrum (*L. F.*). Column B gives the average brain weight by groups, column C the average area of the cortex in the sagittal section, column D the average cortical thickness in the sagittal section (*T*), column F the longitudinal diameter of the cerebrum (*L. F.*), all of these being the corrected values. In column E the value C/D or relative length of the long side, when the cortical area was reduced to a rectangle with the short side equal to the cortical thickness, appears. As shown in column G as E/F , these computed lengths show similar ratios when divided by the actual diameters *L.F.* (column F), that is, 1.16 to 1.24 or on the average 1.20 for Groups N XI–N XXIII, but 1.19 for Groups N XIII–N XX. If necessary, therefore, the cortical area in the sagittal

TABLE 9

Showing the observed and corrected values of the area of the cerebral cortex and of the total section in the frontal section and the percentage of the cortical area in the total frontal section of the Norway rat brain, accompanied by the data for the correction-coefficient in the individual cases and the correction-coefficient for the group. *W. D* is the frontal diameter of the cerebrum,

GROUP	BRAIN WEIGHT	OBSERVED		CORRECTION-COEFFICIENT		CORRECTED		PERCENTAGE OF CORTICAL AREA IN TOTAL SECTION
		Area of cortex	Area of total section	<i>W. D</i> in fresh brain	The same on slide	Area of cortex	Area of total section	
	<i>grams</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>mm.</i>	<i>mm.</i>	<i>mm.</i> ²	<i>mm.</i> ²	<i>per cent</i>
N XI b	1.155	13.8	28.1	13.00	10.00	23.4	47.5	49
a	1.160	12.8	27.9	12.70	9.80	21.5	47.0	46
i	1.175	10.9	23.6	12.50	8.80	22.1	47.7	46
	1.163	12.5	26.5	1.34 ²		22.3	47.4	47
N XII								
N XIII a	1.369	13.7	27.9	13.00	9.80	24.2	49.2	49
	1.369	13.7	27.9	1.33 ²		24.2	49.2	49
N XIV b	1.407	14.0	27.8	13.05	9.50	26.5	52.7	50
g	1.429	14.0	28.5	13.20	9.50	27.1	55.0	49
a	1.431	14.6	30.4	12.85	10.20	23.2	48.4	48
i	1.431	14.9	29.6	13.40	10.30	25.3	50.2	50
e	1.437	12.6	28.7	13.25	9.60	24.1	51.1	44
k	1.445	13.2	28.4	13.30	9.50	26.0	55.8	47
	1.430	13.9	28.9	1.35 ²		25.4	52.7	48
N XV c	1.517	13.0	29.0	13.20	9.60	24.7	55.0	45
e	1.557	12.7	25.7	13.50	9.20	27.4	55.4	49
a	1.564	14.1	29.0	13.50	9.80	26.8	55.0	49
	1.546	13.3	27.9	1.40 ²		26.3	55.1	48
N XVI a	1.619	14.7	31.3	13.80	10.50	25.4	54.2	47
g	1.632	13.8	27.6	13.70	9.50	28.8	57.6	50
e	1.636	13.2	28.2	13.80	9.60	27.3	58.2	47
	1.629	13.9	29.0	1.40 ²		27.2	56.7	48
N XVII e	1.710	13.4	29.5	13.80	9.70	27.2	59.8	44
g	1.721	15.7	32.1	13.60	10.10	28.5	58.4	49
a	1.738	15.2	33.2	14.10	10.60	27.0	58.8	46
c	1.788	15.0	30.7	13.95	10.10	28.6	58.6	49
	1.739	14.8	31.4	1.37 ²		27.8	58.9	47

TABLE 9—Continued

GROUP	BRAIN WEIGHT	OBSERVED		CORRECTION-COEFFICIENT		CORRECTED		PERCENTAGE OF CORTICAL AREA IN TOTAL SECTION
		Area of cortex	Area of total section	W. D in fresh brain	The same on slide	Area of cortex	Area of total section	
	grams	mm. ²	mm. ²	mm.	mm.	mm. ²	mm. ²	per cent
N XVIII c	1.825	15.0	32.3	14.45	10.30	29.6	63.7	47
a	1.833	19.0	39.2	13.95	11.20	29.5	61.0	49
	1.829	17.0	35.8	1.32 ²		29.6	62.4	48
N XIX b	1.962	16.6	36.6	14.60	11.20	28.3	62.3	44
a	1.981	15.3	32.9	13.95	10.30	28.1	60.5	47
	1.972	16.0	34.8	1.33 ²		28.2	61.4	46
N XX c	2.015	14.6	33.1	14.30	10.20	28.7	65.2	44
a	2.089	15.7	35.5	14.50	10.95	27.6	62.3	44
	2.052	15.2	34.3	1.36 ²		28.2	63.8	44
N XXI g	2.156	15.1	35.1	14.75	10.70	28.7	67.0	43
d	2.187	15.3	34.0	15.05	10.70	30.3	67.4	45
	2.172	15.2	34.6	1.39 ²		29.5	67.2	44

section may be calculated by the following formula, in which T_s denotes the average cortical thickness in the sagittal section.

$$L \cdot F \times T_s \times 1.20 \quad (L \cdot F \text{ and } T_s, \text{ in millimeters})$$

The corresponding coefficient was found to be 1.22 in the Albino brains weighing more than 0.5 gram (table 4), but 1.20 for brains weighing more than 1.3 grams (Groups XIII-XX). The coefficients in the two forms may therefore be considered similar, that for the Albino being a trifle the larger.

If comparison is made between the absolute values of the cortical areas in the sagittal sections of the Norway and the Albino brains of like weight, no great difference appears (table 12). In the pair of Groups N XI and XI, the Norway is 10 per cent smaller in the area. This may be explained by the fact that the Norway brain weighing 1.16 grams is in a younger stage of cortical development, as compared with the Albino brain of like weight, the cortex of which is already provided with nearly all its nerve elements. But, in the pairs of Groups N XIII-XIII

TABLE 10

Giving for each individual and for each brain weight group the number of nerve cells in 0.001 mm.³ of the cerebral cortex, in the lamina pyramidalis and in the lamina ganglionaris, and also the number of the ganglion cells only in the same volume of the lamina ganglionaris, counted at locality VII in the frontal section, as shown in fig. 2. Norway rat

GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		NUMBER OF CELLS IN A VOLUME OF CORTEX, 0.001 MM. ³						
		W. D in fresh brain	W. D on slide	Lam. pyramid.		Lam. ganglion.		Ganglion cells in lam. gangl.		
				Ob- served	Cor- rected	Ob- served	Cor- rected	Ob- served	Cor- rected	
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>							
N XI	b	1.155	13.00	10.00	253	115	170	78	44	20
	a	1.160	12.70	9.80	242	111	164	76	41	19
	i	1.175	12.50	8.80	271	95	199	69	48	17
		1.163	(1/1.34) ³		255	107	178	74	44	19
N XII										
N XIII	a	1.369	13.00	9.80	225	96	164	70	45	19
		1.369	(1/1.33) ³		225	96	164	70	45	19
N XIV	b	1.407	13.05	9.50	243	94	174	67	46	18
	g	1.429	13.20	9.50	227	85	176	65	48	18
	a	1.431	12.85	10.20	200	100	142	71	40	20
	i	1.431	13.40	10.30	222	101	175	79	47	21
	e	1.437	13.25	9.60	225	86	165	63	49	19
	k	1.445	13.30	9.50	230	84	178	65	51	19
		1.430	(1/1.35) ³		225	92	168	68	47	19
N XV	e	1.517	13.20	9.60	235	90	169	65	52	20
	e	1.557	13.50	9.20	250	79	176	56	58	18
	a	1.564	13.50	9.80	208	79	166	63	55	21
		1.546	(1/1.40) ³		231	83	170	61	55	20
N XVI	a	1.619	13.80	10.50	203	90	143	63	50	22
	g	1.632	13.70	9.50	235	78	159	56	60	20
	e	1.636	13.80	9.60	214	72	164	55	57	19
		1.629	(1/1.40) ³ ^b		217	80	155	58	56	20
N XVII	e	1.710	13.80	9.70	213	74	155	54	58	20
	g	1.721	13.60	10.10	182	75	147	60	54	22
	a	1.738	14.10	10.60	190	81	131	56	54	23
	c	1.788	13.95	10.10	192	73	142	54	53	20
		1.739	(1/1.37) ³		194	76	144	56	55	21

TABLE 10—Continued

GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT		NUMBER OF CELLS IN A VOLUME OF CORTEX, 0.001 MM. ³					
		W. D in fresh brain	W. D on slide	Lam. pyramid.		Lam. ganglion.		Ganglion cells in lam. gangl.	
				Ob- served	Cor- rected	Ob- served	Cor- rected	Ob- served	Cor- rected
	<i>grams</i>	<i>mm.</i>	<i>mm.</i>						
N XVIII c	1.825	14.45	10.30	200	73	146	53	55	20
	a 1.833	13.95	11.20	147	76	114	59	42	22
	1.829	(1/1.32) ³		174	75	130	56	49	21
N XIX b	1.962	14.60	11.20	164	74	120	54	45	20
	a 1.981	13.95	10.30	176	71	134	54	48	19
	1.972	(1/1.33) ³		170	73	127	54	47	20
N XX c	2.015	14.30	10.20	189	69	140	51	49	18
	a 2.089	14.50	10.95	170	74	116	50	44	19
	2.052	(1/1.36) ³		180	72	128	51	47	19
N XXI g	2.156	14.75	10.70	180	69	118	45	45	17
	d 2.187	15.05	10.70	186	67	120	43	46	17
	2.172	(1/1.39) ³		183	68	119	44	46	17

to N XX-XX the Norway shows a slight excess in the area; on the average 2 per cent.

In spite of the fact that an adult Norway brain has a thicker cortex (by about 6.7 per cent in the sagittal section) than the Albino brain of the same weight, yet between the two a smaller difference in the area of the cortex in the sagittal section is found, because of the shorter longitudinal diameter of the cerebrum (*L. F.*) in the Norway (Sugita, '18).

O. The area of the cortex in the frontal section. Norway rat compared with the Albino

Just as in the case of the sagittal section, table 13 shows relations between the cortical area in the frontal section and the frontal diameter of the cerebrum (*W. D.*). As a result, we see that the relative value C/D or $\frac{\text{Cortical area}}{\text{Cortical thickness}}$ stands almost in a fixed ratio to the frontal diameter *W. D.*, that is, from 0.94

TABLE 11

Showing relations between the cortical area in the sagittal section and the sagittal diameter of the cerebrum (L, F). Column E gives the relative lengths of the long side when the area is reduced to a rectangle with the short side equal to the cortical thickness. These values have almost a fixed ratio to the sagittal diameter of the cerebrum (L, F) in each group, the average being 1.20. For the explanation see the text

A	B	C	D	E	F	G
BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORTICAL AREA IN SAGITTAL SECTION	CORTICAL THICKNESS IN SAGITTAL SECTION	$\frac{C}{D}$	L, F	$\frac{E}{F}$
	grams	mm ²	mm.	mm.	mm.	
N XI	1.163	24.0	1.61	14.9	12.2	1.22
N XII						
N XIII	1.369	27.5	1.73	15.9	13.1	1.21
N XIV	1.430	29.2	1.84	15.9	13.2	1.21
N XV	1.537	28.4	1.82	15.6	13.5	1.16
N XVI	1.629	30.5	1.88	16.2	13.6	1.19
N XVII	1.739	31.8	1.94	16.4	13.9	1.18
N XVIII	1.829	33.0	1.93	17.1	14.3	1.20
N XIX	1.972	33.8	1.97	17.2	14.6	1.18
N XX	2.052	33.8	1.92	17.6	14.7	1.17
N XXI	2.172	35.0	1.99	17.6	15.1	1.17
N XXII						
N XXIII	2.345	35.7	1.86	19.2	15.5	1.24
Average (Groups N XI-N XXIII)						1.20
Average (Groups N XIII-N XX)						1.19

to 1.00 or on the average 0.97 for Groups N XI-N XXI, so that the cortical area in the frontal section may be obtained by the following formula, in which T_F denotes the average cortical thickness in the frontal section:

$$W. D \times T_F \times 0.97 \quad (W, D \text{ and } T_F, \text{ in millimeters})$$

For Groups N XIII-N XX, the coefficient is 0.98 (table 13). The corresponding coefficient in the Albino, Groups XIII-XX, is about 0.93, as shown in table 5. Comparing the absolute values of the cortical area in the frontal sections in two forms of like brain weight group (Groups N XIII-N XX to Groups XIII-XX), we find that in the Norway it is on the average larger by about 10 per cent (table 12).

TABLE 12

Comparison of the Norway rat brain with the Albino rat brain of like weight in the areas of the cortex in the sagittal and the frontal sections and in the area of the total frontal section. The data were taken from tables 1, 2, 8 and 9

BRAIN WEIGHT GROUP	BRAIN WEIGHT		AREA OF CORTEX IN SAGITTAL SECTION		AREA OF CORTEX IN FRONTAL SECTION		AREA OF TOTAL FRONTAL SECTION	
	Albino	Norway	Albino	Norway	Albino	Norway	Albino	Norway
	grams	grams	mm. ²	mm. ²	mm. ²	mm. ²	mm. ²	mm. ²
XI	1.171	1.163	26.6	24.0	21.7	22.3	45.7	47.4
XII	1.253		26.1		23.0		47.2	
XIII	1.335	1.369	27.6	27.5	23.2	24.2	50.2	49.2
XIV	1.445	1.430	28.2	29.2	24.8	25.4	52.3	52.7
XV	1.554	1.542	28.7	28.4	24.3	26.3	54.0	55.1
XVI	1.656	1.629	29.2	30.5	24.3	27.2	54.9	56.7
XVII	1.726	1.739	31.1	31.8	24.6	27.8	56.4	58.9
XVIII	1.839	1.829	32.8	33.0	26.0	29.6	58.9	62.4
XIX	1.924	1.972	32.3	33.8	24.8	28.2	57.0	61.4
XX	2.054	2.052	33.7	33.8	24.9	28.2	63.4	63.8
XXI		2.172		35.0		29.5		67.2
XXII								
XXIII		2.345		35.7				
Average for Groups XIII-XX.....	1.692	1.695	30.5	31.0	24.6	27.1	55.9	57.5

The total area of the frontal section is also slightly in favor of the Norway (table 12).

P. Percentage of the area of the cortex to the total area of the frontal section (one hemisphere). Norway rat compared with the Albino

As for the percentage of the cortical area to the total area of the section, a comparison between the two forms is interesting. In the Albino this percentage value increases from birth to a brain weighing 0.7 to 1.2 grams when it attains the value of about 48 per cent (table 2), but in the Norway the highest percentage is attained in brains weighing 1.1 to 1.8 grams. This indicates that the cortical organization is more retarded in the Norway, if the brain weight be taken as the basis of comparison. In a fully mature Norway brain (from Group N XX onwards,

TABLE 13

Showing relations between the cortical area in the frontal section and the frontal diameter of the cerebrum (*W. D.*). Column *E* gives relative lengths of the long side when the area is reduced to a rectangle with the short side equal to the cortical thickness. These values have almost a fixed ratio to the frontal diameter of the cerebrum (*W. D.*) in each group, the average being 0.97. For the detailed explanation see also the text. Norway rat

A.	B.	C.	D.	E.	F.	G.
BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORTICAL AREA IN FRONTAL SECTION	CORTICAL THICKNESS IN FRONTAL SECTION	$\frac{C}{D}$	<i>W. D.</i>	$\frac{E}{F}$
	<i>grams</i>	<i>mm.²</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	
N XI	1.163	22.3	1.88	11.9	12.7	0.94
N XII						
N XIII	1.369	24.2	1.96	12.3	13.0	0.95
N XIV	1.430	25.4	1.95	13.0	13.2	0.98
N XV	1.546	26.3	2.04	12.9	13.4	0.96
N XVI	1.629	27.2	2.08	13.1	13.7	0.96
N XVII	1.739	27.8	2.07	13.4	13.9	0.96
N XVIII	1.829	29.6	2.08	14.2	14.2	1.00
N XIX	1.972	28.2	2.00	14.1	14.3	0.99
N XX	2.052	28.2	1.96	14.4	14.4	1.00
N XXI	2.172	29.5	2.08	14.2	14.9	0.95
Average (Groups N XI-N XXI)						0.97
Average (Groups N XIII-N XX)						0.98

table 9) this percentage amounts to 44 per cent, which is equal to that seen in the mature Albino brain (Groups XVI to XIX, table 2), if we disregard one case of advanced age (Group XX).

Q. Number of cells in a unit volume of the cortex. Norway rat compared with the Albino

Reviewing table 10 which gives separately the numbers of nerve cells in the unit volume of 0.001 mm.³ of the lamina pyramidalis and the lamina ganglionaris at a fixed locality in the frontal section of the cerebrum and counted by the same method used for the Albino rat and comparing these numbers with those in table 3 in part I, it is easily seen that, if the like brain weight groups of the two forms are paired, the number of cells in the unit volume of both layers is slightly lower in the Norway rat.

These relations are shown in table 14. As for the number of the ganglion cells only in the lamina ganglionaris, it is always lower by 2 to 6 in the Norway and the highest figure (21) in the Norway is seen in Groups N XVII and N XVIII, while in the Albino the highest figure (25) is attained in Groups XIII and XIV and again in Group XVII. In the Albino a temporary increase of cell number in the lamina ganglionaris was seen in Groups XIII and XIV, and in my Norway sections a similar phenomenon is indicated in Groups N XVII and N XVIII. Generally speaking, therefore, the cell density in the cerebral cortex, as far as represented by my observations, is slightly

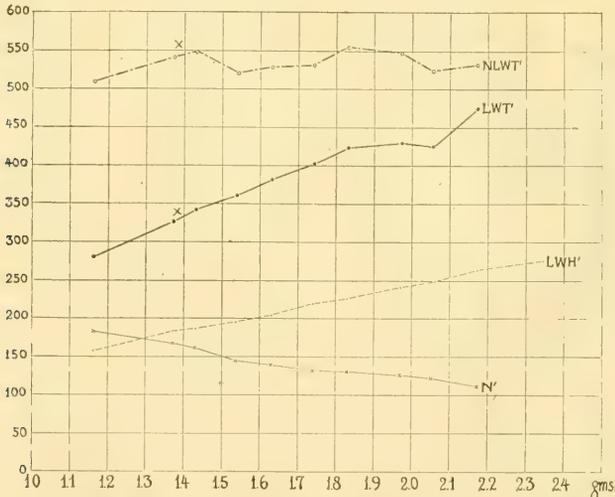


Chart 4 Showing the computed values for the cortical volume, the volume of the cerebrum, the cell density in two unit volumes and the computed number of nerve cells in the entire cortex of the Norway rat, according to the brain weight. This chart is equivalent to, but not directly comparable with chart 2, which gives the similar data in the Albino in ratios of the values at birth. ●—● LWT', The computed volume of the cerebral cortex, based on table 15. - - - - LWH', The relative volume of the entire cerebrum, based on the data presented in a former paper (Sugita, '18) and given also in table 15. ×—× N', The cell density in two unit volumes of the cortex. Graph based on the data given as N in column D, table 16. ○—○ NLWT', The computed number of nerve cells in the entire cortex, based on the figures given in column E, table 16. Mark × shows the phase in growth corresponding to that indicated by the same mark in chart 2, which shows the end of the second developmental phase in the Albino.

TABLE 14.

Comparison of the Norway rat brain with the albino rat brain of like weight for the numbers of nerve cells in the lamina pyramidalis and in the lamina ganglionaris and the number of ganglion cells only in the lamina ganglionaris, in a unit volume of 0.001 mm.³, and also for N, which is the sum of the numbers in the lamina pyramidalis and in the lamina ganglionaris. The data were taken from tables 3 and 10

BRAIN WEIGHT GROUP	BRAIN WEIGHT		NUMBER OF CELLS IN A UNIT VOLUME OF CORTEX, 0.001 MM. ³						N, THE SUM OF NUMBERS OF CELLS IN LAM. PYR. AND IN LAM. GANG.	
			Lam. pyram.		Lam. gangl.		Ganglion cells in lam. gangl.		Albino	Norway
	Albino	Norway	Albino	Norway	Albino	Norway	Albino	Norway		
	<i>grams</i>	<i>grams</i>								
XI	1.171	1.163	113	107	73	74	23	19	186	181
XII	1.253		103		68		23		171	
XIII	1.335	1.369	99	96	77	70	25	19	176	166
XIV	1.445	1.430	94	92	71	68	25	19	165	160
XV	1.554	1.546	87	83	62	61	23	20	149	144
XVI	1.656	1.629	84	80	60	58	24	20	144	138
XVII	1.726	1.739	83	76	63	56	25	21	146	132
XVIII	1.839	1.829	79	75	59	56	23	21	138	131
XIX	1.924	1.972	81	73	51	54	24	20	132	127
XX	2.054	2.052	80	72	51	51	20	19	131	123
XXI		2.172		68		44		17		112
Average for Groups XIII-XX.....	1.692	1.695	86	81	62	60	24	20	148	140

lower in the Norway rat, if the brain weight be selected as a standard of comparison.

R. The computed volume of the entire cerebral cortex. Norway rat compared with the Albino

The computed volume of the cerebral cortex for the Norway may also be obtained and expressed in values comparable among themselves, by the use of the formula: $L. F \times W. D \times T$ (where T denotes the mean thickness of the cortices in the sagittal and the frontal sections), as already explained in detail in part I (see p. 82). But for a comparison between the cortical volumes of the Norway and of the Albino brains, the direct comparison

of the values obtained by the above formulas is not allowable, since, comparing the areas in the Albino among themselves, the fixed coefficients⁵ 1.21 and 0.93 were eliminated from the formula, as already stated, and similarly in the Norway the corresponding coefficients⁵ 1.19 and 0.98 were also eliminated from the formula. In order to compare the areas in these two forms, the coefficients must be taken into consideration. As the product 1.19×0.98 is higher by 3.6 per cent than the product 1.21×0.93 , the value of $L. F \times W. D \times T$ for the Norway should be raised by 3.6 per cent to be directly comparable with the value of $L. F \times W. D \times T$ for the Albino. The ratio $\frac{1.19 \times 0.98}{1.21 \times 0.93}$ ($= 1.036$) being represented by C , the comparable value of the cortical volume for the Norway may be obtained by the corrected formula as follows:

$$L. F \times W. D \times T \times C \quad (C = 1.036)$$

Table 15 gives the computed cortical volume of the Norway brain, obtained according to the above corrected formula, and this is shown graphically in chart 4 (graph LWT').

As the available data in the Norway do not extend to the earlier ages, I could not determine the early increase in the cortical volume of the Norway, but our data show that the cortical volume is increasing somewhat more rapidly during the period when the brain weight is increasing from 1.16 to 1.54 grams and after that it increases more slowly but steadily as the entire cerebral volume increases, as shown in table 15 and in chart 4 (graph LWH'). In the Albino, as has been shown, the cortical volume increases relatively rapidly until the brain attains 1.17 grams in weight, a phase which probably corresponds to the phase in the Norway of 1.43 grams in brain weight.

To compare the cortical volume in the Norway rat with that of the Albino, I have paired, in table 15, the Norway data ($L. F \times W. D \times T \times C$) directly with the corresponding Albino

⁵ For a proper comparison, the coefficients here used are those for the same brain weight groups compared in both forms, being respectively the averages for Groups XIII to XX and for Groups N XIII to N XX, taken from tables 4, 5, 11 and 13.

TABLE 15

Showing the computed volume for the entire cerebral cortex of the Norway rat brain, calculated by the formula: $L.F \times W. D \times T \times C$ for each brain weight group, C being a fixed coefficient used to convert the computed volume of the Norway cortex so as to make it comparable with that of the Albino ($C = 1.036$). The computed volume of the cerebrum is quoted from my previous presentation (Sugita, '18). These values are paired with the corresponding values for the cortical volume of the Albino and the ratios between them calculated

NORWAY RATS							ALBINO RATS	
A	B	C	D	E	F	G	H	I
Brain weight group	Brain weight	Computed volume of cerebrum $L.G \times W.D \times Ht.$	$L. F$ in fresh brain	$W. D$ in fresh brain	T , ¹ average cortical thickness	$L. F \times W. D \times T \times C$ Computed volume of cortex	Corresponding computed volume of the Albino cortex, of the same group number	Ratio of cortical volume of the Norway to that of the Albino
	grams	mm. ³	mm.	mm.	mm.	mm. ³	mm. ³	
N XI	1.163	156	12.2	12.7	1.75	281.00	288.93	0.973
N XII							304.51	
N XIII	1.369	182	13.1	13.0	1.85	326.51	314.03	1.040
N XIV	1.430	185	13.2	13.2	1.90	343.09	329.71	1.040
N XV	1.537	194	13.5	13.4	1.93	361.83	345.86	1.046
N XVI	1.629	203	13.6	13.7	1.98	382.32	359.30	1.064
N XVII	1.739	218	13.9	13.9	2.01	402.47	365.08	1.102
N XVIII	1.829	226	14.3	14.2	2.01	423.00	397.96	1.063
N XIX	1.972	241	14.6	14.3	1.99	430.57	390.39	1.103
N XX	2.052	249	14.7	14.4	1.94	425.59	393.15	1.083
N XXI	2.172	264	15.1	14.9	2.04	475.66		
Average (Groups N XIII-N XX)						386.92	361.94	1.069

¹ T, here entered, is the mean value of T_s and T_F , previously given in tables 11 and 13 and is not the general average thickness of the cortex of the sagittal, frontal and horizontal sections formerly presented in my fourth paper in this series (Sugita, '18 a).

data ($L. F \times W. D \times T$) according to the brain weight groups, quoted from part I. In table 15 the ratios show the volume of the cortex in the Norway to be greater (1.040 to 1.103) in all the comparisons for brain weights above Groups XIII (brain weight 1.37 grams). The average value is about 1.07. In Group XI (brain weight 1.17 grams), the ratio for the Norway is less than 1. At this weight the Norway brain is regarded as less mature than

the corresponding Albino brain. The ratio tends to increase as the brain weight increases, showing roughly the relative growth in the Norway cortex.

Since, as has been shown (Sugita, '18 a), the cortex in the mature Norway is about 8 per cent thicker (average of the sagittal and frontal sections) than in the Albino, and since this value enters as T into the formula under discussion, this would tend to give a greater volume of the cortex in the Norway than in the Albino. The mean value found for the ratio of the cortical volume—1.07—is about that to be expected, in view of the relatively smaller value of $L. F$ in the Norway.

S. Computed number of nerve cells in the entire cortex. Norway rat compared with the Albino

As described in part I, the computed number of nerve cells in the entire cerebral cortex may be obtained by the following formula:⁶

$N \times L. F \times W. D \times T \times C$ ($L. F, W. D$ and T , in millimeters) where $L. F \times W. D \times T \times C$ is the computed volume of the Norway cortex made comparable directly with the corresponding volume for the Albino, as explained in the foregoing chapter, and N is the cell density, represented by the sum of the numbers of cells in a unit volume in the lamina pyramidalis and in a unit volume in the lamina ganglionaris (two unit volumes altogether), given separately in table 10 and combined in table 16.

Table 16 gives the computed value of the cell number in the entire cerebral cortex for each brain weight group of the Norway rats (column E), calculated by the use of the above formula, and also in the corresponding case of the Albino (column G).

On examining table 16, column E, we find the computed number of nerve cells in the cortex to be nearly completed in a brain weighing 1.37 grams (Group N XIII), while in the Albino this condition was reached in a brain weighing 1.17 grams (Group XI). The value of the completed cell number is indicated in

⁶ The formula for the total number of nerve cells in the Norway cortex is like that for the Albino cortex with the addition of the factor C (footnote 4).

TABLE 16

Giving the computed number of nerve cells in the entire cerebral cortex of the Norway rat brain, obtained on the basis of the measurements given in this series of studies. These values are made to be comparable with the corresponding values of the computed number of nerve cells in the cortex of the albino rat brains of like brain weight groups

NORWAY RATS						ALBINO RATS
A	B	C	D	E	F	G
Brain weight group	Brain weight	Computed volume of cortex $L \cdot F \times W \cdot D$ $\times T \times C$	Sum of numbers of cells in lam. pyr. and lam. gang. in two unit volumes, N	Computed number of cells in entire cortex, ¹ $N \times L \cdot F$ $\times W \cdot D \times T$ $\times C \times \frac{1}{100}$	Ratio of number of cells in the Norway to that in the Albino	Corresponding computed number of cells in the Albino, of the same group number
	grams	mm. ³				
N XI	1.163	281.00	181	508.6	0.946	537.4
N XII						520.7
N XIII	1.369	326.51	166	542.0	0.981	552.7
N XIV	1.430	343.09	160	548.9	1.009	544.0
N XV	1.537	361.83	144	521.0	1.011	515.3
N XVI	1.629	382.32	138	527.6	1.020	517.4
N XVII	1.739	402.47	132	531.3	0.997	533.0
N XVIII	1.829	423.00	131	554.1	1.009	549.2
N XIX	1.972	430.57	127	546.8	1.061	515.3
N XX	2.052	425.59	123	523.5	1.016	515.0
N XXI	2.172	475.66	112	532.7		
Average (Groups N XIII-N XX)				536.9	1.013	530.2

¹ As remarked in a note to table 7, the number given in this column corresponds to 1/100 of $N \times L \cdot F \times W \cdot D \times T$, or 1/50,000 of the actual number of cells contained in the computed volume of the cortex.

the Norway by about 537 (the average of Groups N XIII-N XX) or about 1 per cent more than that of the Albino, which has been indicated by about 530 (the average of Groups XIII-XX, see table 7), so that the number of nerve cells in the entire cortex of the mature Norway and of the Albino rats may be regarded as practically the same, as suggested by Donaldson (Donaldson and Hatai, '11).

IX. CONCLUSIONS

Putting together the foregoing observations, we come to the conclusion that in the case of the Norway rat brain the entire volume of the cerebral cortex is actively increasing up to a brain weight of something more than 1.43 grams (Group N XIV) and that the number of nerve cells in the cortex is completed in a brain weighing something less than 1.43 grams (Group N XIV) (chart 4). After this, the increase in cortical volume keeps pace with the enlargement of the entire cerebrum, showing that the cortical mass and the remainder of the cerebrum are growing at the same rate. So, the end of the short period during which the brain has attained 1.37 to 1.54 grams in weight (Groups N XIII to N XV) marks an epoch in the development of the cerebral cortex of the Norway rat, at which the structural completion of the cortex has been acquired and the full preparation for the functional education has been established. This period corresponds approximately to the age of twenty days.

In the Albino, the same degree of development is reached when the brain attains a weight of 1.17 grams or is twenty days old. As I suggested in an earlier paper (Sugita, '18 a), a Norway brain corresponds in the development of the cortex to an Albino brain weighing about 18 per cent less. This assumption has held true in the present examinations of the cortical volume and cell number, because an Albino brain weighing 1.17 grams just corresponds to a Norway brain weighing 1.43 grams.

The number of cells in the Norway cortex has been shown to be but slightly (1 per cent) different from that in the Albino rat cortex and may be regarded as the same in both forms. This fact justifies at the same time a conclusion reached by Donaldson in his former comparison of the Norway with the Albino rats, that the greater weight of the brain in the Norway rat, compared with the Albino of the same body weight or of the same age, is probably due to an enlargement of the constituent neurons rather than to an increase in their number (Donaldson and Hatai, '11). The results of my study regarding the cell size in the cortex in these two forms will be discussed in a forthcoming paper and will support the statement just made.

X. SUMMARY

1. On the sagittal and the frontal sections from 28 Norway rats, whose brain weights fall between 1.1 and 2.4 grams and which were formerly used for the investigation on the cortical thickness (Sugita, '18 a), the area of the cortex was measured and the number of nerve cells, in a unit volume of 0.001 mm.³ at a fixed locality of the cortex, was counted. These values were all later corrected to the corresponding values in the fresh condition of the material, using the correction-coefficients devised for this purpose. These results have been grouped and averaged according to the brain weight and then compared with the corresponding data in the Albino, which were presented in part I of this paper.

2. The actual area of the cortex in the sagittal section may be obtained by the formula: $L. F \times T_s \times 1.20$ ($L. F$ and T_s , in millimeters), where $L. F$ is the longitudinal diameter of the cerebrum, T_s is the thickness of the cortex in the sagittal section and 1.20 is a constant coefficient which was empirically determined (table 11, column G).

3. The actual area of the cortex in the frontal section may be obtained, though less precisely, by the formula: $W. D \times T_f \times 0.97$ ($W. D$ and T_f in millimeters), where $W. D$ is the frontal diameter of the cerebrum, T_f is the thickness of the cortex in the frontal section and 0.97 is a constant coefficient which was determined empirically (table 12, column G).

4. The percentage of the cortical area to the area of the whole frontal section is highest (48 per cent) in brains weighing 1.1 to 1.8 grams. In a fully mature brain it has fallen to 44 per cent.

5. The computed value for the volume of the entire cortex, indicated by the formula: $L. F \times W. D \times T \times C$ ($L. F$, $W. D$ and T , in millimeters), where $L. F$ is the longitudinal diameter, $W. D$ is the frontal diameter of the cerebrum, T is the average thickness of the cortex in the two sections and C a theoretically determined coefficient necessary to make the values directly comparable with the corresponding values for the albino rat, shows that the cortex is increasing relatively rapidly in the

Norway brains weighing less than 1.43 grams. After that stage its increase nearly keeps pace with the increase in the volume of the entire cerebrum.

6. In Norway brains weighing from 1.1 to 2.2 grams, the cell density or the number of nerve cells in a unit volume of the lamina pyramidalis and the lamina ganglionaris, in a fixed locality of the cortex, decreases slowly but steadily as the brain weight advances. It has proved slightly less than that in the Albino (compare table 16, column D, with table 7, column C). In the lamina ganglionaris the number of ganglion cells only in a unit volume is at its highest in the brains weighing 1.7-1.8 grams (table 14).

7. The value for the computed number of nerve cells in the entire Norway cortex, indicated by the formula: $N \times L \cdot F \times W \cdot D \times T \times C$ (L , F , W , D and T , in millimeters), where N is the number of cells in two unit volumes and $L \cdot F \times W \cdot D \times T \times C$ is the computed volume of the cortex, shows that it is almost completed in a brain weighing something more than .37 grams.

8. Comparisons in respect of the above characters between the Norway and the Albino brains of the like weight show that, in the cortical areas in the sagittal and the frontal sections and in the volume of the entire cortex, the Norway rat surpasses the albino rat, but the number of cells as computed for the entire cortex may be regarded as the same in both forms. We conclude therefore that the difference in absolute brain weight between the two forms is not correlated with a difference in the number of nerve cells in the cerebral cortex. In a Norway brain weighing 1.4 to 1.5 grams, which corresponds to an Albino brain weighing 1.17 grams and is about twenty days in age, the elemental organization of the cerebral cortex in the Norway rat is considered to be almost completed.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

VI. PART I. ON THE INCREASE IN SIZE AND ON THE DEVELOPMENTAL CHANGES OF SOME NERVE CELLS IN THE CEREBRAL CORTEX OF THE ALBINO RAT DURING THE GROWTH OF THE BRAIN

VI. PART II. ON THE INCREASE IN SIZE OF SOME NERVE CELLS IN THE CEREBRAL CORTEX OF THE NORWAY RAT (*MUS NORVEGICUS*), COMPARED WITH THE CORRESPONDING CHANGES IN THE ALBINO RAT

NAOKI SUGITA

From the Wistar Institute of Anatomy and Biology

WITH SIX FIGURES AND FOUR CHARTS

PART I

I. PRELIMINARY STUDIES

As a preliminary to the study of cell size, I made a comparison of effects of several fixatives and imbedding media on the size and shape of the cortical nerve cells in a small number of albino rats. These studies were made after considering the results of King ('10) and Allen ('16), both of whom were endeavoring to find methods which caused the minimum alteration in the nerve cells.

For this comparison, ten kinds of preparations were made from albino rat brains of like age: thus, as the fixative, (1) Bouin's fluid, (2) 4 per cent formaldehyde, (3) 95 per cent alcohol, (4) Müller's or Orth's fluid, and (5) Ohlmacher's fluid were successively tried, and each sample was imbedded in (A) parafine and in (B) celloidin.

Formaldehyde fixation and paraffine imbedding (2A) causes considerable shrinkage of nuclei and cell bodies, especially in young brains, but material so prepared takes any aniline dye excellently well (fig. 1, *b*). Fixation in Müller's or Orth's fluid and paraffine imbedding (4A) causes also shrinkage and deformation of the cell bodies and nuclei, the contours of which become zigzag. Formaldehyde fixation and celloidin imbedding (2B) give good figures of cell bodies, which stain excellently with any aniline dye. The shrinkage of cells and nuclei which was seen after paraffine imbedding of the material similarly fixed (2A) is no longer observed. But the size of cell bodies and nuclei seems to have suffered some diminution. Müller or Orth fixation and celloidin imbedding (4B) causes considerable deformation of the contours of the cells and nuclei, which is probably an affect of the potassium bichromate.

In material fixed in 95 per cent alcohol, the brain is subject to much shrinkage, and consequently the cell size and cortical thickness diminish also, though, after paraffine imbedding (3A), the contours of cells and nuclei are preserved pretty well (fig. 1, *a*). Alcohol fixation only or alcohol fixation and celloidin imbedding (3B) is ideal for the study of the cytoplasmic structure as originally emphasized by Nissl. The cell bodies stain very well with aniline dyes, but the section shrinks so that the individual cells must have been more or less reduced in size. Fixation in Ohlmacher's fluid and paraffine imbedding (5A) or celloidin imbedding (5B) proved to be most excellent for cell study, as pointed out by King ('10), but it is followed after fixation by a considerable reduction in the volume of the total brain and some change in shape.

After a number of tests, I decided to use as the fixative Bouin's fluid, which is composed of:

Picric acid, saturated aqueous solution.....	cc.
40 per cent formaldehyde (formalin).....	75
Glacial acetic acid.....	25
	5

Fixed in this fluid the total weight or volume of the brain suffers no significant change after complete fixation and preserves its original shape quite well, though a slight shrinkage occurs,

no matter what the age of the brain is. It takes only a couple of hours to complete fixation in this fluid, if the fluid is kept in the oven at 37°C., but, as a matter of convenience, I left each brain in 20 cc. of this fluid for 24 hours at the room temperature. By this treatment the form of the cells was well preserved, even after imbedding in paraffine (1A) (figs. 3 and 4).

Comparing this with the material which was fixed in the same fluid but imbedded in celloidin (1B), the contours of cell bodies were, in the former, somewhat indistinct and the size of the nuclei somewhat larger (fig. 1, *c*). But after paraffine imbedding the nuclei have yet good contours which are not zigzag and the

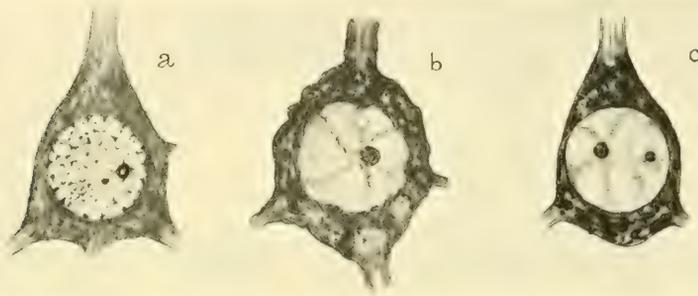


Fig. 1 Showing pyramids from the lamina pyramidalis at a fixed locality (locality VII) of the cerebral cortex of Albino brains weighing 1.3 to 1.5 grams. Magnification of about 950 diameters, measured directly on the slide. *a* = from a brain imbedded in paraffine after fixation in 95 per cent alcohol. *b* = from a brain imbedded in paraffine after fixation in 4 per cent formaldehyde. *c* = from a brain imbedded in celloidin after fixation in Bouin's fluid.

so-called Nissl bodies are also well stained. Since paraffine was used exclusively for the imbedding medium, Bouin's fluid proved to be the best fixative for the albino rat brain, when it is required to follow the growth changes of the cortex by the measurements of the cells of the cortex.

Figure 1 shows a comparison of the effects of several fixatives on the shape and contours of the cell bodies and the nuclei when applied to albino rat brains of like age. The examples are all from Albino brains weighing 1.3 to 1.5 grams and represent pyramids in the lamina pyramidalis taken near the locality VII in frontal sections, being comparable with VII in figure 2, *a* and *b*.

II. MATERIAL

For the present study on cell size in the cerebral cortex, the frontal and horizontal sections of the Albino brains which were used earlier for studies on the cortical thickness, cortical areas, and cell density (Sugita, '17 a, '18 b) were alone taken. No locality in the sagittal sections was examined. These sections were from 128 individuals, sexes combined. The data for these 128 rats appear in tables 1 and 2 in a previous paper (Sugita, '17 a) and it is not thought necessary to repeat the tables here. This study was begun in January, 1916, and carried on with interruptions till February, 1917, at The Wistar Institute of Anatomy and Biology.

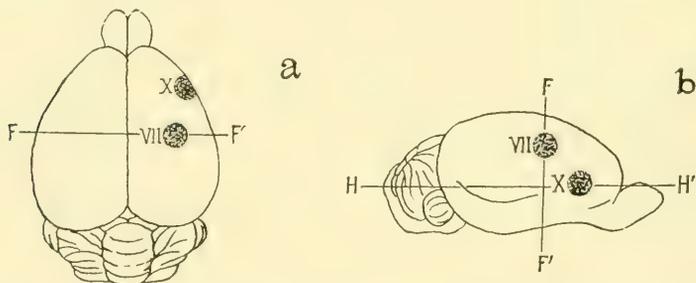


Fig. 2 Showing on the brain surface the localities at which the sizes of the pyramids and the ganglion cells were measured. FF' indicates the level from which the frontal section was taken and HH' indicates the level from which the horizontal section was taken. VII = locality VII; X = locality X. a = the dorsal view of an Albino brain weighing 1.5 grams. Enlarged 1.8 diameters. b = the lateral view of the same.

III. TECHNIQUE

The nerve cells have been measured at fixed localities in the sections; that is, in the frontal sections at locality VII (fig. 4, Sugita, '17 a) and in the horizontal sections at locality X (fig. 6, Sugita, '17 a). For convenience, these localities are here shown on two corresponding figures (fig. 2, a and b). From the lamina pyramidalis and the lamina ganglionaris at each of these localities, ten of the largest cells were selected and measured. The cells in the other layers were not systematically investigated,

but in several stages of growth, a few were measured, in order to be able to make some comparisons.

The study of the cells under the microscope was made with a Zeiss Comp. Ocular no. 6 with a micrometer, combined with the objective 2 mm., oil immersion. Each division in the micrometer scale was equal to two micra. The measurement of the cell size was executed in the following way: the transverse diameter of the cell body (the greatest width of the cell body) was measured on a line, parallel to the base line, which crossed about the middle of the nucleus. For the longitudinal diameter the measurement was made vertical to the transverse diameter from the base of the cell body to the beginning of the apical dendrite. This last limit was assumed to be at the point where the Nissl bodies are no more to be seen and the side lines of the apical dendrite begin to run nearly parallel to each other. Sometimes this upper limit was very hard to determine, especially in fully grown cells, because of the irregularity of the cell outline and the relatively slow transition from cell body to the apical dendrite. In these latter cases, the upper limit was somewhat arbitrarily fixed, but this procedure has apparently been without much effect on the results.

The measurements of the ten largest cells of the same kind from within the fixed locality in the same individual were then averaged for each diameter and recorded on cards without any correction. The average measurements from the frontal section and the horizontal section are denoted in the records by the letters F and H, respectively. The individual averages for each series of ten cells in each section have all been tabulated and the respective averages for the brain-weight groups found. The values for the individuals in each brain-weight group are so well correlated with their respective individual brain weights that it has seemed necessary to publish only the averages for the successive brain-weight groups. Table 1 contains the cell measurements on the frontal section averaged for each brain-weight group. The results of the measurements on the horizontal sections, which were taken from the other individuals,

are given in table 2, and here also only the averages for the brain-weight groups are given.¹

The maximal diameters of the nuclei of the same cells were measured in the two directions in which the cell measurements were made. The nuclei have sharp contours, so that it was always easy to find the border points of the diameters. The results of the nuclear measurements have been treated in the same manner as the cell-body measurements and the average values are recorded also in the same way—without any correction—in tables 1 and 2.

In table 3 the final average diameters of the cell bodies and their nuclei for each brain-weight group are given for each section. These final average values were obtained by multiplying the values of the transverse and longitudinal diameters together and by extracting the square root of the product, thus assuming the cell- and nucleus-figures to form a plane instead of a solid body. By this treatment, the results for the nucleus do not differ much from those which would be obtained by using a planimeter, because the nucleus has a nearly spherical or ellipsoidal form. The cell body, on the contrary, appears as a somewhat irregular cone or pyramid in the outline. Nevertheless, its relative volume may be denoted by a^2b , or its area by ab , in which a is the transverse and b the longitudinal diameter. Accordingly, the relative values of the average diameter may be represented by \sqrt{ab} , but these values should not be compared directly with the average diameter of the nucleus, because the forms of the cell body and of the nucleus are quite different. The size of cell bodies and their nuclei was assumed to have shrunk in the same proportion as the total brain volume during the procedure of fixation, imbedding and mounting and the values observed were therefore corrected for the fresh condition of the material by the use of the correction-coefficient which was formerly used for the correction of the cortical thickness or other measurements made on the same section. The cell bodies and nuclei were assumed to have shrunk similarly in transverse and

¹ The detailed data for tables 1 and 2 and also for tables 6 and 7 have all been tabulated and are on file at The Wistar Institute of Anatomy and Biology.

TABLE 1

Giving the average uncorrected diameters of the nerve cells and their nuclei in the lamina pyramidalis and the lamina ganglionaris measured at the fixed locality (locality VII) on the frontal sections of the albino rat brain. The data are given for each brain weight group only

BRAIN WEIGHT GROUP	NO. OF CASES	BRAIN WEIGHT	LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
			Cell body diameter		Nucleus diameter		Cell body diameter		Nucleus diameter	
			Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	Transv.	Longit.
		<i>grams</i>	μ	μ	μ	μ	μ	μ	μ	μ
I	3	0.161	7.5	10.7	6.6	7.6	10.1	14.1	8.7	10.5
II (B)	5	0.251	10.3	13.0	9.2	10.3	14.4	18.2	12.0	13.6
III	5	0.358	11.9	15.5	10.7	12.4	16.1	20.6	13.5	15.0
IV	6	0.432	14.1	17.3	12.4	13.5	18.4	23.3	15.5	17.1
V	9	0.542	14.4	17.3	12.4	13.4	19.5	23.4	16.2	17.4
VI	3	0.639	15.0	17.7	12.9	13.9	19.4	23.7	16.2	17.2
VII	2	0.750	15.2	18.7	13.5	14.2	20.2	25.7	16.1	16.9
VIII	6	0.841	16.5	19.4	14.0	14.8	20.8	26.7	17.4	18.3
IX	3	0.964	16.9	20.2	15.7	16.4	21.4	28.6	19.1	19.6
X	3	1.040	16.6	20.1	14.8	15.3	21.0	27.7	17.8	18.6
XI	4	1.171	16.8	20.6	14.7	16.1	21.5	28.6	18.2	19.4
XII	2	1.253	16.2	20.7	14.6	15.4	21.1 ¹	27.7	18.0	18.6
XIII	5	1.335	16.0	20.7	14.6	15.2	20.4 ¹	26.8	17.8	18.4
XIV	3	1.445	15.4	20.4	14.3	15.1	20.1 ¹	27.0	17.5	18.3
XV	5	1.554	15.5	20.0	14.2	14.8	21.2	27.4	18.0	18.6
XVI	4	1.656	15.0	19.6	13.8	14.7	21.7	29.1	18.1	19.4
XVII	4	1.726	15.7	19.9	14.3	15.2	22.0	28.0	18.7	19.5
XVIII	3	1.839	14.7	19.4	13.6	14.5	22.3	28.5	18.4	19.0
XIX	1	1.924	15.6	19.9	14.0	14.3	22.7	29.3	18.8	19.4
XX	2	2.054	15.2	19.5	13.5	14.3	23.2	31.4	19.3	20.2

¹ The uncorrected measurements of the cell body and the nucleus of the ganglion cells in these groups (Groups XII–XIV) show a slight decrease, while in the corrected measurements (see table 3) no diminution in cell size has occurred in this stage. This slight decrease in size on the slide is probably due to some chemical changes which takes place in cytoplasm during this phase of development. The same phenomenon is to be seen also in the ganglion cells measured on the horizontal section, given in table 2, in Groups XII–XVI.

longitudinal diameters and in the same proportion as the width of the brain has shrunken. As in the other measurements (Sugita, '17 a, '18 a, '18 b), the correction-coefficient was based on $\frac{W. D. \text{ in fresh brain}}{W. D. \text{ on the slide}}$ for the frontal section and on

TABLE 2

Giving the average uncorrected diameters of the nerve cells and their nuclei in the lamina pyramidalis and the lamina ganglionaris measured at the fixed locality (locality X) on the horizontal sections of the albino rat brain. The data are given for each brain weight group only

BRAIN WEIGHT GROUP	NO. OF CASES	BRAIN WEIGHT	LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
			Cell body diameter		Nucleus diameter		Cell body diameter		Nucleus diameter	
			Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	Transv.	Longit.
			<i>grams</i>	μ	μ	μ	μ	μ	μ	μ
II (B)	2	0.292	9.9	12.7	8.5	9.8	15.4	19.3	13.0	14.2
III	3	0.317	10.6	13.8	9.4	10.9	14.6	19.0	12.7	14.4
IV	3	0.419	13.0	14.0	10.2	12.9	16.0	21.4	14.2	16.3
V	5	0.546	13.9	16.5	12.5	13.5	18.7	23.5	16.0	17.5
VI	2	0.631	15.6	18.1	13.8	15.2	19.7	23.7	17.2	18.3
VII	2	0.761	15.6	18.5	14.3	15.7	19.4	24.9	17.6	19.0
VIII	4	0.848	15.5	19.1	14.4	15.8	20.1	26.3	18.1	19.3
IX	2	0.939	15.9	19.8	14.8	16.0	20.9	28.1	18.8	19.6
X	3	1.054	16.1	20.6	14.9	15.7	20.7	28.5	18.8	19.8
XI	1	1.121	16.5	21.2	15.6	16.6	20.8	28.8	19.1	19.9
XII	3	1.240	16.0	20.5	14.7	15.9	19.5 ¹	27.8	17.6	19.2
XIII	3	1.351	15.9	20.9	14.6	15.5	20.3 ¹	29.1	17.6	19.0
XIV	2	1.455	15.1	20.1	13.9	14.9	20.7	28.4	18.1	19.1
XV	2	1.566	15.3	20.8	14.0	15.1	20.7	29.5	18.2	19.4
XVI	4	1.678	15.2	19.9	14.0	15.0	20.4	27.9	17.8	19.3
XVII	2	1.730	15.3	20.3	14.1	15.1	20.8	29.6	18.2	19.5
XVIII	2	1.823	15.5	20.5	14.3	15.1	21.1	29.9	18.4	19.6
XX	1	2.004	14.6	19.3	13.5	14.0	21.5	31.0	18.4	19.6

¹ See note on table 1.

W. B in fresh brain
W. B on the slide for the horizontal section, and applied directly to the final average diameters for the cell bodies and the nuclei. The corrected results, with the average correction-coefficient for each brain-weight group, taken from previous papers (Sugita, '17 a, '18 b), are tabulated in table 3, accompanied with the averages of all the diameters in both sections for each brain-weight group.

TABLE 3

Giving the corrected final average diameters of the nerve cells and their nuclei of the lamina pyramidalis and the lamina ganglionaris measured on the frontal and the horizontal sections of the albino rat brain. The average values of the two for each brain weight group are also given. The correction-coefficient for each brain weight group was taken from previous papers (Sugita, '17 a, '18 b). *F* = the frontal section. *H* = the horizontal section.

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT	LAMINA PYRAMIDALIS		LAMINA GANGLIONARIS	
			Cell body diameter	Nucleus diameter	Cell body diameter	Nucleus diameter
	<i>grams</i>		μ	μ	μ	μ
F I	0.161	1.14	10.3 °	8.1	13.6	10.9
H I	—	—	—	—	—	—
	0.161		10.3	8.1	13.6	10.9
F II	0.251	1.16	13.5	11.2	18.8	14.8
H II	0.292	1.10	12.3	10.0	18.9	15.0
(Birth)	0.272		12.9	10.6	18.9	14.9
F III	0.358	1.13	15.4	13.0	20.6	16.0
H III	0.317	1.21	14.6	12.2	20.1	16.3
	0.338		15.0	12.6	20.4	16.2
F IV	0.432	1.10	17.2	14.2	22.8	17.9
H IV	0.419	1.30	17.5	14.8	24.0	19.6
	0.426		17.4	14.5	23.4	18.8
F V	0.542	1.13	17.9	14.6	24.2	19.0
H V	0.546	1.22	18.5	15.9	25.6	20.4
	0.544		18.2	15.3	24.9	19.7
F VI	0.639	1.19	19.4	16.0	25.4	19.9
H VI	0.631	1.24	20.4	18.0	26.8	21.9
	0.635		19.9	17.0	26.1	20.9
F VII	0.750	1.24	21.0	17.2	28.2	20.5
H VII	0.761	1.27	21.6	19.0	28.0	23.2
	0.756		21.3	18.1	28.1	21.9
F VIII	0.841	1.20	21.5	17.3	28.3	21.4
H VIII	0.848	1.38	23.7	20.8	31.8	25.8
	0.845		22.6	19.1	30.1	23.6
F IX	0.964	1.21	22.4	19.4	29.9	23.4
H IX	0.939	1.31	23.2	20.2	31.7	25.2
(10 days)	0.952		22.8	19.8	30.8	24.3

TABLE 3—Continued

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT	LAMINA PYRAMIDALIS		LAMINA GANGLIONARIS	
			Cell body diameter	Nucleus diameter	Cell body diameter	Nucleus diameter
	<i>grams</i>		μ	μ	μ	μ
F X	1.040	1.23	22.5	18.6	29.6	22.4
H X	1.054	1.36	24.8	20.8	33.0	26.3
	1.047		23.7	19.7	31.3	24.4
F XI	1.171	1.26	23.4	19.4	31.4	23.8
H XI	1.121	1.26	23.7	20.4	31.0	24.6
(20 days)	1.146		23.6	19.9	31.2	24.2
F XII	1.253	1.31	24.0	19.6	31.6	24.0
H XII	1.240	1.36	24.6	20.0	31.7	25.9
	1.247		24.3	20.3	31.7	24.5
F XIII	1.335	1.29	23.4	19.2	30.2	23.4
H XIII	1.351	1.34	24.4	20.2	32.6	24.5
	1.343		23.9	19.7	31.4	24.0
F XIV	1.445	1.34	23.8	19.7	31.2	24.0
H XIV	1.455	1.31	22.8	18.9	31.7	24.4
	1.450		23.3	19.3	31.5	24.2
F XV	1.554	1.30	22.9	18.9	31.4	23.8
H XV	1.566	1.28	22.9	18.6	31.6	24.1
	1.560		22.9	18.8	31.5	24.0
F XVI	1.656	1.33	22.9	19.0	33.4	24.8
H XVI	1.678	1.32	23.0	19.2	31.4	24.4
	1.667		23.0	19.1	32.4	24.6
F XVII	1.726	1.26	22.3	18.6	31.3	24.1
H XVII	1.730	1.36	23.9	19.8	33.7	25.6
	1.728		23.1	19.2	32.5	24.9
F XVIII	1.839	1.32	22.3	18.5	33.2	24.7
H XVIII	1.823	1.29	23.0	19.0	32.4	24.5
	1.831		22.7	18.8	32.8	24.6
F XIX	1.924	1.29	22.7	18.2	33.2	24.6
H XIX	—	—	—	—	—	—
	1.924		22.7	18.2	33.2	24.6
F XX	2.054	1.23	21.2	17.1	33.2	24.2
H XX	2.004	1.31	22.0	17.9	33.8	24.9
	2.029		21.6	17.5	33.5	24.6

IV. GROWTH IN THE DIAMETERS OF THE CELL BODY AND OF THE NUCLEUS

Chart 1 shows graphically the data given in table 3. As ordinates the average diameters of the cell body and of the nucleus of the pyramids (lamina pyramidalis) and of the ganglion cells (lamina ganglionaris) are plotted on the abscissa for the average brain weights.



Chart 1 Showing the corrected average diameters of the cell body and the nucleus of the cortical nerve cells of the albino rat, plotted according to increasing brain weight. Based on the data in table 3. Graph GC, average diameter of the cell body of the ganglion cells in the lamina ganglionaris. Graph GN, average diameter of the nuclei of the ganglion cells in the lamina ganglionaris. Graph PC, average diameter of the cell body of the pyramids in the lamina pyramidalis. Graph PN, average diameter of the nuclei of the pyramids in the lamina pyramidalis. X, 10 days of age. XX and *, 20 days of age. **, 30 days of age.

If the length of the average diameters represents relatively the cube root of the volume of the cell body or of the nucleus, the actual volume of them may be comparable among themselves by the cube of the diameters. It is clearly seen from the chart that the pyramids in the lamina pyramidalis of the Albino cortex attain their maximum size in a brain weighing from 1.1 to 1.3 grams or 20 to 30 days in age, the curve showing the maximum size in a brain weighing about 1.25 grams, and after that they diminish slightly but steadily in size as the age (brain weight) advances, while, on the other hand, the ganglion cells in the lamina ganglionaris attain nearly their full size in a brain weighing about 0.95 gram or ten days in age; that is, earlier than the pyramids, and after that slowly but steadily increase their size as the brain weight increases. The nuclei in the pyramids and in the ganglion cells change their sizes in much the same way as the cell bodies to which they belong, the graphs for the cell body and that for the nucleus for each kind of cell running nearly similar courses (chart 1).

As shown in chart 1, the graphs suggest that both kinds of cells increase in size very rapidly during the first ten days after birth, and then the rate diminishes rather abruptly during the following ten days (0.95 to 1.15 grams in brain weight) or more, at the end of which phase the pyramids reach the maximum size, after which they decrease slowly, while the ganglion cells still continue to increase somewhat even after this phase.

On examining all the sections which I made, it was seen that the ground tone of the sections uniformly stained with the carbol-thionine has been gradually changing as the age of the brain, from which the sections were taken, increases. In successfully stained sections—even if stained by decoloration—of brains from birth to those weighing less than 1.0 gram, the ground tone is rather purple or violet, when viewed with the naked eye by transmitted light. On the other hand, the sections from brains weighing more than 1.3 grams have a rather distinctly blue tone. The intercellular tissue takes more easily the pale blue color—owing to a less decoloration—in older brains, while in younger brains the intercellular tissue remains

quite unstained. The period during which the brain weight increases from 1.1 to 1.3 grams coincides with a transitional phase of the color. I regret that I have not been able to reproduce these distinctions of color for the illustration of this paper.

These changes in color suggest that at the 20 to 30 day phase some chemical changes in the structure of the cell body and the nucleus have been occurring.² At this phase of growth, the cells having attained nearly the full size, the rate of increase in size abruptly diminishes, suggesting that during this phase important changes have occurred. Myelination is proceeding very actively after the brain has attained the weight of 1.0 gram (Sugita, '17 a), and the fact that the cell bodies and nuclei of the pyramids decrease in size as the brain weight passes 1.3 grams while the growth of the cell body and of the nucleus of the ganglion cells become very slow may have some connection with the myelin formation.

Table 3 enables us to examine the measurements for the frontal and for the horizontal sections separately. Generally speaking, at the locality VII, measured in the frontal section (lines denoted by *F* in table 3) and at the locality X measured in the horizontal section (see lines denoted by *H* in table 3), the corrected sizes of the cell body and of the nucleus show some differences in the younger brains, but the sizes may be regarded on the whole as practically the same in these two localities in mature brains. If stated more minutely according to the data presented in table 3, the pyramids and the ganglion cells at locality VII (frontal section) grow in size somewhat more slowly as compared with those at locality X (horizontal section), so that in Groups IV to X the diameters are all smaller for the frontal section than for the horizontal section, in averaged values (see table 3). But if these slight discrepancies be not

² As noticed in tables 1 and 2, the size of the ganglion cells directly measured on the slides shows a slight decrease during this phase (1.0 to 1.3 grams in brain weight), while, in corrected measurements given in table 3, there cannot be detected any diminution in cell size during the same phase. This decrease in size of the ganglion cells on the slide may have some connection with the chemical changes occurring in the cytoplasm and karyoplasm, which cause different reactions to the reagents used for fixation.

taken too seriously, it may be stated that on the average the cell bodies and the nuclei of the pyramids attain their maximum size at about twenty-five days (brain weight, 1.25 grams) and those of the ganglion cells attain nearly the full size at about ten days of age (brain weight, 0.95 gram).

The largest ganglion cells (lamina ganglionaris) in the cerebral cortex of the adult albino rat brain are found in the middle part of the sagittal section, denoted by locality III (Sugita, '17 a). The size of these largest cells at different ages was not systematically investigated by me, but a careful comparison of them with the ganglion cells at localities VII and X, tabulated in this study, show them to be on the average (in brains weighing more than 1.3 grams) 4 to 7 micra greater in the transverse diameter, 7 to 10 micra greater in the longitudinal diameter of the cell body, and 3 to 5 micra greater in both diameters of the nucleus—all in corrected values—than the corresponding diameters of the ganglion cells in localities VII and X, as shown in the following summary:

Average corrected diameters of the cell body and of the nucleus of the ganglion cells in the lamina ganglionaris (Groups XIII-XX)

	LOCALITIES VII AND X	LOCALITY III
Cell body.....	28 x 37 μ (average 32.4 μ)	33 x 46 μ (average 39.0 μ)
Nucleus.....	24 x 25 μ (average 24.4 μ)	28 x 30 μ (average 29.0 μ)

The size of the cell bodies and their nuclei in the other layers of the Albino cortex will be considered in a later chapter in this paper.

Figures 3 and 4 give the typical appearance of the pyramids and the ganglion cells, respectively, for each brain-weight group (with a few omissions), all drawn proportional in size to the uncorrected diameters and magnified about 950 times.

V. MORPHOLOGICAL CHANGES IN THE CORTICAL NERVE CELLS DURING GROWTH

Figures 3 and 4 illustrate the typical pyramids and the ganglion cells from each brain-weight group, as seen in the sections pre-

pared by me, from the material fixed in Bouin's fluid, imbedded in paraffine, stained with the carbol-thionine, and projected and enlarged by a fixed number of diameters. The size of the pictures, therefore, corresponds to the uncorrected measurements given in tables 1 and 2.

Though they are increasing in volume very rapidly after birth, the pyramids in the lamina pyramidalis retain up to a brain weight of 0.6 gram (VI, 6 days in age) the characteristics of the

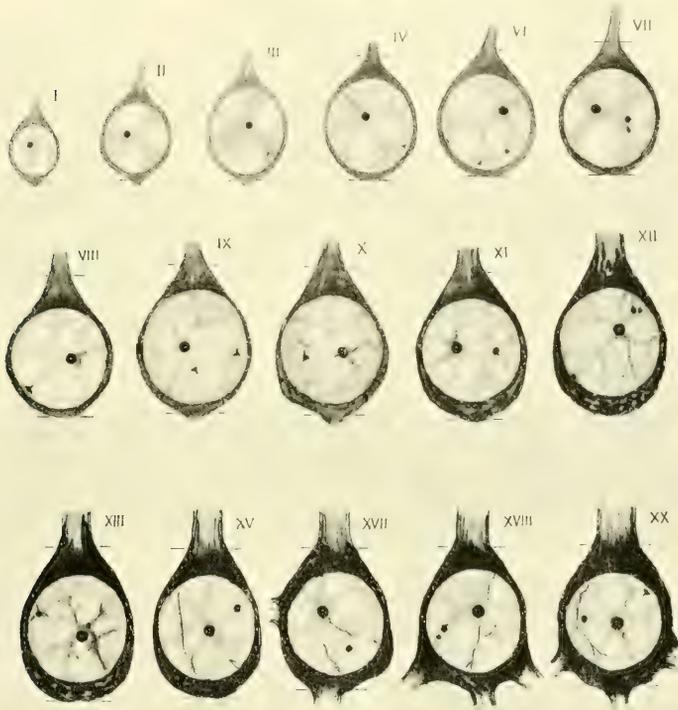


Fig. 3 Showing semi-diagrammatically the increase in size and the morphological changes, in the typical pyramids in the lamina pyramidalis of the cerebral cortex of the albino rat. The Roman number by each cell figure indicates the brain weight group from which the typical pyramid was selected and the drawing made. All cell figures have been uniformly magnified to 950 diameters, according to the uncorrected measurements.

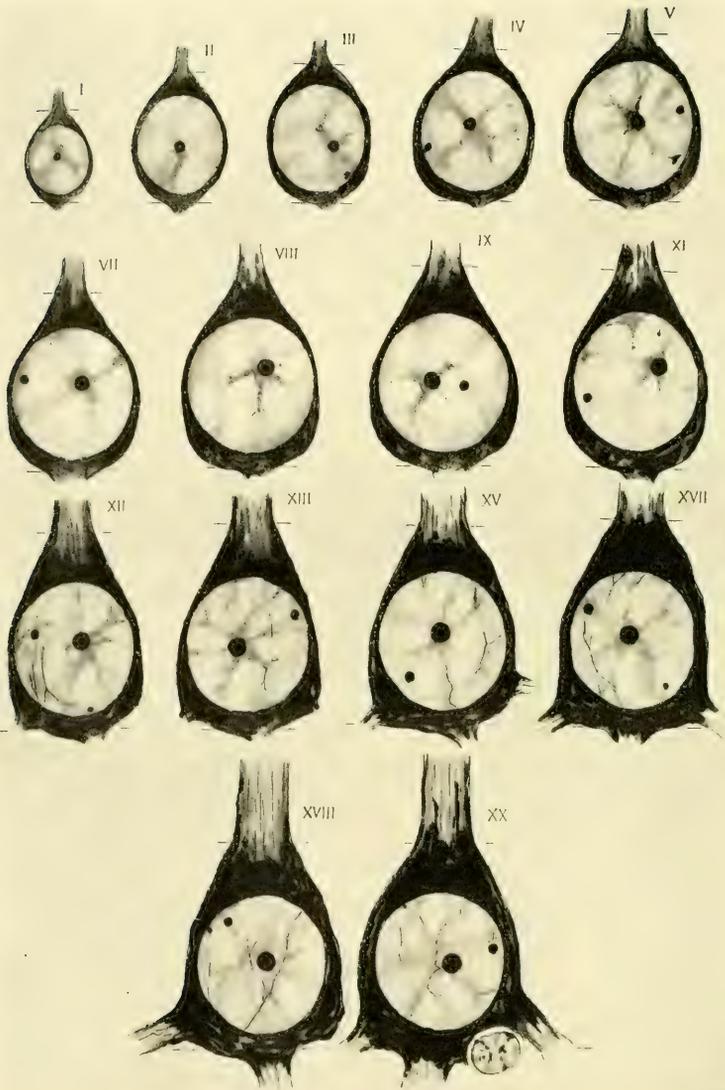


Fig. 4 Showing semi-diagrammatically the increase in size and the morphological changes in the typical ganglion cells in the lamina ganglionaris of the cerebral cortex of the albino rat. The Roman number by each cell figure indicates the brain-weight group from which the typical ganglion cell was selected and the drawing made. All cell figures have been uniformly magnified to 950 diameters, according to the uncorrected measurements.

fetal form of the cells,³ represented by a relatively large, round nucleus thinly enveloped by a small amount of homogeneous cytoplasm and with processes from both poles. The Nissl bodies begin to appear first in a brain weighing 0.8 gram (VIII), showing first in a part of cytoplasm adjoining the nucleus at the apical pole and forming the so-called 'Kernkappe.' The cytoplasm matures rapidly in structure as the brain weight increases from 0.8 to 1.2 grams. As the measurements show, the nucleus attains nearly the full size when the brain weighs 0.95 gram (10 days), but at that phase the cytoplasm has not yet been fully developed. It is meagre in mass, enveloping the nucleus thinly,

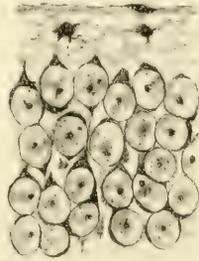


Fig. 5 Showing the cerebral cortex proper at the locality II (fig. 2, Sugita, '17 a) on a fetal brain of the albino rat. Body weight about 1.0 gram, body length (neck-rump) about 19.5 mm., eighteenth day of gestation. Magnification of about 500 diameters, measured directly on the slide.

the Nissl bodies not being yet fully differentiated, but only suggesting the 'Kernkappe.' The cell continues to grow very slowly up to a brain weight of 1.1 to 1.3 grams or about 20 to 30 days in age. Then, as the age advances, the sizes of both the cell body and of the nucleus slowly diminish, while within the cytoplasm the differentiation of the Nissl bodies progresses. As the differentiation progresses, the general tone of color of the section

³ The form of the fetal nerve cells from the locality II of the cerebral cortex of the albino rat is shown diagrammatically in figure 5, which was taken from an Albino fetus of 1.0 gram in body weight, 19.5 mm. in body length at the eighteenth day of gestation. The cortex proper, not regarding the transitional layer, consists of four or five rows of cells with scanty cytoplasm. The average diameter of the nucleus is about 5 to 7 micra on the slide and the thickness of the cortex at this age is about 0.06 mm. on the slide.

changes from violet to blue, owing to the deeper staining of the Nissl bodies and of the intercellular tissue with the carbol-thionine. The apical dendrite thickens rapidly during the period in which the brain weight increases from 1.0 to 1.3 grams, but the basal dendrites are not clearly stained until the brain attains 1.6 grams in weight. Throughout the later life, the cytoplasm is slowly but continuously decreasing in the absolute mass as the age advances, and the size of the nucleus is also diminishing. The nucleolus in the nucleus attains also its full size (the diameter is somewhat less than 2 micra) at the time when the nucleus has attained the maximum size, but it tends to grow slightly in late rages, while the nucleus show some decrease in size.

The structure of the nucleus of the pyramids is not clearly demonstrable with this stain. As far as can be judged from the present preparations, the chromatin substance in the nucleus begins to develop notably only after the brain has attained the weight of 1.0 gram, and after the nucleus has passed its phase of rapid enlargement.

From the foregoing it will be seen that up to a brain weight of 0.95 gram, the pyramids may be regarded as in the preparatory stage of structural development, attaining at the end of this period nearly the full size of the cell body and of the nucleus. And after this stage increase and differentiation in the cytoplasm and the nucleus chromatin continue slowly until a brain weight of 1.1 to 1.3 grams. After that time they begin rather to diminish in size, but nevertheless, to advance more and more in differentiation, which latter change probably indicates the maturing of the function of the pyramids. Morphologically, the pyramids first attain their fully mature aspects at a brain weight of about 1.6 grams (about 50 days in age).

In my previous studies on the development of the cortex (Sugita, '17 a, '18 b), I named three phases of cortical growth in the early life of the albino rat; the first phase: from birth to the tenth day; the second phase: from the tenth to the twentieth day, and the third phase: from the twentieth to the ninetieth day. Applying this series of phases to the cytological development of the pyramids, the following appears.

In the first phase occurs the rapid enlargement of the cell body and the nucleus, the cell retaining still the fetal form, and not showing any significant differentiation in the internal structure. The Nissl bodies first appear as the so-called 'Kernkappé' at the end of this phase. The tone of color of the sections stained with the carbol-thionine is rather violet.

In the second phase, the size of the cell body and of the nucleus continues to increase, but very slowly, and both attain their maximum sizes at the end of this phase. The differentiation in cytoplasm goes slowly on and the chromatin in the nucleus begins also to differentiate. The tone of the stain is transitional from violet to blue.

Throughout the third phase and afterwards, the size of the cell body and of the nucleus decreases slowly from the maximum values attached at the end of the second phase. But the differentiations of the cytoplasm and the nucleus chromatin steadily continue as the age advances. The apical dendrites gain in diameter and the basal dendrites begin to take the stain. The nucleus sometimes shows the 'Kernfalte.' The tone of the stain is rather blue and the contour of the pyramids clear cut.

The ganglion cells of the lamina ganglionaris enlarge very rapidly and attain nearly their full size at the age of ten days—somewhat earlier than do the pyramids. But the morphological changes which take place in the ganglion cell body and the nucleus are similar to those just described in the pyramids. In the lamina ganglionaris there can be recognized two distinct kinds of nerve cells, one the smaller-sized pyramids, which seem to be very like the pyramids in the lamina pyramidalis, and the other, the larger-sized neurons, which are usually called ganglion cells or giant cells and which characterize the layer. Some of the cells found in the lamina ganglionaris and which grow to be the ganglion cells are from the first somewhat large-sized. These develop more rapidly than the other small cells in this layer, which are intermingled with them. In earlier stages the ganglion cells manifest no structural difference or characteristics marking them off from the smaller cells, but differ only in the size of the cell body and of the nucleus. They retain their fetal

appearance, that is, an ovoid form with a relatively large nucleus also ovoid or ellipsoid in form and a small amount of enveloping cytoplasm, which seems almost homogeneous in its staining, together with slender processes, until a brain weight of 0.75 gram. The Nissl bodies begin at first to appear in a brain weighing 0.9 gram, as the 'Kernkappe' covering the apical part of the nucleus. The differentiation of the cytoplasm becomes more and more distinct as the brain weight increases and, in brains weighing more than 1.3 grams, the section as a whole takes a blue tone. This change in color tone is probably due to the development of the Nissl bodies in the cytoplasm and the structural changes in the intercellular tissue. The apical dendrites rapidly thicken in brains weighing 1.1 to 1.3 grams and, in brains weighing more than 1.3 grams, we see distinctly some relatively thick basal dendrites and the axis-cylinder becomes visible. The mass of the cytoplasm and the differentiation of the Nissl bodies proceeds steadily as the age advances. In the fully grown brain we see very often small satellite cells surrounding or indenting the cytoplasm of the ganglion cells, though satellite cells appear in relation to some other types of neurons also. Whatever the significance of these satellite cells, it is to be noted that in younger brains they are very rarely seen. The outline of the ganglion cell body is not necessarily sharp nor is the form regularly pyramidal, being sometimes indeed quite irregular and often appearing ovoid or ellipsoid in shape. Lipochrome or fat pigment, usually seen in the adult human cells of this type, is never seen in those of the adult albino rat, even in old age.

The nucleus of the young ganglion cell seems quite simple in structure and it attains nearly the full size in a brain weighing 0.95 gram. After passing this stage, the chromatin structure of the nucleus begins to appear. The size of the nucleus may be said to remain practically the same after this stage, while the cytoplasmic development continues relatively rapidly. The 'Kernfalte' is sometimes visible in brains weighing more than 1.5 grams. The nucleolus in the nucleus of the ganglion cells attains also nearly the full size (diameter is somewhat less than 4 micra) at the phase when the nucleus has reached nearly

the full size (10 days), but continues to grow steadily, though slightly, throughout later life. The size of the nucleolus in the ganglion cells is relatively much larger than in the pyramids.

As for the developmental phases of the ganglion cells according to age, a statement similar to that made concerning the pyramids of the lamina pyramidalis holds true, though in the ganglion cells the size development seems to be accomplished in general somewhat earlier. In a brain under 1.2 grams in weight, more mature ganglion cells are seen mixed up with those less mature, indicating that the development of the ganglion cells is not uniform, but that some progress more slowly. In a brain weighing more than 1.3 grams, all the ganglion cells seem to have already passed the first phase of development in size, and all the cells are now of full size and probably fully functional.

One observation which I think it important to notice here is that cells in the same layer but in different parts of the cortex do not always show a like degree of development at a given age. Some cells or some cell groups are more precocious or more retarded than their neighbors. My observations apply only to the size and morphology of the most developed cells found together in a selected locality, regardless of the relative maturity of that locality. So the statement that the ganglion cells attain full size at ten days does not necessarily mean that the lamina ganglionaris is completely mature at that age, but it only applies to the size or morphology of the most advanced cells found in the layer. As a matter of fact, the lamina ganglionaris matures in toto earliest, so that in a brain weighing 1.3 grams all the ganglion cells found in the lamina ganglionaris are apparently completely mature, while at the same age the lamina pyramidalis still contains many immature cells among the mature ones, and the full maturity of the latter layer is attained only in a brain weighing more than 1.6 grams (more than 50 days in age).

In respect of cell size and morphological changes, the lamina ganglionaris and the lamina multiformis are the earliest to mature all the elements in them, while the lamina pyramidalis matures more slowly, for example, and in a section from a brain twenty days old, we can still see many immature cells mixed with the mature ones in this latter layer.

VI. ON THE NERVE CELLS IN OTHER LAYERS OF THE CEREBRAL CORTEX

Figure 6 shows a diagram of cell-lamination of the adult albino rat brain, taken from locality II of the sagittal section (fig. 2, Sugita, '17 a). In comparison with the data on the pyramids in the lamina pyramidalis (III) and the ganglion cells in the lamina ganglionaris (V), the measurements of the cells found in the lamina granularis interna (IV) and the lamina multiformis (VI) show nothing peculiar. Generally speaking, the cell body and the nucleus of the granules do not take the stain as well as in the case of the pyramids and remain rather pale in color. The cells of the lamina multiformis, on the other hand, generally stain deeply. Especially the cytoplasm of the cells forming the inner (ental) sublayer of the lamina multiformis tints very well, so that this sublayer is easily distinguished even at a low magnification by the deep staining of the elements.

The granules in the lamina granularis interna (IV) are smaller in size and lie more crowded than do the pyramids. This layer is not clearly differentiated in brains weighing less than 0.6 gram or less than six days of age, at which stage the immature cells of fetal form prevail in both the lamina pyramidalis and the lamina granularis interna and no characteristic granules are shown. On the sections from a brain weighing 0.5 to 0.6 gram, which had been fixed in formaldehyde and imbedded in paraffine, I could see distinctly a dark band due to the deep staining of the ground substance and characteristic for the adult lamina granularis interna (cf. Sugita, '17 a, p. 526), though the contained cells do not show any of the characteristics of the granules. This is probably the first step in the differentiation of the granular layer. Later we see that the cells lying near the lamina ganglionaris become more and more crowded and somewhat small in size compared with the cells lying in the lamina pyramidalis. In an adult brain weighing more than 1.3 grams, a distinct band of smaller-sized cells (the lamina granularis interna) appears above the lamina ganglionaris.

Fig. 6 Diagram of cell-lamination of the frontal cerebral cortex (locality II, fig. 2, Sugita, '17 a) of the adult albino rat brain weighing 1.8 grams, schematically enlarged 66 diameters. I = lamina zonalis, III = lamina pyramidalis, IV = lamina granularis interna, V = lamina ganglionaris, VI = lamina multiformis, which is divided into two sublayers at * by a band poor in cells.

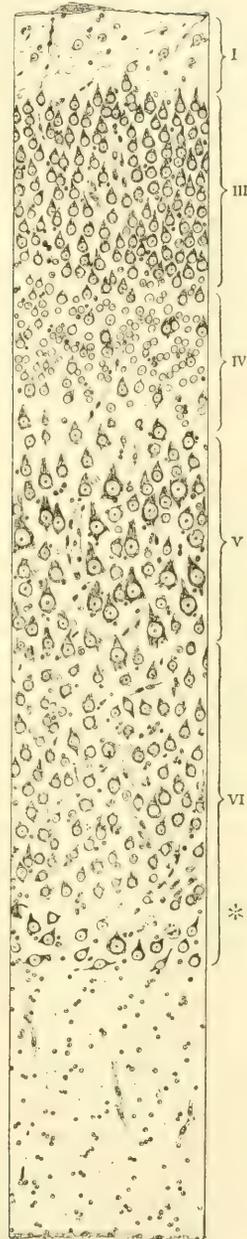


TABLE 4

Giving both corrected and the uncorrected values for the two diameters of the cell body and the nucleus respectively, of the granule cells in the lamina granularis interna (IV, fig. 6) for several brain weight groups

BRAIN WEIGHT GROUP	CELL BODY		NUCLEUS	
	Corrected	On the slide	Corrected	On the slide
	μ	μ	μ	μ
Group II (birth).....	12 x 15	(10 x 12)	11 x 12	(9 x 10)
Group III.....	14 x 16	(11 x 13)	12 x 14	(10 x 11)
Group V.....	15 x 18	(12 x 14)	14 x 15	(11 x 12)
Groups VI-VIII.....	16 x 20	(13 x 16)	15 x 16	(12 x 13)
Groups X-XIII.....	19 x 21	(15 x 17)	16 x 19	(13 x 15)
Groups XIII-XV.....	16 x 20	(13 x 16)	15 x 16	(12 x 13)
Groups XVI and above.....	15 x 20	(12 x 16)	14 x 16	(11 x 13)

The average size of the granules measured on the sections here used is given in table 4. In brain-weight Groups II-V, at which stages the layer is not yet clearly differentiated, the measurements were made on the small cells which lie nearest to the lamina ganglionaris and the cells were assumed to be the future granules.

So, in brains weighing more than 1.6 grams (Group XVI), the size of the granules diminishes slightly as the age advances. Most of the nuclei of the granules are more or less elongated or elliptical in shape and the cytoplasm is very scanty, so that sometimes there can be seen only a thin envelope of the cytoplasm around the nucleus.

In short, the granules at the earlier age are almost equal to the growing pyramids in size, but they increase in size somewhat less rapidly as compared with the pyramids, among which they are interspersed at first. They reach their maximum size in a grain weighing between 1.2 and 1.4 grams, and after that period the size decreases as the age advances, showing a somewhat compact nucleus.

As already indicated in a former paper (Sugita, '17 a), the lamina multiformis is divided by a pale band (fig. 6,*), poor in cells, into two sublayers. The polymorphous cells in the ectal sublayer have the shapes indicated by their name, but in general they are pyramidal in form, the apex directed ectally, being somewhat flattened and rich in cytoplasm, as compared with the

pyramids. The density of the polymorphous cells in this sublayer is greatest at the earlier ages. During the early ages the most densely crowded pyramids are in the lamina pyramidalis, while by contrast the lamina multiformis seems rather poor in cells. But in adults the cell population of the ectal sublayer of the lamina multiformis appears to be only slightly less than that of the lamina pyramidalis and the size of the polymorphous cells appears nearly equal to that of the pyramids, though, by an exact measurement, they prove to be slightly larger (fig. 6). The shape of polymorphous cells is not uniform and they show many dendritic processes, irregularly arranged. Some, though pyramidal, lie obliquely or transversely, while some hold a reversed position, with the apical dendrite directed entally (Martiniotti's cells).

The cells of the ental sublayer of the lamina multiformis are quite different in their appearance. They are polygonal or spindle-shaped and generally lie with their long axis in the plane of the lamina. The cytoplasm of the cells is massive and takes the stain well. The Nissl bodies, however, are not well differentiated. Though not always pyramidal in shape, the assumed apex of the cells appears to be directed towards the occipital pole in the sagittal and the horizontal sections or towards the ventral surface in the frontal section, thus indicating the direction of the migration of the nerve cells from the matrix to the cortex proper. As already stated by me (Sugita, '17a), this sublayer probably serves as a secondary station for cells migrating from the matrix at the ventricular wall to their final destination in the cortex and the number of cells in this sublayer diminishes as the age of the brain advances. So one has some reason to think that a fraction of the cells found in this sublayer are still in transit, at least during the early ages. It should be noted at least that the cells of this sublayer have a morphology in respect of the mass and the staining reaction of their cytoplasm which indicates the stage of migration.

The neuroglia nuclei are abundantly scattered in the ental cortical layers (that is, in the lamina multiformis and the lamina ganglionaris) as compared with the ectal layers (that is, in the

TABLE 5

Giving the cubes of the average diameters of the cell bodies and of the nuclei of both the pyramids (lamina pyramidalis) and the ganglion cells (lamina ganglionaris) at birth, 10 days, 20 days and 90 days, the ages indicating respectively the beginning of each developmental phase. The values given represent merely the relative volumes of the cell bodies and of the nuclei. Ratios based on the initial value taken as unity are given for each column. The data, on the basis of which the calculations were made, were taken from table 3

AGE INDICATING THE BEGINNING OF EACH DEVELOPMENTAL STAGE	BRAIN WEIGHT GROUP	PYRAMIDS IN THE LAMINA PYRAMIDALIS				GANGLION CELLS IN THE LAMINA GANGLIONARIS			
		Cell body		Nucleus		Cell body		Nucleus	
		Relative volumes	Ratio	Relative volumes	Ratio	Relative volumes	Ratio	Relative volumes	Ratio
		μ^3		μ^3		μ^3		μ^3	
Birth.....	II	215	1.00	119	1.00	675	1.00	330	1.00
10 days.....	IX	1185	5.51	775	6.50	2925	4.33	1440	4.36
20 days.....	XI	1315	6.12	790	6.63	3070	4.55	1415	4.29
90 days.....	XVIII	1170	5.44	665	5.58	3530	5.23	1490	4.52

lamina granularis interna and the lamina pyramidalis) (see fig. 6). At earlier ages, neuroglia nuclei are comparatively scarce in the lamina pyramidalis, but at maturity they are well distributed in this layer, though in the lamina multiformis they are found always abundantly. With the method of staining here used, we can distinguish two kinds of the neuroglia nuclei, one staining a relatively deep blue, which is the smaller in size (2 to 5 micra in diameter on the slide), with crowded granules in the chromatin sometimes arranged radially ('Radkern'), and surrounded by evident cytoplasm, and the other staining rather paler and with a violet tone, vesicular ('blasig') in appearance, somewhat larger in size (3 to 6 micra in diameter on the slide), with scanty chromatin and enveloped by a small amount of cytoplasm. This metachromatism in the staining of the two kinds is very remarkable. Both kinds are found intermingled. In the white matter glia cells are distributed in rough chains, while in the cortex they are, under normal conditions, less well distributed than in the white matter. Sometimes, especially in old age, the glia cells are found gathered around the ganglion cells or the pyramids or near the blood-vessels. The satellite cells which are attached to or

even invade the cytoplasm of the nerve cells, are usually regarded as neuroglia cells.

The method here used, of staining with the carbol-thionine the material fixed in Bouin's fluid and imbedded in paraffine, reveals clearly only the size and shape of the nerve cells in the cerebral cortex. The more detailed structure of the cytoplasm and of the nucleus or the structure of the axis-cylinder and dendrites is not brought out by this method, and for the investigation of these characters other methods are required.

VII. DISCUSSION

According to the foregoing observation, the full size of the largest pyramids in the lamina pyramidalis (about 25 days in age)⁴ is about $21 \times 27 \mu$ for the cell body and $19 \times 21 \mu$ for the nucleus, and the measurement of those largest at birth⁵ is $11 \times 15 \mu$ for the cell body and $10 \times 11 \mu$ for the nucleus, in the fresh condition of the material. The full size of the largest ganglion cells in the lamina ganglionaris (at localities VII and X, about 25 days, for example)⁴ is $27 \times 37 \mu$ for the cell body and $24 \times 25 \mu$ for the nucleus, and the measurement of the largest ganglion cells at birth⁵ is $17 \times 21 \mu$ for the cell body and $14 \times 16 \mu$ for the nucleus, all in the fresh condition of the brain.

If the volume of the cell bodies or of the nuclei be comparable among themselves according to the cubes of their average diameters, the figures given in table 5 which presents the cubes of the average diameters of the cell bodies and of the nuclei of the nerve cells at different ages, and which were calculated from the data in table 3, may be used as the basis of discussions on the volume development of the cells. It will be seen from table 5, by a

⁴ To obtain the values here given, the uncorrected diameters of the cell body and the nucleus in Groups XI-XIII in the frontal and the horizontal sections (tables 1 and 2) were respectively averaged and the results were corrected by multiplying by the mean correction-coefficient of Groups XI-XIII for the frontal and the horizontal sections (see table 3).

⁵ To obtain the values here given, the uncorrected diameters of the cell body and the nucleus in Group II in the frontal and the horizontal sections (tables 1 and 2) were respectively averaged and the results were corrected by multiplying by the mean correction-coefficient of Group II for the frontal and the horizontal sections (see table 3).

simple calculation, that at birth the largest ganglion cells are almost 3.1 times as voluminous, at 20 days about 2.3 times, and at 90 days 3.0 times, as the pyramids of the same stage, and the nuclei of the ganglion cells are at birth 2.8 times as voluminous, at 20 days 1.8 times, and at 90 days, 2.2 times as the nuclei of the pyramids of the same stage, if both kinds of cells are assumed to have the similar forms throughout their enlargement.⁶ It is also seen that, using the same method, the cell body of the pyramids has increased from birth 6.1 times in volume at 20 days and 5.4 times at 90 days, and the nuclei 6.6 times at 20 days and 5.6 times at 90 days, while the cell body of the ganglion cells has increased only 4.6 times at 20 days, 5.2 times at 90 days and the nuclei of the ganglion cells 4.3 times at 20 days and 4.5 times at 90 days, as compared with their initial volumes at birth.

It may therefore be concluded that, throughout the developmental stage of the nerve cells after birth, the rate of enlargement is almost similar in the nuclei and in the cell bodies of both kinds of cells, though the rate is slightly higher in the pyramids than in the ganglion cells in both the cell body and the nucleus during the first twenty days after birth, because the initial volume of the pyramids is small at birth.

As the shape of the cell body is different from that of the nucleus, it is not proper to compare directly their respective volumes as determined by the foregoing use of their diameters, but they must be first reduced to forms which are comparable as

⁶ Here the nucleus was considered as an ellipsoid, the volume of which is to be calculated by the formula $\frac{4}{3}\pi a^2b$, when b is the long radius and a is the short radius of the body. As the transverse diameter (n_1) of the nucleus is equal to $2a$ and the longitudinal diameter (n_2) is equal to $2b$ the volumes of the nuclei may be compared among themselves simply by the factor a^2b or $n_1^2n_2$.

On the other hand, if the volume of the cell body was considered as a circular cone, in which the diameter of the basic circle is equal to the transverse diameter (c_1) of the cell body and the height of the cone is equal to the longitudinal diameter (c_2) of the cell body, then the volume of the cell body will be $\frac{1}{3}\pi\left(\frac{c_1}{2}\right)^2c_2$, and the values for the relative volumes of the cell bodies may be compared on the basis of the factor $c_1^2c_2$.

As the average diameters given in table 3 are respectively the square roots of the products n_1n_2 and c_1c_2 , the cubes of the average diameters will be approximately proportional to the values $n_1^2n_2$ and $c_1^2c_2$, respectively.

explained in the accompanying note and then table 5 may be consulted again.⁷ It is seen from table 5 that at birth the entire cell has almost double the volume of the nucleus, so that the cytoplasm and the nucleus have nearly the same volume. The nucleus-plasm relation changes according to the brain weight. In the pyramids, the total cell body comes to 1.7 times at 20 days and to 1.8 times at 90 days, compared with the volume of the nucleus at the same age. This is owing to the relatively rapid growth of the nucleus. In the ganglion cells, on the other hand, the total cell body is 2.2 times at 20 days and 2.4 times at 90 days, compared with the volume of the nucleus at the same stage. As the pyramids decreases in size after 30 days, the cell size of the pyramids in old age (brain weight more than 2.0 grams) becomes almost equal to that at 8 days of age, but the nucleus-plasm relation is quite different at the two stages. At 8 days the nucleus is relatively large (total cell body is 1.7 or less times the nuclear volume), but in old age the volume of cytoplasm has increased somewhat in relation to the nuclear volume (total cell body is nearly 2.0 times the nuclear volume).

These values for comparison were taken from the data here used alone, but, as already noted, sections which were taken from material fixed in 95 per cent alcohol or in Bouin's fluid and imbedded in celloidin show a nucleus which is relatively smaller. In series of sections which have been prepared by methods other than that used by me, the volume relations between the cell body and the nucleus (nucleus-plasm relation) would probably be different from those which I have reported here, but I think it will be fair to assume that the growth changes in the cell body on

⁷ If the cell body were considered as having an ellipsoidal form with diameters equal to c_1 and c_2 which denote respectively the transverse longitudinal diameters measured on the cell body the volume, would be $\frac{3}{4}\pi\left(\frac{c_1}{2}\right)^2\left(\frac{c_2}{2}\right)$ or $\frac{3}{32}\pi c_1^2 c_2$. And if, on the other hand, the same cell body were considered as a circular cone, the volume may be calculated by $\frac{1}{3}\pi\left(\frac{c_1}{2}\right)^2 c_2$, or $\frac{1}{12}\pi c_1^2 c_2$. As the difference between these two formulas is not higher than $\frac{\pi}{96}$ of $c_1^2 c_2$, I have here compared the volumes of the cell body and of the nucleus under the assumption that both have the ellipsoidal form, employing once more the figures given in table 5 as the basis of comparison.

one hand and in the nucleus on the other would probably be similar by the use of any uniform method, even if the absolute values differed for the different methods, and none of them gave exactly the fresh values.

It is remarkable that both the cell body and the nucleus of the cortical cells attain nearly their full size at an early stage of development (at about ten days of age) and then continue to undergo cytomorphic development, without much change in cell size (chart 1). As already pointed out in former papers (Sugita, '17 a, '18 b), the elementary completeness of the cerebral cortex of the albino rat is attained at the age of twenty days, the final thickness of the cortex and the total number of the cortical nerve cells being apparently reached at this age. After this age, the volume of the cortex increases as the age advances nearly in proportion to, or at a slightly slower rate than, the total volume of the cerebrum. As noted, the size of the pyramidal cells in the lamina pyramidalis attains the maximum size in brains weighing 1.1 to 1.3 grams and the volume of the cell body and the nucleus becomes slightly less during later phases, while the size of the ganglion cells in the lamina ganglionaris increases slightly as the age advances, even after the above-named stage. It must be concluded, therefore, that the subsequent increase in cortical volume is effected by changes in structures other than the cell bodies themselves. And, as a consequence, in mature brains, the cell density in the cortex diminishes more and more, as has been already pointed out in a previous paper (table 3, Sugita, '18 b).

It is very interesting to find that the thickness of the cortex, the total number of the cortical nerve cells, and the size of the cortical cells all have reached nearly their maximum at the same age of twenty days, which is the weaning time of the rat. These relations appear also in the mouse. According to the results obtained by Isenschmid ('11), the thickness of the cerebral cortex of the mouse, measured at a fixed locality—corresponding to locality VII in my sections—attains nearly its full value something before seventeen days in age. And according to the systematic work of Stefanowska ('98), who has studied the devel-

opment of the cortical nerve cells by the method of silver impregnation of Golgi, the cortical nerve cells of the mouse have completed their development in respect of their attachments at the age of fifteen days, and the age of fifteen days is the weaning time of the mouse. It appears, therefore, that the completion of certain features of cortical development in relation to the weaning time, the time when the young become independent of the mother, is similar in both the albino rat and the mouse.

VIII. SUMMARY

1. The size of the nerve cells most advanced in development from a fixed locality of the cerebral cortex was systematically measured and the developmental changes during postnatal growth studied on the material represented by the grains of 128 albino rats of different ages. The data have been averaged for each brain-weight group and then corrected for the fresh condition of the material, using the correction-coefficients devised for this purpose. The results are given in tables and charts.

2. The full size of the pyramids in the lamina pyramidalis (about twenty-five days in age, average of Groups XI-XIII) is cell body $21 \times 27 \mu$ and nucleus $19 \times 21 \mu$ and the largest size at birth is cell body $11 \times 15 \mu$ and nucleus $10 \times 11 \mu$. The size of the ganglion cells in the lamina ganglionaris at the same stage (about twenty-five days in age, average of Groups XI-XIII) is cell body $27 \times 37 \mu$ and nucleus $24 \times 25 \mu$, while the largest size at birth is cell body $17 \times 21 \mu$ and nucleus $14 \times 16 \mu$.

In the full-grown albino rat (Groups XVI-XX), the average size of the pyramids is cell body $20 \times 26 \mu$, nucleus $18 \times 19 \mu$ and the average size of the ganglion cells is cell body $28 \times 38 \mu$, nucleus $24 \times 25 \mu$.

3. The cell body and the nucleus of the pyramids attain their maximum size at twenty to thirty days in age (1.1 to 1.3 grams in brain weight). Up to the tenth day of age they retain their fetal morphology. After having passed the maximum at twenty to thirty days, they diminish in size, but the internal structure matures more and more as the age advances.

4. The cell body and the nucleus of the ganglion cells attain nearly their full size at ten days (0.95 gram in brain weight), when they still show the fetal appearance. After this stage, the size of the cell body increases slowly but steadily as the age advances, while the nucleus remains nearly unchanged in size throughout life.

5. Both the pyramids and the ganglion cells retain clearly the fetal character of form until the brain weighs 0.6 gram or more. The differentiation of the cytoplasm and the Nissl bodies begins to appear in my preparations first in a brain weighing something more than 0.9 gram, the latter showing first as the 'Kernkappe' at the apex of the nucleus. The cells exhibit the mature appearance in a brain weighing more than 1.4 grams.

6. As for the maturation of the several layers, in general, disregarding the maturation of the individual cells in them, the lamina ganglionaris is completed earliest, so that in a brain weighing 1.3 grams (thirty days in age) all the ganglion cells in this layer are apparently mature, while at the same age the lamina pyramidalis is less mature as it contains relatively many immature cells mingled with the others. The full maturity of the lamina pyramidalis is attained, probably, in a brain weighing 1.6 grams (more than fifty days in age).

7. Throughout the developmental stage of the nerve cells, the rate of enlargement is almost similar in the nucleus and in the cell body in both the pyramids and the ganglion cells; but when the pyramids are compared with the ganglion cells it appears that the rate is more rapid in the pyramids than in the ganglion cells in both the cell body and the nucleus during the first ten days after birth.

8. The lamina granularis interna is first differentiated in brains weighing more than 0.6 gram. In younger brains it is confused with the pyramidal layer and cannot be clearly discriminated. The granules attain their maximum size in brains weighing 1.0 to 1.3 grams and then diminish slightly. The final size (corrected) of the granules in Groups XVI and above, is cell body $15 \times 20 \mu$ and nucleus $14 \times 16 \mu$.

9. The polymorphous cells in the ectal sublayer of the lamina multiformis are slightly larger than the pyramids of the same age. The polymorphous cells in the ental sublayer of the lamina multiformis are somewhat larger than those of the ectal sublayer, but are irregular in shape and rich in cytoplasm.

10. Two kinds of the neuroglia nuclei are found in the cortex. One staining deep blue with the carbol-thionine, smaller in size (2 to 5 micra in diameter on the slide) and having a radiating structure of the chromatin, and the other staining paler, swollen ('blasig') and somewhat larger in size (3 to 6 micra in diameter on the slide).

11. Taking a general view of the data already presented in this series of studies, it is very interesting to note that the thickness of the cortex, the total number of the cortical nerve cells, and the size of the cortical cells all attain nearly their full values at the same age of twenty days (1.15 grams in brain weight); that is, at the weaning time of the albino rat.

PART II

ON THE INCREASE IN SIZE OF SOME NERVE CELLS IN THE CEREBRAL CORTEX OF THE NORWAY RAT (*MUS NORVEGICUS*) COMPARED WITH THE CORRESPONDING CHANGES IN THE ALBINO RAT

To compare with the results of the preceding study on the growth in size of the cortical nerve cells in the albino rat brain, data were gathered for the cortical cells of the Norway rat also. According to my previous studies (Sugita, '17 a, '18 a, '18 b), the measurements of the cerebral cortex in the Norway rat in thickness, in total number of cells, etc., have shown some interesting relations to the corresponding measurements for the Albino. Donaldson and Hatai ('11) made a comparison of these two animals in respect of their body measurements and the size of the central nervous system, and concluded that the greater weight of the brain in the Norway rat is probably due to an enlargement of the constituent neurons rather than to an increase in their number. As my former study (Sugita, '18 b) has de-

TABLE 6

Giving the average uncorrected diameters of the nerve cells and their nuclei in the lamina pyramidalis and the lamina ganglionaris measured at the fixed locality (locality VII) on the frontal sections of the Norway rat brain. The data are given for each brain weight group only. This table is comparable with table 1

BRAIN WEIGHT GROUP	NO. OF CASES	BRAIN WEIGHT	LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
			Cell body diameter		Nucleus diameter		Cell body diameter		Nucleus diameter	
			Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	Transv.	Longit.
			<i>grams</i>		μ	μ	μ	μ	μ	μ
N XI	3	1.164	15.2	20.8	14.5	15.5	20.5	29.0	18.1	19.3
N XIII	1	1.369	15.5	20.9	14.4	15.5	20.6	29.9	18.3	20.2
N XIV	6	1.430	15.4	20.6	14.2	15.1	21.6	29.6	18.4	19.4
N XV	3	1.546	14.8	19.8	13.8	15.1	20.5	28.9	17.8	19.6
N XVI	3	1.629	14.6	19.8	13.4	14.1	21.2	29.0	17.8	19.2
N XVII	4	1.739	14.9	20.4	13.8	14.7	21.9	29.8	18.9	20.2
N XVIII	2	1.829	15.0	20.7	14.1	14.8	23.5	32.8	20.7	21.5
N XIX	2	1.972	14.8	19.4	13.9	14.3	24.3	33.7	20.3	21.6
N XX	2	2.052	14.5	19.8	13.6	14.3	23.9	33.2	20.3	21.6
N XXI	2	2.172	14.3	20.0	13.3	14.2	23.9	34.0	19.4	21.0
N XXIII	1	2.345	14.6	21.0	13.3	13.9	25.0	36.0	18.5 ¹	20.5 ¹

¹ In this group the size of the nucleus of the ganglion cells has fallen down remarkably (see also chart 2), which fact was not seen in the Albino (Group XX). Whether this is due to an actual change in old age or due to incidental variation cannot be definitely affirmed here.

terminated that in both forms the total number of the nerve cells in the cerebral cortex is practically the same, it becomes desirable to compare the size of the nerve cells in the two animals in order to test the assumption of the above authors.

The material used in this study comprised 54 Norway rats, sexes combined, the data for which are given in tables 1 and 2 in a former paper (Sugita, '18 a) and which are the same material that was formerly employed for the other measurements on the cortex. It seems unnecessary to repeat these tables here.

In the selection of the localities in which the largest cells in the lamina pyramidalis and the lamina ganglionaris were measured and in making the measurements, the same procedure was followed as has been described minutely for the albino rat in part I of this paper.

TABLE 7

Giving the average uncorrected diameters of the nerve cells and their nuclei in the lamina pyramidalis and the lamina ganglionaris measured at the fixed locality (locality X) on the horizontal sections of the Norway rat brain. The data are given for each brain weight group only. This table is comparable with table 2

BRAIN WEIGHT GROUP	NO. OF CASES	BRAIN WEIGHT	LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
			Cell body diameter		Nucleus diameter		Cell body diameter		Nucleus diameter	
			Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	Transv.	Longit.
		<i>grams</i>	μ	μ	μ	μ	μ	μ	μ	μ
N XI	3	1.164	15.4	20.3	14.1	15.4	20.6	29.3	18.0	19.2
N XIII	1	1.343	15.2	19.9	14.1	15.1	20.4	28.2	17.8	19.0
N XIV	5	1.447	15.4	20.6	14.4	15.3	20.8	29.0	18.4	19.7
N XV	2	1.520	14.8	20.2	13.9	15.1	20.5	28.8	18.2	19.0
N XVI	4	1.663	14.9	20.0	13.8	14.9	21.0	29.8	18.3	19.3
N XVII	4	1.747	14.8	20.0	13.7	15.0	20.9	29.5	18.5	19.5
N XVIII	2	1.843	14.5	20.2	13.8	14.7	20.2	29.4	18.0	19.5
N XIX	1	1.953	15.1	20.8	14.5	15.3	23.5	30.5	19.5	20.3
N XX	2	2.018	15.5	21.1	14.2	14.7	23.5	31.0	18.8	19.0
N XXI	2	2.156	14.7	20.9	13.8	14.4	23.0	29.4	18.8	20.0
N XXIII	1	2.345	15.0	20.8	13.4	14.0	25.8	32.0	18.4 ¹	19.2 ¹

¹ See note on table 6.

The results of the measurements are presented in tables 6 and 7 arranged in the same way as in the corresponding tables 1 and 2 for the Albino. Chart 2 shows graphically the data presented in table 8 which gives the average diameters of the cell bodies and the nuclei for each brain-weight group, corrected for the fresh condition of the material, by multiplying by the correction-coefficient for the group, which is cited from my previous paper (Sugita, '18 a) and explicitly given in table 8 also. Charts 3 and 4 show some comparisons in cell sizes in the two forms. Chart 3 was plotted according to the actual brain weights of the two forms, and chart 4 was plotted, using the same data for the Norway, but entering these according to the brain weights reduced by 18 per cent, which presumably correspond to the brain weights of the Albino at the same age (see Sugita, '18 a), while the data of the Albino were plotted according to the actual brain weight.

TABLE 8

Giving the corrected final average diameters of the nerve cells and their nuclei in the lamina pyramidalis and the lamina ganglionaris measured on the frontal and the horizontal sections of the Norway rat brain. The average values of the two for each brain weight group are also given. The correction-coefficient for each brain weight group, was taken from previous papers (Sugita, '18 a, '18 b). F = frontal section. H = horizontal section.

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT	LAMINA PYRAMIDALIS		LAMINA GANGLIONARIS	
			Cell body diameter	Nucleus diameter	Cell body diameter	Nucleus diameter
	<i>grams</i>		μ	μ	μ	μ
F N XI	1.164	1.34	23.8	20.1	32.7	25.0
H N XI	1.164	1.30	23.0	19.1	31.8	24.2
	<i>1.164</i>		<i>23.4</i>	<i>19.6</i>	<i>32.3</i>	<i>24.6</i>
F N XIII	1.369	1.33	23.9	19.8	33.0	25.5
H N XIII	1.343	1.39	24.2	20.3	33.4	25.6
	<i>1.356</i>		<i>24.1</i>	<i>20.1</i>	<i>33.2</i>	<i>25.6</i>
F N XIV	1.430	1.35	24.0	19.7	34.2	25.5
H N XIV	1.447	1.36	24.2	20.3	33.5	25.9
	<i>1.439</i>		<i>24.1</i>	<i>20.0</i>	<i>33.9</i>	<i>25.7</i>
F N XV	1.546	1.40	23.9	20.2	34.2	26.2
H N XV	1.520	1.42	24.5	20.5	34.5	26.4
	<i>1.533</i>		<i>24.2</i>	<i>20.4</i>	<i>34.4</i>	<i>26.3</i>
F N XVI	1.629	1.40	23.8	19.3	34.7	25.9
H N XVI	1.663	1.34	23.2	19.2	33.5	25.2
	<i>1.646</i>		<i>23.5</i>	<i>19.3</i>	<i>34.1</i>	<i>25.6</i>
F N XVII	1.739	1.37	23.8	19.5	35.1	26.7
H N XVII	1.747	1.35	23.4	19.3	33.5	25.7
	<i>1.743</i>		<i>23.6</i>	<i>19.4</i>	<i>34.3</i>	<i>26.2</i>
F N XVIII	1.829	1.32	23.2	19.0	36.7	27.8
H N XVIII	1.843	1.39	23.8	19.7	34.0	26.0
	<i>1.836</i>		<i>23.5</i>	<i>19.4</i>	<i>35.4</i>	<i>26.9</i>
F N XIX	1.972	1.33	22.5	18.8	38.0	27.9
H N XIX	1.953	1.34	23.6	19.8	35.7	26.5
	<i>1.963</i>		<i>23.1</i>	<i>19.3</i>	<i>36.8</i>	<i>27.2</i>
F N XX	2.052	1.36	23.1	18.9	38.3	28.5
H N XX	2.018	1.32	23.9	19.0	35.6	25.0
	<i>2.035</i>		<i>23.5</i>	<i>19.0</i>	<i>37.0</i>	<i>26.8</i>

TABLE 8—Continued

BRAIN WEIGHT GROUP	BRAIN WEIGHT	CORRECTION-COEFFICIENT	LAMINA PYRAMIDALIS		LAMINA GANGLIONARIS	
			Cell body diameter	Nucleus diameter	Cell body diameter	Nucleus diameter
	<i>grams</i>		μ	μ	μ	μ
F N XXI	2.172	1.39	23.5	19.2	39.6	28.1
H N XXI	2.156	1.34	23.5	18.9	34.8	26.0
	<i>2.164</i>		<i>23.5</i>	<i>19.1</i>	<i>37.2</i>	<i>27.1</i>
F N XXIII	2.345	1.26	22.0	17.2	37.8	24.6
H N XXIII	2.345	1.28	22.6	17.4	36.8	24.1
	<i>2.345</i>		<i>22.3</i>	<i>17.3</i>	<i>37.3</i>	<i>24.4</i> ¹

¹See note on table 6.

Chart 2 shows for the Norway also that the ganglion cells are enlarging slowly but steadily throughout life, while the pyramids rather decrease in size slightly in later life, after having attained the maximum size in brains weighing 1.3 to 1.5 grams. So, in the Norway as in the case of the Albino, the pyramidal cells in the lamina pyramidalis undergo some diminution in the adult brain.

Chart 3 gives a comparison of the cell sizes in brains of like weight in the two forms. In Group N XI, the sizes of the cell body and the nucleus of the pyramids are slightly smaller in the Norway than in the Albino. This is probably explicable by the fact that the Norway brain at this stage is still immature and younger than the Albino brain of like weight. Such a relation has been revealed in other measurements also; for example, in the cortical thickness, the cortical area, etc. (Sugita, '17 a, '18 b). The ganglion cells in the Norway are larger than in the Albino and the difference in the size of the ganglion cells in the two forms increases somewhat as the brain weight advances.

In Groups above N XIII, the cell size (pyramidal and ganglion cells) in the Norway proved to be generally larger than that in the Albino of the same brain weight.

The summary in table 9 gives the average diameters for the adult Albino (Groups XIII to XX) and the adult Norway (Groups N XIII to N XX).

TABLE 9

Comparison of diameters of cortical cells in the Norway and the albino rats. The data used here are the averages in Groups XIII to XX and in Groups N XIII to N XX, taken from tables 3 and 8. Differences in diameter and in volume are calculated here, the data of the Albino being taken as the standard of comparison

	AVERAGE BRAIN WEIGHT	PYRAMIDS		GANGLION CELLS	
		Cell body	Nucleus	Cell body	Nucleus
	<i>grams</i>	μ	μ	μ	μ
Albino.....	1.691	22.9	18.8	32.4	24.9
Norway.....	1.694	23.7	19.6	34.9	26.3
Difference in diameter.....		3.5%	4.2%	7.7%	5.6%
Difference in volume.....		10.9%	13.1%	24.9%	17.8%

This summary shows that in mature brains of like weight, the pyramids (cell body and nucleus) in the Norway exceed those in the Albino in average diameters by about 4 per cent and in volume by about 12 per cent, and the ganglion cells (cell body and nucleus) in the Norway exceed those in the Albino in average diameters by about 7 per cent and in volume by about 20 per cent, if the Albino be taken as the standard of comparison. It may be said, therefore, that in the Norway the ganglion cells in the lamina ganglionaris exceed much in size those in the Albino, while the pyramids in the Norway are only somewhat greater than those in the Albino.

In chart 4, which gives a comparison of the nerve-cell sizes between brains of presumably the same age in the two forms, it is shown clearly that the changes in sizes of cell body and the nucleus according to age are quite similar in both forms. The pyramids attain the maximum size at about twenty to thirty days (in the Albino in brains weighing 1.1 to 1.3 grams, in the Norway in brains weighing 1.3 to 1.5 grams, which both come to the same relative position in the curves), and after that they decrease slowly. The ganglion cells in the Norway grow more rapidly than those in the Albino, even in later life. In the latter the ganglion cells remain almost unchanged in size in brains weighing 1.0 to 1.6 grams, while those in the Norway increase in size rather steadily as the age advances.

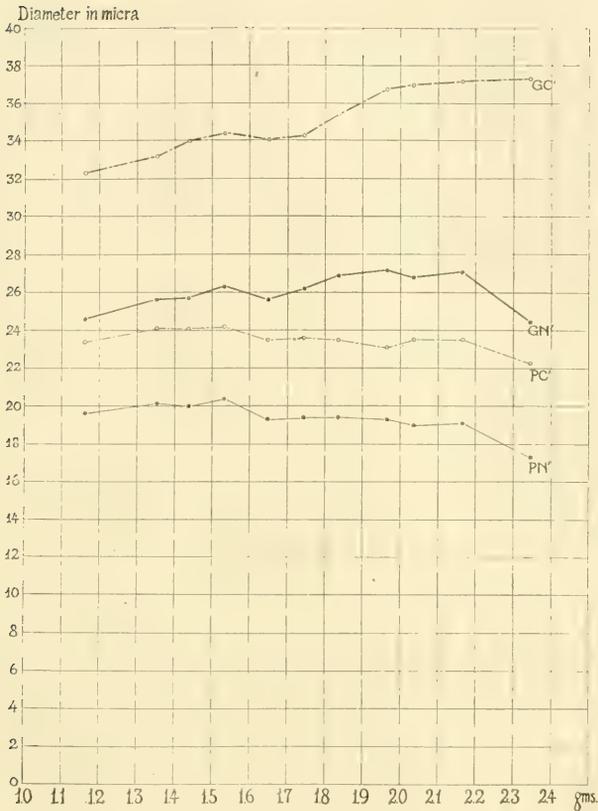


Chart 2 Showing the corrected average diameters of the cell body and the nucleus of the cortical nerve cells of the Norway rat, plotted according to increasing brain weight. Based on the data in table 7. Graph GC', average diameter of the cell body of the ganglion cells in the lamina ganglionaris. Graph GN', average diameter of the nucleus of the ganglion cells in the lamina ganglionaris. Graph PC', average diameter of the cell body of the pyramids in the lamina pyramidalis. Graph PN', average diameter of the nucleus of the pyramids in the lamina pyramidalis.



Chart 3 Showing a comparison of sizes of the cell bodies and of the nuclei of the ganglion cells in the lamina ganglionaris and of the pyramids in the lamina pyramidalis in brains of the Norway and the Albino, according to the actual brain weights. The data are taken from tables 3 and 7. The chart has been divided and the values 22-26 on the ordinate repeated to prevent confusion among graphs for the cell bodies of the pyramids, PC and PC', and the graphs for the nuclei of the ganglion cells, GN and GN'. In the upper chart: Graph GC', cell body of the ganglion cells in the Norway. Graph GC, cell body of the ganglion cells in the Albino. Graph GN', nucleus of the ganglion cells in the Norway. Graph GN, nucleus of the ganglion cells in the Albino. In the lower chart: Graph PC', cell body of the pyramids in the Norway. Graph PC, cell body of the pyramids in the Albino. Graph PN', nucleus of the pyramids in the Norway. Graph PN, nucleus of the pyramids in the Albino.

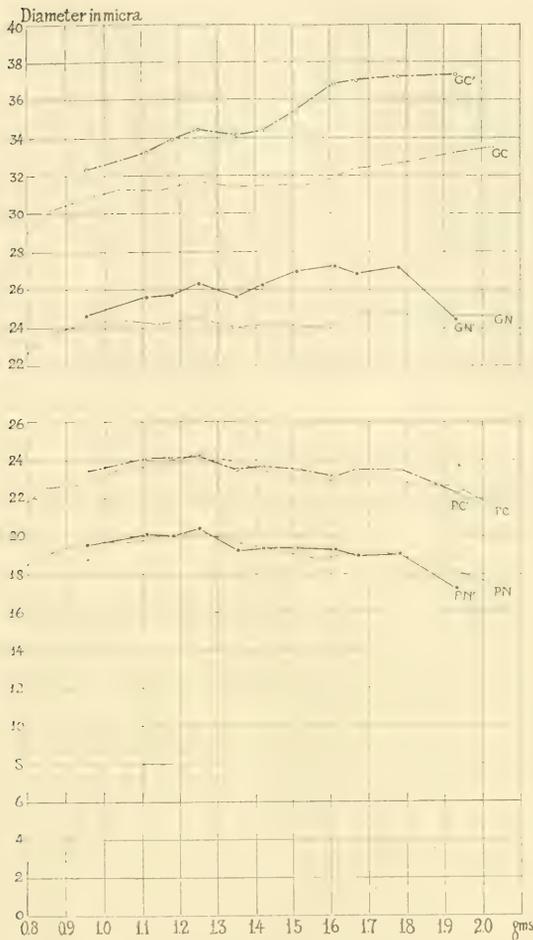


Chart 4. Showing a comparison of sizes of the cell bodies and of the nuclei of the ganglion cells in the lamina ganglionaris and of the pyramids in the lamina pyramidalis in brains of the Norway and the Albino, according to age. The Norway brain weight was reduced by 18 per cent and entered at the corresponding brain weight of the Albino. The data were taken from tables 3 and 7. The chart has been divided and the values 22-26 on the ordinate repeated to prevent confusion among the graphs for the cell bodies of the pyramids, PC and PC', and the graphs for the nuclei of the ganglion cells, GN and GN'. In the upper chart: Graph GC', cell body of the ganglion cells in the Albino. Graph GC, cell body of the ganglion cells in the Norway. Graph GN', nucleus of the ganglion cells in the Norway. Graph GN, nucleus of the ganglion cells in the Albino. In the lower chart: Graph PC', cell body of the pyramids in the Norway. Graph PC, cell body of the pyramids in the Albino. Graph PN', nucleus of the pyramids in the Norway. Graph PN, nucleus of the pyramids in the Albino.

My study of the Norway cortex did not extend to the early life of the animal, but, from the courses of the curves shown in chart 4, it seems probable that, in early life, before ten days after birth, the developmental changes in the cell size would be quite similar to those in the Albino, which have been minutely described in part I, and that we may therefore apply to the Norway rat also the same developmental phases as were formerly applied to the Albino.

Morphological changes in the cytoplasmic and nuclear structures in the Norway rat cells are similar to those in the Albino, if the comparison is made at like ages, so that figures 3 and 4 in part I of this paper may be considered to represent Norway cells as well.

Briefly stated, in the case of the Norway rat, the maximum size of the pyramids in the lamina pyramidalis (in brains weighing 1.3 to 1.5 grams) is cell body $21 \times 28 \mu$ and nucleus $20 \times 21 \mu$; values only slightly larger than those in the Albino. The final size of the ganglion cells in the lamina ganglionaris (in brains weighing 1.9 to 2.3 grams) is cell body $32 \times 43 \mu$ and nucleus $26 \times 27 \mu$, which is much larger than the corresponding measurements for the Albino.

Nissl bodies are already seen in brains weighing 1.13 grams—the youngest case in my material—but these bodies assume their mature appearance first in brains weighing more than 1.6 grams. As regards other developmental changes both in the cytoplasm and in the nucleus, the statements made for the Albino are all applicable to the Norway, if the comparison is made at like ages.

SUMMARY

1. In the full-grown Norway rat (Groups N XIX to N XXIII), the average size of the pyramids in the lamina pyramidalis is cell body $20 \times 27 \mu$, nucleus $18 \times 19 \mu$, and the average size of the ganglion cells in the lamina ganglionaris is cell body $32 \times 43 \mu$, nucleus $26 \times 27 \mu$.
2. The cell body and the nucleus of the pyramids attain their maximum size (cell body $21 \times 28 \mu$, nucleus $20 \times 21 \mu$) in brains weighing 1.3 to 1.5 grams, and after that they slightly diminish

in size, but the internal structure matures progressively as the brain weight increases. The cell body and the nucleus of the ganglion cells increases in size continuously throughout life. The last entry for the nucleus of the ganglion cells is an exception to this statement.

3. As compared with the corresponding cells in the albino rat, the pyramids in the adult Norway rat (Groups N XIII to N XX) exceed those in the Albino in diameter on the average by 4 per cent and in volume by 12 per cent and the ganglion cells also exceed in diameter on the average by 7 per cent and in volume by 20 or more per cent.

4. The course of development and the morphological changes in the Norway cells are similar to those in the albino rat, if compared at like ages. At the same age, the Norway brain weight, less 18 per cent, is taken as equal to the brain weight of the Albino.

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ON TACTILE RESPONSES OF THE DE-EYED HAMLET (EPINEPHELUS STRIATUS)¹

W. J. CROZIER

1. The observations herein discussed grew out of a first attempt to examine the physiology of excitation of the 'common chemical' sense in a teleost bearing a well-developed investment of scales. The work contemplated was rendered impossible, for reasons which will shortly appear, but the cause of the failure has a distinct bearing upon the original problem and a certain significance in several other directions as well.

Epinephelus striatus Bloch, the 'hamlet' or 'grouper,' was used in these experiments. The tests which were contemplated involved the local application of solutions to the skin of the hamlet, and it was necessary to employ fishes in which the chance of visual response had been eliminated. Recourse was had to the removal of the eyes rather than to the use of temporary blinding devices. Hamlets are exceedingly handy, and the removal of one or both eyes, usually while under chlorotone anaesthesia, was followed by quick recovery. Blinded individuals lived in the laboratory for more than four months.

In preliminary tests different regions of the surface of de-eyed hamlets were examined by applying to them from a pipette small volumes of acid and other solutions. Control experiments quickly demonstrated, however, that these fishes were reactive to the mere presence (or near approach) of the undischarged pipette, even when it contained only sea-water. A thoroughly cleaned glass rod, when carefully brought near a de-eyed hamlet, also induced responses of a deliberate and well-defined character.

A very pronounced degree of sensitivity is manifest in these responses, and the source of stimulation is rather precisely located

¹ Contributions from the Bermuda Biological Station for Research. No. 86.

by the blind fish. When a clean glass rod is carefully and very slowly brought near one side of the head, say to within 4.5 or 5 cm. of the gill cover, the fish bends in the opposite direction and swims slowly backward; or it may back deliberately away for 10 or 15 cm., then abruptly turn away from the side stimulated and assume a position at right angles to that held before being stimulated. When one side of the caudal peduncle is stimulated in this way, the tail is caused to bend away from that side, and the fish swims forward and usually turns in a complete half-circle away from the area of activation.

Unblinded fishes, when not resting on the bottom, usually give somewhat similar responses, although rarely so if any region other than the anterior end is being 'stimulated' by the near approach of a glass rod. With de-eyed individuals the best results are obtained when the fish is quietly swimming or is stationary in mid-water. As noted by Jordan ('17, p. 447), the normal hamlet usually lies on the bottom of an aquarium, particularly in the angle between a wall and the base of the container. When in the latter position, the hamlet does not usually react by body movements to the close approach of a glass or metal rod, although eye movements and increased vibrations of the pectoral or other fins may show that the foreign object is seen and perhaps also sensed in some additional manner. It frequently happened that responses of the kind described were not obtained from totally blinded hamlets when they were in a similar position; that is, when they were resting in a corner of the aquarium.

This applies also to hamlets from which only one eye had been removed; animals so prepared characteristically seek a corner of the aquarium²—a dark corner, if such be available—and for long periods remain in a fixed position with the side

² The aquarium used in most of these experiments was that already described in Jordan's paper ('17). It had solid wooden ends and plane glass sides. In working with hamlets having one or both eyes functional the arrangements were such that the experimenter was screened from the fish, and the glass, or other, rod was suspended from above and moved about by an appropriate arrangement of strings.

carrying the intact eye pressed against the confining wall. They seldom, if ever, moved in any way as the result of a solid object being brought near them on the *blind* side, although when actually touched on that side, however lightly, they made exceedingly violent escaping movements—much more vigorous movements, in fact, than are ordinarily evidenced by the normal seeing fish.

Whether or not the delicate form of sensitivity described for the completely blinded hamlet is present and actively functional in the unblinded animal cannot be decided from the facts so far given; but it can be shown that the responses in question are not the result of special sensory alterations determined by or during anaesthesia, since 1) different anaesthetics (chloroform, ether, chloretone) and various degrees of narcosis could be used for the de-eying operation without affecting the result in any way; 2) there is no discernible increase in sensitivity after a fish previously de-eyed has recovered from a second anaesthetization; 3) a non-de-eyed fish does not give responses of the character under discussion after recovery from (chloretone) anaesthesia; 4) several hamlets from which the eyes were removed *without* anaesthesia, gave well-defined reactions of this nature.

Inasmuch as the reactions to the careful approximation of solid bodies were secured very shortly after the operation, and were evident almost to their maximal extent within twenty-four hours, it is doubtful if the mere absence of the eyes has produced this form of sensitivity; the following results, as well as the studies upon normal individuals, support such a conclusion:

a) When the eyes of a medium-sized hamlet were covered by a cap of black velvet, the fish became very restless (owing to mechanical irritation of the harness required to fasten the cap); but after about ten hours, good 'avoiding reactions' were obtained upon the careful approach of a glass rod, both at the snout and at the caudal peduncle.

b) In several hamlets the cornea of either eye, or of both eyes, was rendered opaque by searing with a hot iron. The fishes so treated behaved respectively as did those with one or both eyes removed.

The delicate sensitivity manifested in the responses of the blind hamlet upon the near approach of foreign objects is therefore not induced by the absence of the eyes or by procedures incidental to their removal; it is present in the normal seeing fish, although reactions to which it might give rise are largely inhibited through visual and coarse mechanical stimulations (touch). It is obvious that this form of irritability, if present but unrecognized, might lead to serious errors in the interpretation of different phases of behavior not only in the hamlet, but also in other fishes where it may occur.

2. De-eyed hamlets, stationary in mid-water or slowly swimming, but not in contact with the bottom or walls of the aquarium, were found to show the following regional distribution of sensitivity to the gentle approach of the rounded end of a clean glass rod (3 mm. diameter): tip of the snout, side of head, caudal peduncle, top of head, side of body (especially in the region covered by the pectoral fin when it is folded back on to the body), anterior edge of the erect spinous dorsal fin, soft dorsal fin, caudal fin (except near its distal extremity).

The parts are arranged in the foregoing list according to the vigor of the reactions induced. No well-defined responses could be secured from the ventral surface of the animal nor from the pectoral or pelvic fins. The nature of the response varies with the different regions of the animal; thus, the spinous dorsal was pulled down close to the body when its anterior edge was approached, while the soft dorsal responded by vibratory movements.

About twenty-five individuals were carefully studied to determine the distribution of this sensitivity to 'contact at a distance.' The critical tests were made in filtered 'outside' sea-water (the circulating water of the laboratory being less alkaline than normal sea-water), and the conditions were so arranged that no shadows from the body of the experimenter or from the glass rod fell upon the surface of the fish. These tests were made upon single isolated fishes in non-running water.

Rods or wires of a number of different materials were found to induce reactions of this type. In all cases the rods were well

cleaned; metal rods or wires were brightly polished and the strips of wood were freshly planed. Tests were made with rods immediately after cleaning and also when they had lain in sea-water for an hour or more. The substances used were:

Metals: copper, platinum, gold, zinc, cadmium, aluminum, wrought iron, steel, galvanized iron, and brass.

Woods: 'cedar,' spruce, oak, elm and cypress.

Miscellaneous: glass, hard rubber, sealing-wax, soft rubber (red, white, and black tubing), porcelain, hard paraffin, sandstone, and compressed carbon.

The great variety of materials which induced the same response is sufficient to show that the process of stimulation did not depend upon the diffusion of chemical excitants nor (in the case of the metals) upon any 'action at a distance,' either primarily electrical or through the escape of charged atoms of metal (cf. Mathews, '07). The cadmium stick and the wires of platinum used in the tests were particularly pure, and no difference in the response they induced could be detected after they had been covered with neutral paraffin. The reactions are somewhat variable, and it is conceivable that some substance may stimulate in this fashion (i.e., 'chemically') more than others, but I could find no evidence of it in the hamlet. This point was tested with some care, because I had learned from Prof. G. H. Parker of reactions found by him with the catfish when approached by metal rods. Nor could I find anything of this sort in *Amphioxus*, *Balanoglossus*, sea-anemones, crabs (blinded), the 'rhizophores' of nudibranchs, or several teleosts that were examined.

Rods of brass, iron, glass, or wood of different diameters and shapes were then tried. Fishes of fairly uniform size (about 30 cm. length) were used in comparative experiments. To avoid, as far as possible, communicating undesired trembling movements to the rods, and thus to the water, the rods were in many tests clamped firmly in the middle of the aquarium and the behavior of the blinded hamlet when approaching them during slow swimming movements was compared with the result when a rod was carefully brought near a part of the body. The result was in

either case the same; when slowly swimming the de-eyed hamlet will most often neatly avoid contact with a rod or wire situated in its path, but more successfully if the end or edge of the rod presents a sharp corner. Similarly, in many cases, the fish is somewhat better stimulated by a thin wire (less than 1 mm. in diameter) than by a thicker one and by a rod of square cross section than by one of similar size (several centimeters in diameter) but with a smoothly rounded end and circular cross section.

The inference from these tests is, unavoidably, that mechanical deformations in the water, of a somewhat *irregular* character, are the means of stimulation. It was shown by appropriate elimination experiments that the nostrils and lateral-line organs could not be concerned, and this is further made obvious from a consideration of the local nature and manner of distribution of these reactions over the body of the fish.³

The mode of excitation in these reactions is in certain particulars significantly different from that in some reactions which have previously been attributed to tactile excitation of the skin in teleosts (cf. Parker, '04, pp. 61, 62; Jordan, '17). A current from a pipette or ripples at the water surface frequently failed to induce any perceptible reaction in a de-eyed hamlet, although immediately after this, or immediately before, a slender rod or wire slowly brought to within 5 cm. of the snout or caudal peduncle led to well-defined reactions. Moreover, it was often possible to get good reactions to a thin rod in water much disturbed by a current of relatively large volume.

The snout and lips of the hamlet were the most sensitive regions of the animal's surface. There is thus a general parallelism between the distribution of this delicate tactile sensitivity and that of skin sensitivity to currents, as described by Jordan ('17). Whether or not this indicates the activity of the tactile corpuscles in the reactions herein discussed, I am not sure; but I suspect that the tactile corpuscles may not be involved, although con-

³ It may be suggested that the reactions of Amoebae to insoluble substances, as described by Schaeffer ('16), are possibly due to some such form of irritability as that herein considered. Certain peculiar phenomena obtainable with human erythrocytes (Oliver, '14; Kite) are also suggestive in this connection.

clusive evidence for this belief cannot be adduced. The higher sensitivity of the anterior end of the de-eyed hamlet was not occasioned by the presence of freshly exposed tissue surfaces in the orbits or by other injuries, since in several cases the animals were kept in aquaria for more than four months, long after the orbit surfaces had cleanly healed, and their reactions were as distinct as those of recently de-eyed fishes.

The relatively acute sensitivity of the region behind each pectoral fin, as judged by the reactions obtained when it was approached by a rod, is probably a secondary condition, due to the fact that the pectoral fins are usually in slight motion, creating in the water waves which impinge upon these surfaces; any disturbance of these wave fronts or fin currents would result in a greater stimulus than that afforded by the near approach of a rod or wire to a stationary part.

3. I have ventured to describe these tactile reactions of the de-eyed hamlet at some length, because the fine, 'epieritic' nature of the sensitivity evidenced toward minute mechanical disturbances in the water is of particular use for the purposes of certain critical experiments regarding chemical stimulation of the skin of fishes. It will be observed that crude tests made by applying solutions from a pipette to the skin of *Epinephelus* would be quite pointless, since the blinded fish reacts with precision to the presence of the undischarged pipette. The degree of sensitivity in these delicate tactile reactions is nevertheless rather definitely fixed at a uniform level, as seen in the more than twenty-five individuals I have examined. The speed, vigor, and amplitude of these reactions give them a perfectly definite character. It is conceivable that this tactile sensitivity might be enhanced or diminished under various conditions and that such variations would be reflected in the behavior of the de-eyed fishes, and that, in fact, a good opportunity would be offered for discovering the way in which tactile terminals may be influenced by such treatment of the skin as is involved in the local application of chemical excitants. If, as is supposed by Coghill ('14, p. 197; '16, p. 302), those responses of fishes and amphibians usually regarded as being initiated through excitation of ter-

minals representing a 'common chemical sense,' are in reality due to the heterologous activation of tactile and pain terminals,⁴ owing to destruction of the epithelium, then it would be expected that the local application of irritants to the skin of the hamlet would produce one of two effects: either tactile sensitivity would be noticeably increased immediately thereafter or, following relatively severe treatment, it would be found more difficult to bring about tactile activation. In the former case it *might* be held that excitants for the 'common chemical' sense are capable of acting upon tactile receptors in a sensory way.

In testing this matter, my experiments dealt mainly with the areas of skin on either side of the caudal peduncle, although other regions were also examined, notably, the lips and gill-covers.

In different individuals these areas were treated with solutions of cocaine hydrochloride in sea-water by painting the surface in question (held out of water) with a brush. The dermal chromatopores in the region cocainized quickly contract and remain contracted for some hours. The area treated is sharply outlined by the blanching of the skin. The narcotized area is thus clearly delimited for reference in stimulation trials.

Even slight cocainization causes a complete suppression of the sensitivity to rods or wires, as well as to water currents; slightly stronger narcosis obliterates all responses to touch. Even then, however, the anaesthetized surface is fully active in the reception of stimulation from acid and alkaline solutions (HCl, NaOH, NH₄OH, n 20 n 40) or from dilute solutions of quinine. The sensitivity to delicate mechanical stimulation in these experiments returns with equal rapidity whether or not the narcotized area has been stimulated chemically while under anaesthesia.

The hamlet, normal or de-eyed, reacts to local treatment with n 20 NaOH or NH₄OH on the caudal peduncle after the spinal cord has been transected, but this operation obliterates the sensitivity to minute mechanical disturbances at all levels posterior to the cut and decreases the amplitude of responses of this nature in other regions.

⁴ A view suggested also by Watson ('14, pp. 419) and apparently accepted in some degree by Herrick ('16, pp. 85).

By several stimulations in rapid succession the vigor of the response elicited upon the near approach of a glass rod may be to some extent heightened. Such reactions are never so vigorous as those called forth by acid or alkali. If, however, tactile stimulation by this means be induced immediately after relatively severe chemical irritation (n 10 HCl from a pipette), it is found either that the local irritability is quite unaffected or that it is slightly decreased. With weaker acid, inducing, nevertheless, very vigorous reactions, no effect could be detected upon subsequent excitability by the near presence of glass rods or wires.

The results of the test thus briefly outlined are uniformly in agreement with the idea that (within physiological limits) the excitation of the 'common chemical sense' has nothing to do with tactile receptors or with the destruction of the epithelium, since the delicate form of 'touch at a distance' employed in the de-eyed hamlet shows no specific effects of a sort otherwise to be expected when the receptive areas of this sense are bathed with chemical excitants. These results make it impossible to suppose that acid, for example, could disorganize the skin (as suggested by Coghill) sufficiently to induce violent painful excitation and yet at the same time leave sensitivity to minute mechanical disturbances practically unaffected.

And if acid acted directly upon tactile receptors, it would be expected that organs of delicate tactile receptivity would behave toward subsequent mechanical activation as if they had recently been activated; as previously described, this is apparently not the case. It might be objected that the source of stimulation could not, in the 'tactile' experiments with wires and rods, be localized with sufficient precision for critical use. Yet this would be incorrect, as could very nicely be shown in tests made upon small narcotized areas of the skin. Regions (on the caudal peduncle) not more than 2 cm. in diameter were painted with cocaine, and when the pale anaesthetized part was approached with the end of a thin rod, no reactions followed, although similar spots 3 cm. away were of fully normal sensitivity.

This result confirms the conclusion which I supported in a previous paper ('16), to which Coghill ('16) has made further and (it

seems to me) quite unwarranted objection. According to a conception first formally advanced by Botezat ('10) and later applied by Parker ('12) to the general chemical irritability of moist surfaces in vertebrates, the stimulation of epithelial free nerve terminals is accomplished secondarily through the activity of substances diffusing from the more external epithelial cells (some of which may be supposed to be in a special receptive state, although this is not necessary) to deeper parts. There is obviously no necessity that the nerve terminals concerned be situated near the surface immediately exposed to the activating agent. The cells primarily activated by acid or alkali in the 'common chemical sense' experiments are undoubtedly those of the very outermost layer of the skin. A study of the conditions of chemical activation in primary receptors (of the earthworm) shows, or seems to show, that a chemical reaction occurs between the activating agent and some receptor constituent.⁵

This means that the acid or other agent stimulates after union with, or penetration of, the surface of the superficial cells. The acid or other substance does not act directly upon deeper layers of the skin, for the good and sufficient reason that the stimulation time is utterly inadequate for any such process, even though the changed condition in the cell primarily affected can obviously be transmitted from cell to cell through the whole depth of the epidermis in a very brief time.⁶ The fact that one small area of the skin may be excited repeatedly by acid or by alkali shows that no destructive action is wrought by these excitants (within reasonable limits of concentration).

It is becoming more and more necessary to recognize that receptor organs depend for their differential irritability upon the possession of specific substances which enter into excitation reactions. There is reason to suppose that in mechanical stimulation surfaces (intracellular, intercellular, or both) are tempo-

⁵ Some of the results of this investigation are in course of publication.

⁶ This primary effect may or may not be an increase in cell permeability, but it undoubtedly does involve an alteration in the relations between ions at the surfaces of the stimulated cells; hence the violent stimulating effect of distilled water under certain circumstances, as Loeb long ago found in the case of the frog's foot.

rarily broken down, to a certain extent, so that substances normally kept apart are free to intermix and react. There is no reason to expect that the products of the chemical activation of epithelial cells should be able to bring about a specific action upon tactile nerve endings or upon the specialized accessory end organs of the tactile sense. Tactile organs, 'corpuseles,' or what not may obviously be (and in fact frequently are) situated at some distance from the outer epithelial surface; it is probable, however, that the 'epieritic' form of irritability described in the hamlet depends upon very superficial structures; hence their particular value for the present research.

These considerations may enable one to see why it would be somewhat surprising to find tactile organs in fishes capable of being normally excited by acids, for example.

It is easily seen that differential anaesthesia is, by itself, in many cases a poor criterion of sensory differentiation; and yet, in the case of cocaine, when the results obtained by this method agree perfectly with other and quite independent methods of analysis, the results must perforce be accepted. In the present case it is rendered probable that the production of stimulation by chemical irritants applied to the general surface of *Epinephelus* has nothing to do with tactile receptors, and that the obliteration of tactile ('epieritic') sensitivity by cocaine is not an 'artifact' due to the specifically more intense action of the chemical irritants. Even in coelenterates there are indications that irritant chemicals and mechanical agencies respectively act in a sensory way upon differentiated receptors having diverse internal connections (Parker, '17), and the present observations confirm the idea that these agencies have modes of action in lower vertebrates as separate as they are in man.

4. Responses similar to those described for the de-eyed hamlet are exhibited by the normally blind cave fishes, according to Eigenmann (cited by Whitman, '99, p. 303). The parallelism is striking, since in both cases the direction from which a rod is being brought near is accurately located, while vibrations of a coarser order may not be responded to. In the blind fishes, however, this form of sensitivity is said to be more active in younger individuals than in adults.

Inasmuch as tactile sensitivity of a very highly developed character is present in the hamlet possessing well-developed functional eyes, there is no reason to believe that a similar superior degree of tactile irritability has been developed in the blind cave fishes as the result of their lack of vision.⁷

Concerning the function of this sense in *Epinephelus*, it may be suggested that it is useful at night or when the fish is maneuvering in darkened crannies of the 'coral reefs.'

SUMMARY

The de-eyed hamlet (*Epinephelus striatus*) gives well-defined reactions to the near approach of solid bodies. In the seeing fish this form of sensitivity is present, but motor effects which it might induce are almost completely inhibited. Mechanical deformations in the water of very minute amplitude and of a somewhat irregular nature are the source of stimulation in these responses, which cannot be attributed to chemical or to electrical disturbances. The presence of this exceedingly delicate form of sensitivity, generally distributed over the surface of the fish and leading to deliberate reactions of a well-defined character, has been used to discover any influence of chemical excitants, locally applied, upon the end organs of tactile sensitivity. Although the existence of this 'epicritic' form of irritability interferes with any direct study of the mode of excitation in 'common chemical sense' reactions, it can nevertheless be shown, with its aid, that the generally distributed 'common chemical' irritability of this fish does not involve tactile receptors. Since the hamlet with well-developed eyes exhibits a high degree of tactile discrimination, such as has been described for blind cave fishes,—although the existence of this sensitivity would be quite overlooked unless

⁷ It should be added that after living in the laboratory for more than four months after the removal of the eyes, three hamlets were carefully compared with several others recently de-eyed as regards their comparative 'tactile' irritability; no differences could be detected. Hence continued lack of vision does not lead to an increased development of the hamlet's 'epicritic' tactile irritability.

blinded animals were studied, —it is unnecessary to suppose that sensory structures appropriate to this type of irritability have been determined either by blindness or by life in caves.

AGAR'S ISLAND, BERMUDA.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

VII. ON THE INFLUENCE OF STARVATION AT AN EARLY AGE UPON THE DEVELOPMENT OF THE CEREBRAL CORTEX. ALBINO RAT

NAOKI SUGITA

From The Wistar Institute of Anatomy and Biology

TWO CHARTS

1. INTRODUCTION

Investigations on the influence of partial or complete starvation upon the growth of the body under various conditions have been made by many authors, and it has long been known that of all the organs the brain is least affected in weight by underfeeding while, in younger animals in active growth, the brain weight may even increase during severe underfeeding. These facts were early observed by Chossat ('43) in pigeons, Falek ('54) in dogs and Voit ('66) in cats, later by Bechterew ('95) in kittens and puppies and Lassarew ('97) in guinea-pigs, and recently by Hatai ('04, '08, '15), Donaldson ('11), Jackson ('15 a, '15 b), and others working in the albino rat. Jackson made experiments with complete and partial starvation on adult albino rats and also held the young albino rats at constant body weight for a considerable period by partial underfeeding, and in all his experiments the brain was found to be only slightly affected in weight. Hatai underfed young rats so as to cause a reduction of 30 per cent in total body weight, while the average loss in brain weight was only 5 per cent. According to Donaldson's experiments on the young albino rats (thirty days old) under moderate underfeeding for three weeks, it was found that the underfed are on the average 41.2 per cent less in body weight than the controls and nevertheless only 7.7 per cent less in brain weight.

According to my previous studies on the normal development of the cerebral cortex during the period of most active growth (Sugita, '17, '17 a, '18 a, '18 b, '18 c), it was found that the growth of the cortex is precocious and that its elementary organization (that is, the cortical thickness, the cortical cell number and cell size, etc.) is nearly completed at the time of weaning, when the albino rat is twenty days of age. The investigations by the several authors cited above were, however, made mostly on animals which were already weaned, because, of course, feeding experiments necessitate a strict food control. But at this stage (after weaning), the elementary organization of the cerebral cortex is already completed. For my object, which was to determine the effect of starvation on the early development of the cerebral cortex, it was necessary to use animals in which the growth of the cerebral cortex was still in active progress and to note the influence upon the organization of the cortex of longer and shorter periods of inadequate feeding.

For this it is necessary to use the very young animals, still dependent on the mother. During this period the growth impulse in the brain is especially strong and the results of underfeeding are somewhat peculiar, as the brain weight may even increase under severe underfeeding. In complete starvation, growth is stopped and the brain weight remains constant. Thus, von Bechterew ('95) studied on new-born kittens and puppies the influence of complete starvation upon the brain weight. His results were that the brain weight, at the time of death after three or four days of starvation, was like the initial weight of the organ at birth. The brain had not grown, but also it had not lost in weight.

By applying severe starvation to the albino rat immediately after birth, it has been my object in the present study to obtain answers to the following questions:

1. How far will the growth of the body and of the brain be arrested?
2. Will the normal relation between body weight, body length, and tail length be modified?

3. What will be the relation between body weight and brain weight in the underfed rats?
4. How far will the size and shape of the cerebrum be influenced?
5. Will the thickness of the cortex of the stunted rats be different from that of the standard?
6. How far will the volume of the cerebral cortex be modified?
7. Will the number of the cortical cells increase normally according to age?
8. Will the development in the size of the nerve cells be influenced by starvation?
9. What will be the effect of the starvation on the percentage of water and on the alcohol extractives?

2. THE TEST ANIMALS

After several preliminary tests on producing underfed young, I adopted the following three procedures, which are fairly reliable:

I. Separation of the young from the nursing mother for a maximum period each day.

II. Entrusting one mother with an excessive number of young and thus reducing the amount of milk available for each of the young.

III. Underfeeding the nursing mother and thus reducing the quantity of milk secreted.

I treated five litters by the first method (Series I), two litters by the second method (Series II), and one litter by the third method (Series III). The detailed records of these experiments are on file at The Wistar Institute of Anatomy and Biology. All the material, consisting of forty-six test individuals and fourteen controls, from the above eight litters, was supplied from the rat colony at The Wistar Institute. They are all from mothers of standard size which were kept throughout the experiment under good sanitary conditions.

This study was carried on from October, 1916 to July, 1917, at The Wistar Institute of Anatomy and Biology.

3. MATERIAL

Series I (Litters A, B, C, D, and E, table 1)

Procedure. In each litter, half of the young were selected for the experiment and marked with hectograph ink on the back and the remaining individuals were used as the controls. The young under experiment were taken away from the mother each day and kept packed in cotton in a warm place, but without any food or water, for the time which had been determined. Table 1 contains the records of the number of hours during which each test individual in this series was isolated each day.

Litter A (born October 16, 1916) was composed of nine young. Five (c, a, d, f, and h) were subjected to experiment and were separated from the mother daily beginning on the very day of birth, the foodless interval being increased day by day, as recorded in table 1. Sundays were excluded from any experimentation. The duration of starvation, daily and total, and the age at which the animals were killed is recorded also in table 1. Four controls (b, e, g, and i) were also killed one by one at the same ages as the test animals. The total hours of isolation, the average per day, and the percentage of hours isolated during the total life of the individual in hours, are given in the lower part of the table. As the young are not fed continuously, even when they were with the mother, this percentage will but roughly indicate the grade of underfeeding to which the young were subjected. They were killed for examination at the ages of 3, 4, 9, 11, and 15 days (see \times in table 1).

Litter B (born October 15, 1916) consisted of ten young. Five (a, c, e, f and i) were separated daily from their mother, as in the case of Litter A, and the remaining young (b, d, g, h, and j) were used as controls. The experiment was begun at the age of one day in Litter B, a day later than in the case of Litter A. They were killed for examination at the ages of 4, 8, 11, 12, and 19 days.

Litter A and B represent groups in which mild starvation was instituted from a very early age.

Litter C (born October 18, 1916) was composed of seven young, of which four (a, c, d, and f) were used for experiment and three

(b, e, and g) for control. The experiment was begun five days after birth. One test rat (f) and one control (g) were killed by the mother. For the first three days mild starvation was tried, and then, from the age of nine days, severe starvation was instituted. They were killed for examination at the ages of 15, 17, and 28 days.

Litter D (born October 23, 1916) consisted initially of eight young, of which five (a, c, d, e, and g) were used for experiment and three (b, f, and h) for control. One underfed (g) and one control (h) were killed by the mother. In this litter severe starvation was begun at the age of three days. The animals were killed at the ages of 9, 10, 16, and 18 days.

Litter E (born November 4, 1916) was composed of eight rats, of which six (a, b, c, d, g, and h) were selected for experiment and two (e and f) for control. Severe starvation with some intervals of feeding was begun at the age of three days. In this litter pairs of test rats of the same age were killed for examination (on the 7th, 10th, and 17th days of the experiment) to determine individual variations.

Litters D and E represent groups in which relatively severe starvation was begun at an early age.

Series II (Litters F and H)

Procedure. In this series one nursing mother was placed in charge of an excessive number of young. The results were not very good, because some relatively lucky or strong ones always got more than their share of milk, while the others were in a condition of severe underfeeding.

Litter F (born October 15, 1916). To a young small primipara, which had just given birth to ten young, were entrusted ten more young from two other litters which had been born on the same day. Unhappily, the young from three different litters were not separately marked. The rate of growth among them was later found to be unequal, owing probably partly to litter characteristics and partly to the inequality of the milk ration. Individuals were selected arbitrarily and killed for examination at intervals of one to three days (at the ages of 11, 14, 17, 19,

TABLE 1

Showing for each test individual in Series I the daily duration of starvation, total starved hours, their percentage to the entire duration of the test, all in the form of a diary, according to the age in days. The observed body and brain weights are also given for each individual. The dates of birth and of the beginning of the test are recorded in calendar days. X indicates the date of examination.

AGE, DAYS	LITTER A						LITTER B						LITTER C			LITTER D			LITTER E					
	Born October 16, 1916 Experiment began October 16, 1916						Born October 15, 1916 Experiment began October 16, 1916						Born October 18, 1916 Experiment began October 23, 1916			Born October 23, 1916 Experiment began October 26, 1916			Born November 4, 1916 Experiment began November 7, 1916					
	c♀	a♀	d♂	f♀	h♀		a♂	c♂	o♂	f♀	i♂	a♂	c♀	d♂	a♂	c♀	d♀	o♂	a♂	b♂	c♀	d♂	g♀	h♀
Birth	4	4	4	4	4		4	4	4	4	4		18	18	20	20	20	20	20	20	20	20	20	20
1	6	6	6	6	6		6	6	6	6	6		20	20	20	20	20	20	20	20	20	20	20	20
2	6	6	6	6	6		6	6	6	6	6		20	20	20	20	20	20	20	20	20	20	20	20
3	X	7	7	7	7		6	6	6	6	6		20	20	20	20	20	20	20	20	20	20	20	20
4		X	8	8	8		X	7	7	7	7		20	20	20	20	20	20	20	20	20	20	20	20
5			9	9	9			8	8	8	8		20	20	20	20	20	20	20	20	20	20	20	20
6			0	0	0			8	8	8	8		20	20	20	20	20	20	20	20	20	20	20	20
7			24	24	24			9	9	9	9		20	20	20	20	20	20	20	20	20	20	20	20
8			17	17	17		X	0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
9			X	18	18			24	24	24	24		20	20	20	20	20	20	20	20	20	20	20	20
10				18	18			0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
11				18	18			X	24	24	24		20	20	20	20	20	20	20	20	20	20	20	20
12				X	0			0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
13					0			0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
14					20			0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
15					X			20	20	20	20		20	20	20	20	20	20	20	20	20	20	20	20
16								20	20	20	20		20	20	20	20	20	20	20	20	20	20	20	20
17								16	16	16	16		20	20	20	20	20	20	20	20	20	20	20	20
18								20	20	20	20		20	20	20	20	20	20	20	20	20	20	20	20
19								0	0	0	0		20	20	20	20	20	20	20	20	20	20	20	20
20								22	22	22	22		20	20	20	20	20	20	20	20	20	20	20	20
21								20	20	20	20		20	20	20	20	20	20	20	20	20	20	20	20
22								22	22	22	22		20	20	20	20	20	20	20	20	20	20	20	20
23								20	20	20	20		20	20	20	20	20	20	20	20	20	20	20	20

20, 23, 24, 26, 30, and 40 days). Those killed were replaced by individuals of like age from other litters, so as to keep the number in this litter always above thirteen. After twenty days, the mother was removed and the young fed with a small amount of ordinary food. The last eight young, which survived beyond the age of forty days, were rejected as too old for the purpose of this study.

Litter H (born January 2, 1917). A mother having just given birth to eight young was entrusted with nine more young from another litter which had been born on the same day. The underfed young of this litter were all employed for the study on the percentage of water and for the histological study of myelination in the brain and not included in the study of the cerebral cortex.

Series III (Litter G)

Litter G (born October 23, 1916). In this series a nursing mother was severely underfed immediately after the parturition. This litter consisted of eleven young. Only a fraction (one-tenth to one-twentieth) of the ordinary diet with unlimited water was supplied daily to the mother. She was found to lose slowly in body weight day by day. The amount of milk was consequently much reduced, but not completely stopped, as could be determined by examining daily the stomach contents of the young. By this method I was able to get a series of young which were very poorly developed. The young were killed for examination at the ages of 8, 10, 11, 12, 15, 16, 18, 22, and 25 days.

Table 2 contains the observed body weight and brain weight of the young in Litters F, G, and H, when examined, for a comparison with table 1.

4. BODY WEIGHT, BODY LENGTH AND TAIL LENGTH

Table 3a (not published, because of its complexity, but on file at The Wistar Institute) gives for each individual in this study the sex, age, observed body length, tail length, and brain weight. The standard tail length and the standard brain weight for the observed body length were also entered for comparison, the

TABLE 2

Showing for each test individual in Series II and III (Litters F, G, and H) the sex, age, and body and brain weights, at time of examination

LITTER (SERIES II AND III)	SEX	AGE OF KILLING	BODY WEIGHT	BRAIN WEIGHT
		<i>days</i>	<i>grams *</i>	<i>grams</i>
F a	m	11	8.5	0.709
b	f	14	9.8	0.954
c	f	17	13.5	1.106
d	f	19	13.3	1.218
e	m	20	12.4	1.148
f	m	23	11.2	1.230
g	f	23	14.2	1.224
h	m	24	13.5	1.170
i	f	26	17.0	1.197
j	f	30	24.2	1.219
k	m	30	18.7	1.222
l	f	40	40.0	1.310
G a	m	8	7.5	0.679
b	f	8	7.4	0.703
c	f	10	10.3	0.864
d	m	11	9.8	0.929
e	f	12	8.8	0.907
f	m	15	7.3	0.881
g	m	16	7.3	0.948
h	m	18	9.6	1.119
i	f	22	12.2	1.110
j	m	25	17.2	1.234
H a	f	13	8.8	0.880
b	f	17	10.8	1.024
c	f	23	14.7	1.135
d	f	28	17.2	1.166
e	m	32	20.0	1.215
f	f	37	19.3	1.101
g	m	43	21.1	1.295

values having been calculated for each individual by the use of formulas given in 'The Rat' (Donaldson, '15). Here the body length was chosen as the basis for comparison, because the increase in body length has proved less variable than body weight. Table 3 was condensed from the original complete table (table 3a) by dividing the individuals, the tests, and controls within each litter into two groups, according to the observed brain

weight and taking averages for each group. Group I consists of those which have brains weighing less than 1.0 gram and presumably still in the first phases of cortical development (Sugita, '17 a) and Group II those which have brains weighing more than 1.0 gram and probably in the second or third phase of cortical development. So, one litter in Series I was divided into four groups, the tests having brain weights less than 1.0 gram (T. I), the tests having brain weights more than 1.0 gram (T. II), the controls having brain weights less than 1.0 gram (C. I) and the controls having brain weights more than 1.0 gram (C. II). This grouping prevails throughout all condensed tables (tables 3 to 13, 16 and 17) published in this paper. The average values were all obtained according to individual measurements, and the average standard values were also obtained by averaging from the full tables, which give the individual cases. As the standard values were not based on the average measurements given in the condensed tables, those standards given in the condensed tables sometimes deviate slightly from the standard values which would be directly obtained for the given average measurements.

On comparing, in table 3, the observed measurements with the corresponding standards, no significant difference between them has been detected, either in the underfed or in the controls. Only the body weight in the underfed is slightly lower as compared with the standard for the same body length, but it amounts to no more than 8 per cent.

This comparison indicates that, though the underfed young show a considerable retardation in total growth according to age (see table 4), yet the relation between the body and the tail lengths and the body weight is but little affected, at least during the early period of active growth. So the only marked difference between the underfed and the controls of the same body length or body weight would be the age, if their brain weights are disregarded. The effect on the brain weight will be discussed in the next chapter.

TABLE 3

Giving for each litter group in this study the average age, body length, tail length, and body weight, the last two compared with the corresponding standard measurements for the observed body length, calculated according to sex by the use of formulas given in 'The Rat' (Donaldson, '15). The general averages for the test and the control groups are given at the foot of the table. T = test, C = control.

SERIES, LITTER AND GROUP	TEST CONTROL	SEX	AVERAGE AGE	BODY LENGTH	TAIL LENGTH		BODY WEIGHT	
					Observed	Standard according to body length	Observed	Standard according to body length
<i>Series I</i>			<i>days</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>grams</i>	<i>grams</i>
A c, a, d, f h	T. I	1 m, 3 f	7-	56.3	26.5	26.3	7.2	7.1
	T. II	1 f	15	74.0	48.0	47.0	13.9	13.9
b, e, g i	C. I	3 m	8	66.7	31.7	37.0	11.7	10.2
	C. II	1 f	17	96.0	62.0	71.0	30.1	26.3
<i>Series I</i>								
B a, c, e, f i	T. I	3 m, 1 f	9-	59.8	27.8	29.8	7.3	7.9
	T. II	1 m	19	75.0	50.0	46.0	12.7	13.6
b, d g, h, j	C. I	2 f	6	57.0	25.5	27.5	7.1	7.0
	C. II	3 f	18-	86.3	53.3	61.3	20.5	20.3
<i>Series I</i>								
C a, e, d	T. II	2 m, 1 f	20	82.0	51.7	54.3	15.1	17.5
b, e	C. II	2 f	22-	98.5	71.5	73.5	27.6	29.4
<i>Series I</i>								
D a, e, d e	T. I	1 m, 2 f	12-	61.0	39.0	31.7	6.9	8.2
	T. II	1 m	18	78.0	54.0	49.0	13.0	15.0
b f	C. I	1 m	9	69.0	39.0	40.0	11.2	1.0
	C. II	1 m	22	91.0	65.0	63.0	24.0	21.9
<i>Series I</i>								
E a, b, c, d g, h	T. I	3 m, 1 f	12-	65.8	35.0	36.8	9.7	9.9
	T. II	2 f	20	82.0	58.0	56.0	16.2	17.9
e, f	C. II	1 m, 1 f	17-	87.0	56.5	60.0	21.6	20.4
<i>Series II</i>								
F a, b c-1	T. I	1 m, 1 f	13-	63.5	33.0	34.5	9.2	9.1
	T. II	4 m, 6 f	25+	83.9	61.5	57.1	18.1	19.4

TABLE 3—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	SEX	AVERAGE AGE	BODY LENGTH	TAIL LENGTH		BODY WEIGHT	
					Observed	Standard according to body length	Observed	Standard according to body length
			days	mm.	mm.	mm.	grams	grams
<i>Series III</i>								
G a-g	T. I	4 m, 3 f	11+	63.0	32.9	33.7	8.3	8.8
h-j	T. II	2 m, 1 f	22-	75.0	48.7	46.7	13.0	14.1
<i>Series II</i>								
H a	T. I	1 f	13	63.0	33.0	34.7	8.8	9.
b-g	T. II	2 m, 4 f	30	81.7	64.0	53.8	17.2	17.1
Average } (Series I-III)								
	T. I		11-	61.8	32.5	32.5	8.2	8.6
	T. II		21+	79.0	54.5	51.2	14.9	16.1
Average } (Series I)								
	C. I		8-	64.2	32.1	34.8	10.0	9.4
	C. II		19+	91.8	61.7	65.8	24.8	23.7

5. BODY WEIGHT AND BRAIN WEIGHT

Table 4 was condensed from table 4 a (unpublished), which gives data for each individual in this study, and shows for each group, in the three series, the sexes, average age, average duration of starvation (denoted by percentage value of the hours of isolation), and the observed body and brain weights, accompanied by the average values for the group of the individual standard weights, for the same ages, and of the individual standard brain weights for the same ages and for the same body weights. For the calculation of the standard values for each individual the sex was regarded, because in body and brain weights the sex difference is clear ('The Rat,' Donaldson, '15). The average differences of the observed values from the standards are given for each group in percentage, the standards being taken, respectively, as the norms for comparison.

A glance at the table reveals three differences which are clearly marked:

1. The underfed rats have, as a rule, body weights considerably less than the standard values for the same age.

2. The underfed rats have brain weights somewhat less than the standard values for the same age.

3. The underfed rats have brain weights markedly higher than the standard values for their observed body weight.

It was already noted in the introduction that the central nervous system as represented by the brain suffers little or no loss of initial weight even in the case of severe starvation. In my series—underfeeding of the albino rat at an early age—the body weight of the rats stunted by starvation, as compared with the standards for the same age, were deficient (on the average by litters, table 4) by from 19 to 44 per cent. On the other hand, the brain weights were less than the standards for the same age by from 4 to 12 per cent (for litters, table 4, but by from 3 to 17 per cent for individuals, table 4 a), while for the same body weights they were from 15 to 29 per cent (for litters, table 4, but up to 65 per cent for individuals, table 4 a) above the standard values.

Considering together all the five litters (A to E) of Series I, in which the young were starved by separating them at an early age from the mother daily, it appears that the underfed rats at the end of the first twenty days after birth (during the suckling period) are about 29 per cent (average of A, T. I and II, B, T. I and II, C, T. II, D, T. I and II, and E, T. I and II) behind the standards in body weight, while they are only 8 per cent (average of the above-cited cases) behind in the brain weight. In Series II and III, in both of which the young were subjected to early and continuous underfeeding, increasing in intensity, by the method of reducing the ration of milk, but without removal from the nest, the underfed young have shown a slightly better development in brain weight (in relation to body weight), the average being also 8 per cent (average of F, T. I and II, G, T. I and II, and H, T. I and II) less than the standard for the same age, while the body weight is on the average as much as 39 per cent (average of the above-cited cases) below the standard value. Whether removing the young from the nest increases the relative effect of underfeeding on the brain, as these results suggest, can be determined only by experiments with that question as the main point in view.

In connection with the underfeeding, as practiced in Series I, some interesting results of overfeeding have been noticed in the control animals; overfeeding having taken place in the case of the controls of Litters A to E on account of the periodic isolation of a number of the members of the litter. The controls have shown generally, as seen in table 4 a (unpublished) and also in table 4, some excess in body and brain weights, as compared with the standard values for the same age. The excess in body weight is on the average 19 per cent (average of A, C. I and II, B, C. I and II, C, C. II, D, C. I and II, and E, C. II), while the brain weight is on the average 6 per cent (average of the above-cited cases) higher than the standard for the same age and 2 per cent higher than the standard for the same body weight. Thus, by moderate overfeeding, the growth in body weight is definitely accelerated and, at the same time, the growth in brain weight is also accelerated, nearly in proportion to the increase in body weight.

If the observed brain weights are compared with the standard brain weights for the observed body weight, it is clearly seen that the observed brain weights are higher than the standard by 24 per cent (average of all eight litters T. groups only). Of course, the younger the individual, the higher is the percentage, because the standard brain weight is smaller in the young animals and they are not increasing in direct proportion to the body weight, but nearly as the logarithm of the latter value. So it may be roughly stated that the brain weights in the underfed young albino rats have values below the standard weights for the same age and above those for the same body weights, but always falling nearer to the standard age values.

6. THE SIZE AND SHAPE OF THE CEREBRUM

The five diameters of the cerebrum of the underfed young were measured and recorded according to the procedure already described in my first paper of this series (Sugita, '17, figs. 1 and 2). The measurement *W.B.*, represents the greatest frontal diameter; the measurement *W.D.*, the frontal diameter passing the middle point of the fissura sagittalis; the measurement *L.G.*, the greatest distance from the frontal pole to the occipital

TABLE 4

Showing for each litter group in this study the average age, duration of isolation denoted by the percentage of the life span, observed body weight, compared with the standard body weight for the same age, and observed brain weight, compared with the standard values for the same age and the observed body weight, respectively. Standard values were all calculated by the use of the formulas given in 'The Rat' (Donaldson, '15). Within each litter the starved animals were divided into two groups, T. I having brains weighing less than 1.0 gram and T. II having brains weighing more than 1.0 gram. The control animals were also grouped in the same way into two groups, C. I and C. II. Averages were taken within each group. In lines designated 'percentage difference' (abbreviated 'per. diff. '), the deviations of the observed measurements from the standard values were given in percentage, the respective standard values being taken as standards of comparison. At the foot of the table, the average as to the test and control groups are given and the percentage differences from the standards are also calculated.

SERIES, LITTER AND GROUP	TEST CONTROL	SEX	AVERAGE AGE	STARVED: DURATION IN PERCENTAGE OF HOURS OF LIFE		BODY WEIGHT		BRAIN WEIGHT		
				Observed	Standard according to age	Observed	Standard according to age	Standard according to observed body weight		
			days	per cent	grams	grams	grams	grams	grams	
<i>Series I</i>										
A e, a, d, f	T. I	1 m, 3 f	7-	32	7.2	9.7	0.584	0.644	0.441	
h	T. II	1 f	15	44	13.9	16.5	1.024	1.048	0.952	
(per. diff.)						(-19)		(-5)	(+15)	
b, e, g	C. I	3 m	8		11.7	10.9	0.740	0.750	0.790	
i	C. II	1 f	17		30.1	18.1	1.278	1.099	1.301	
(per. diff.)						(+44)		(+9)	(-4)	
<i>Series I</i>										
B a, c, e, f	T. I	3 m, 1 f	9-	30	7.3	11.4	0.644	0.775	0.468	
i	T. II	1 m	19	44	12.7	18.7	1.052	1.131	0.901	
(per. diff.)						(-34)		(-11)	(+24)	
b, d	C. I	2 f	6		7.1	8.6	0.543	0.559	0.437	
g, h, j	C. II	3 f	18-		20.5	18.7	1.144	1.112	1.148	
(per. diff.)						(+1)		(+1)	(+6)	
<i>Series I</i>										
C a, c, d	T. II	2 m, 1 f	20	44	15.1	20.4	1.105	1.146	0.946	
(per. diff.)						(-26)		(-4)	(+17)	
b, e	C. II	2 f	22-		27.6	22.6	1.307	1.165	1.234	
(per. diff.)						(+22)		(+12)	(+6)	

TABLE 4—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	SEX	AVERAGE AGE	STARVED: DURATION IN PERCENTAGE OF HOURS OF LIFE	BODY WEIGHT		BRAIN WEIGHT		
					Observed	Standard according to age	Observed	Standard according to age	Standard according to observed body weight
			days	per cent	grams	grams	grams	grams	grams
<i>Series I</i> D a, c, d e (per. diff.)	T. I	1 m, 2 f	12—	57	6.9	14.0	0.778	0.943	0.437
	T. II	1 m	18	65	13.0	18.0 (-38)	1.089	1.112 (- 9)	0.921 (+37)
b f (per. diff.)	C. I	1 m	9		11.2	11.8	0.870	0.840	0.782
	C. II	1 m	22		24.0	21.1 (+ 7)	1.220	1.184 (+ 3)	1.237 (+ 4)
<i>Series I</i> E a, b, c, d g, h (per. diff.)	T. I	3 m, 1 f	12—	46	9.7	14.3	0.835	0.977	0.664
	T. II	2 f	20	44	16.2	20.7 (-26)	1.122	1.159 (- 8)	1.042 (+15)
e. f (per. diff.)	C. II	1 m, 1 f	17—		21.6	17.3 (+25)	1.179	1.077 (+ 9)	1.171 (+ 1)
<i>Series II</i> F a, b c-l (per. diff.)	T. I	1 m, 1 f	13—		9.2	14.9	0.832	1.000	0.631
	T. II	4 m, 6 f	25+		18.1	25.6 (-33)	1.204	1.231 (- 9)	1.046 (+21)
<i>Series III</i> G a-g h-j (per. diff.)	T. I	4 m, 3 f	11+		8.3	13.6	0.844	0.914	0.561
	T. II	2 m, 1 f	22—		13.0	21.5 (-39)	1.154	1.181 (- 5)	0.871 (+39)
<i>Series II</i> H a b-g (per. diff.)	T. I	1 f	13		8.8	15.1	0.880	1.003	0.600
	T. II	2 m, 4 f	30		17.2	31.5 (-44)	1.156	1.298 (-12)	1.045 (+24)
Average (Series I-III) (per. diff.)	T. I		11—		8.2	13.3 (-38)	0.771	0.895 (-14)	0.543 (+42)
Average (Series I-III) (per. diff.)	T. II		21+		14.9	21.6 (-31)	1.113	1.163 (- 4)	0.966 (+15)

TABLE 4—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	SEX	AVERAGE AGE	STARVED: DURATION IN PERCENTAGE OF HOURS OF LIFE	BODY WEIGHT		BRAIN WEIGHT		
					Observed	Standard according to age	Observed	Standard according to age	Standard according to observed body weight
			days	per cent	grams	grams	grams	grams	grams
Average (Series I) (per. diff.)	C. I		8-		10.0	10.4	0.718	0.716	0.670
						(- 4)		(+ 0)	(+ 7)
Average (Series I) (per. diff.)	C. II		19+		24.8	19.6	1.226	1.127	1.218
						(+27)		(+ 9)	(+ 1)

pole; the measurement *L.F.*, the sagittal diameter from the frontal to the occipital pole running parallel to the sagittal fissure, and the measurement *Ht.* is the greatest vertical height at the stalk of the hypophysis. In table 5, which was condensed from table 5 a (unpublished) for each individual, the average brain weight, the average measurements *W.B.*, *L.G.* and *Ht.* are given for each group, both test and control, compared with the corresponding standard measurements for the brains of the same weight, which were originally calculated for each individual using the formulas formerly presented by me (Sugita, '17), and then condensed. The measurements *L.F.* and *W.D.* are given, also condensed for each group, in table 9.

On examining table 5, it appears that the measurement *W.B.* of the underfed is smaller on the average by 2 per cent (average of all eight litters, T. groups only) than standard for the brains of the same weight, while the measurement *L.G.* of the underfed is greater on the average by 2 per cent (average of all eight litters, T. groups only). The height in the underfed seems to be slightly less, by about 1 per cent on the average. On the other hand, if the controls be considered in the same way, they show also slight deviations from the calculated standard values, thus, on the average (Litters A to E, C. groups only), *W.B.* is smaller by 1 per cent, *L.G.* greater by 0.8 per cent and *Ht.* smaller by about 3 per

cent in the controls. As a matter of fact, the measurement of *Ht.* could not be so accurate on account of difficulty in fixing the dorsal limit, so that these slight differences in *Ht.* should not be taken too seriously. The measurement of *L.G* and *W.G* can be made accurately so that these results are trustworthy.

Taking these deviations in the controls into account, the general statement may be made that underfeeding alters the shape of the cerebrum, so that it becomes slightly elongated, when compared with the normal cerebrum of the same weight. This difference is probably due to the fact that, although the underfed cerebrum is arrested in growth, it nevertheless tends to enlarge normally and, as already determined (Sugita, '17) becomes more and more elongated as the age advances.

If, for the brains of like weight, the width-length indices obtained by the formula $\frac{W.D \times 100}{L.F}$ are compared between the underfed and the controls (compare table 9) or the standard values (based on table 3, Sugita, '17), it will be seen that the index value tends to be lower in the underfed, especially in the members of Litters F and G which were underfed continuously and rather severely. In the latter litters the index values for each individual are smaller by 2 to 7 points than the index values for the standard brains of like weights (the data for these calculations are contained in table 9 a, not here published). The average index values in Litters F and G are 102 (for T. I groups) and 97 (for T. II groups), while the corresponding standard values are, respectively, 106 and 103 (Sugita, '17).

7. THICKNESS OF THE CEREBRAL CORTEX

Tables 6 a, 6 b, and 6 c (all unpublished) were originally prepared to give the cortical thickness for each individual as measured at the localities I to VIII in the sagittal and frontal sections and to give the average cortical thickness in each section and the general average thickness, to be compared with the respective standards presented in a former paper (Sugita, '17a). Table 6, which follows, contains in condensed form the corrected data for the thickness of the cerebral cortex of the underfed Albinos and that of

TABLE 5

Giving for each litter group in this study the average brain weight and the average measurements L.G, W.B and Ht. of the cerebrum, each compared with the corresponding standard values for the same brain weight, calculated by the use of the formulas given by me (Sugita, '17). The averages for the test and control groups are given at the foot of the table.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE BRAIN WEIGHT	W. B.		L. G.		Ht.	
			Observed	Standard	Observed	Standard	Observed	Standard
		grams	mm.	mm.	mm.	mm.	mm.	mm.
<i>Series I</i>								
A c, a, d, f h	T. I	0.584	10.79	10.94	9.69	9.20	6.99	7.06
	T. II	1.024	13.05	13.00	12.30	12.30	8.45	8.70
b, e, g i	C. I	0.740	11.63	11.90	10.73	10.63	7.50	7.68
	C. II	1.278	13.85	14.00	13.15	13.25	8.95	9.30
<i>Series I</i>								
B a, c, e, f i	T. I	0.644	11.11	11.38	10.25	9.96	7.36	7.38
	T. II	1.052	13.20	13.15	12.35	12.40	8.50	8.75
b, d g, h, j	C. I	0.543	10.50	10.78	9.73	9.18	6.90	6.95
	C. II	1.144	13.47	13.48	12.75	12.77	8.68	9.00
<i>Series I</i>								
C a, c, d	T. II	1.105	13.10	13.35	12.72	12.62	8.70	8.88
	C. II	1.307	13.78	14.10	13.63	13.33	8.83	9.40
<i>Series I</i>								
D a, c, d e	T. I	0.778	11.67	12.17	11.25	10.80	7.98	7.92
	T. II	1.089	12.90	13.30	12.75	12.55	8.60	8.85
b f	C. I	0.870	12.25	12.60	11.40	11.65	8.00	8.20
	C. II	1.220	13.95	13.80	13.30	13.05	8.80	9.20
<i>Series I</i>								
E a, b, c, d g, h	T. I	0.835	12.08	12.41	11.35	11.16	8.29	8.10
	T. II	1.122	13.35	13.40	12.68	12.70	8.98	8.95
e, f	C. II	1.179	13.55	13.60	12.78	12.85	8.88	9.05
<i>Series II</i>								
F a, b c-l	T. I	0.832	12.00	12.53	11.50	11.13	7.95	8.05
	T. II	1.204	13.30	13.73	13.11	12.98	9.30	9.15
<i>Series III</i>								
G a-g h-j	T. I	0.844	12.22	12.46	11.46	11.32	8.13	8.69
	T. II	1.154	13.27	13.53	13.03	12.80	8.95	9.00
Average (Ser. I-III)	T. I	0.753	11.65	11.98	10.92	10.60	7.78	7.87
	T. II	1.107	13.17	13.35	12.71	12.62	8.78	8.90
Average (Ser. I)	C. I	0.718	11.46	11.76	10.62	10.49	7.47	7.61
	C. II	1.226	13.72	13.80	13.12	13.05	8.83	9.19

the controls from the same litter, and it gives for each group, underfed and controls, the average brain weight and the corrected cortical thickness in the sagittal and frontal sections of the brain, together with the average thickness. The data for obtaining the correction-coefficient are given in the full table for each individual, but in the condensed table 6 only the average values of the correction-coefficients for each group appear. The application of the correction-coefficient was made in the way formerly described (Sugita, '17 a). The horizontal sections of underfed brains were not prepared for this study.

Table 6 shows also a comparison of the average thickness of the cortex in the underfed young with that for the standard Albino of the same brain weights. As the present study was not extended to the horizontal sections, the average thickness of the cortex was determined from only the two kinds of sections from the same individual and it was compared with the corresponding average for the standards. In the standards, these values proved to be within 0.5 per cent of the general average thickness of the cortex based on the three kinds of sections. Here, in table 6, the standard values were obtained from the somewhat smoothed curve based on the data formerly presented (table 9 and chart 9, Sugita, '17a).

Table 6 a (unpublished) for the sagittal section showed for the underfed that the cortical thickness at the frontal pole (locality I) is evidently very much greater than that of the controls or the corresponding standard value for the same brain weight, comparison having been made on the basis of the data given formerly (table 6 and chart 4, Sugita, '17 a). Locality II was the next which exceeds in the cortical thickness on the side of the underfed. Localities III and IV stand in general slightly in favor of the underfed, but at locality V, the occipital pole, there was found no notable difference in the cortical thickness between the underfed and the standard. As a rule, the cortical thickness of the normal Albino diminishes from the frontal to the occipital pole—from locality I to locality V—and the cortex at the frontal pole increases most rapidly in the early age. This is also just the order of the excesses in the cortical thickness of the underfed

when compared with the standard values for the brains weighing the same. The cortical thickness at each locality of the controls was on the average fairly in accord with the standard (the detailed evidence for these conclusions is contained in table 6 a, not here published).

In table 6 b (unpublished), in which the cortical thickness at localities VI, VII, and VIII of the frontal section was given, it was also clearly seen that the localities VI and VII are much greater in the cortical thickness, compared with those of the controls or the standard values of the same brain weight. The excess amounts on the average to more than 10 per cent. The locality VIII, at which the cortex is heterogeneous in laminar structure, did not show any significant difference in the cortical thickness, compared with the normal, though in some cases here and there it was found somewhat thicker in the underfed (the evidence for these determinations is contained in table 6 b, not here published).

One more notable thing found in the cerebral cortex of the underfed was that, while in the controls and standards the locality VII is always somewhat greater in thickness than the locality VI, the relation has, in many cases (18 out of 44) of the underfed, proved to be reversed (A a, h; B i; C a, c; D d, e; E c, h; F b, c, f, h; G a, e, g, e and h).

Generally considered, the localities which are situated nearer to the ventricular wall, the locus of the cell division, seem to have gained much more in the cortical thickness in the case of the underfed, while the localities remote from the matrix (for example, locality V) or the part constructed heterogeneously (for example, locality VIII) appear to be modified but little by underfeeding.

As is to be seen in table 6, the average thickness of the cortex is in favor of the underfed Albinos. If compared with the standard values for the same brain weight, the average cortical thickness in the underfed young (table 6) is greater than the standard on the average by 7 per cent (average of all eight litters, T. groups only), while the controls are greater on the average by only 1.8 per cent (average of Litters A to E; C. groups only). According

TABLE 6

Giving for each litter group in this study the average age, brain weight, and the average cortical thickness in the sagittal and frontal sections. The general average cortical thickness was obtained and compared with the standard value for the same brain weight, quoted from a previous paper (Sugita, '17a). The data for each individual and for each locality of the cortex were originally tabulated in three full tables (tables 6a, 6b and 6c) which are on file at The Wistar Institute and from which this table 6 was condensed. The correction-coefficients are given in averages for each litter group for each kind of section. The averages for the test and control groups are given at the end of the table.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	SAGITTAL SECTION		FRONTAL SECTION		AVERAGE	
				Correction coefficient	Cortical thickness	Correction coefficient	Cortical thickness	Cortical thickness	Standard for the same brain weight
		days	grams		mm.		mm.	mm.	mm.
<i>Series I</i> A c, a, d, f h	T. I	7--	0.584	1.16	1.24	1.18	1.47	1.35	1.69
	T. II	15	1.024	1.21	1.64	1.28	2.05	1.85	1.73
	C. I	8--	0.688	1.09	1.34	1.14	1.46	1.40	1.38
	C. II	17	1.278	1.23	1.77	1.26	2.00	1.89	1.84
<i>Series I</i> B a, c, e, f i	T. I	9--	0.644	1.12	1.33	1.17	1.53	1.43	1.40
	T. II	19	1.052	1.20	1.66	1.37	2.15	1.91	1.74
	C. I	6	0.543	1.08	1.18	1.09	1.32	1.25	1.25
	C. II	18--	1.144	1.24	1.74	1.31	2.01	1.88	1.80
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	1.17	1.74	1.25	2.08	1.91	1.77
	C. II	22--	1.307	1.17	1.76	1.16	1.97	1.87	1.85
<i>Series I</i> D a, e, d e	T. I	12--	0.778	1.15	1.54	1.24	1.89	1.72	1.61
	T. II	18	1.089	1.17	1.73	1.28	2.10	1.92	1.77
	C. I	9	0.870	1.13	1.55	1.22	1.87	1.71	1.67
	C. II	22	1.220	1.14	1.78	—	—	—	1.82
<i>Series I</i> E b, e, d, g, h	T. I	12	0.867	1.11	1.53	1.23	1.95	1.74	1.66
	T. II	20	1.122	1.20	1.81	1.26	2.15	1.98	1.79
	C. II	17--	1.179	1.10	1.68	1.21	1.94	1.81	1.79

TABLE 6—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	SAGITTAL SECTION		FRONTAL SECTION		AVERAGE	
				Correction coefficient	Cortical thickness	Correction coefficient	Cortical thickness	Cortical thickness	Standard for the same brain weight
		<i>days</i>	<i>grams</i>		<i>mm.</i>		<i>mm.</i>	<i>mm.</i>	<i>mm.</i>
<i>Series II</i>									
F a, b	T. I	13—	0.832	1.17	1.57	1.21	1.8	1.72	1.62
c-l	T. II	25+	1.204	1.24	1.81	1.32	2.15	1.98	1.82
<i>Series III</i>									
G a-g	T. I	11+	0.844	1.14	1.55	1.24	1.89	1.72	1.63
h-j	T. II	22—	1.154	1.19	1.78	1.26	2.15	1.97	1.80
Average } (Ser. I-III)	T. I	11—	0.758	1.14	1.46	1.21	1.77	1.61	1.54
	T. II	20—	1.107	1.20	1.74	1.29	2.2	1.93	1.77
Average } (Ser. I)	C. I	8—	0.700	1.10	1.36	1.15	.55	1.45	1.43
	C. II	19+	1.226	1.18	1.75	1.4	1.98	1.86	1.82

to table 6 c (unpublished), which gives comparisons of cortical thickness of the underfed with the standard in each section, the average cortical thickness in the sagittal section of the underfed exceeds the standard on the average by 5.3 per cent and that in the frontal section of the underfed on the average by 8.7 per cent.

8. AREA OF THE CORTEX IN THE SAGITTAL AND FRONTAL SECTIONS

Following the procedures which have been described earlier for the measurement of the area of the cortex in the sagittal and frontal sections of the Albino brains (Sugita, '18 b), the data for the underfed Albinos were obtained. Table 7 presents in condensed form for each group the averaged data on the corrected area of the cortex together with the average correction-coefficient for each group, in the sagittal and frontal sections, respectively. The observed data, as measured on the slides, and the data for correction-coefficient for each individual were tabulated in tables 7 a and 7 b (unpublished), on the basis of which table 7 was made. In table 7 (and in table 7 b) the total areas of the frontal sections (one hemisphere) and the percentage of the cortical area to the total area of the section are also entered.

TABLE 7

Giving for each litter group in this study the average brain weight, the corrected areas of the cortex in the sagittal and frontal sections, and the total area of the frontal section and the average correction-coefficients for each group for each kind of section. The percentage values of the cortical area to the area of the total section in the frontal section are also given for each group. This table was condensed from two detailed tables for individual observed data and the data for the correction-coefficients. The averages for the test and control groups are given at the foot of the table

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE BRAIN WEIGHT	SAGITTAL SECTION		FRONTAL SECTION			
			Correc-tion-co-efficient	Area of cortex	Correc-tion-co-efficient	Area of cortex	Total area of section	Percent-age of cortical area to the total area
		grams		mm. ²		mm. ²	mm. ²	per cent
<i>Series I</i> A c, a, d, f h b, g i	T. I	0.584	1.16	14.6	1.18	13.4	28.8	45
	T. II	1.024	1.21	22.2	1.28	22.8	45.0	51
	C. I	0.688	1.09	17.4	1.14	15.2	31.9	46
	C. II	1.278	1.23	27.4	1.26	21.7	43.6	50
<i>Series I</i> B a, c, e, f i b, d g, h, j	T. I	0.644	1.12	16.9	1.17	15.0	31.6	47
	T. II	1.052	1.20	23.3	1.37	23.4	45.7	51
	C. I	0.543	1.08	9.1	1.09	11.6	25.1	46
	C. II	1.144	1.24	24.6	1.31	21.7	45.3	47
<i>Series I</i> C a, c, d b, e	T. II	1.105	1.17	24.5	1.25	22.0	43.6	50
	C. II	1.307	1.17	27.8	1.16	22.2	46.0	48
<i>Series I</i> D a, c, d e b f	T. I	0.778	1.15	19.4	1.24	17.9	36.1	50
	T. II	1.089	1.17	24.2	1.28	20.0	41.0	49
	C. I	0.870	1.13	20.6	1.11	18.7	38.8	48
	C. II	1.220	1.14	26.7	—	—	—	—
<i>Series I</i> E b, c, d g, h e, f	T. I	0.867	1.11	19.9	1.23	19.8	38.4	52
	T. II	1.122	1.20	25.9	1.26	23.4	45.9	51
	C. II	1.179	1.10	24.2	1.21	22.2	45.2	49
<i>Series II</i> F a, b c-l	T. I	0.832	1.17	20.8	1.21	18.6	38.0	50
	T. II	1.204	1.24	26.0	1.32	23.4	47.3	50

TABLE 7—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	SAGITTAL SECTION			FRONTAL SECTION			Percentage of cortical area to the total area
		AVERAGE BRAIN WEIGHT	Correc-tion-co-efficient	Area of cortex	Correc-tion-co-efficient	Area of cortex	Total area of section	
		<i>grams</i>		<i>mm²</i>		<i>mm.²</i>	<i>mm.²</i>	<i>per cent</i>
<i>Series III</i> G aag h-j	T. I	0.844	1.14	20.1	1.24	19.2	38.5	50
	T. II	1.154	1.19	25.6	1.26	22.9	46.2	50
Average (Ser. I-III)	T. I	0.758	1.14	18.6	1.21	17.3	35.2	49
	T. II	1.107	1.20	24.5	1.29	22.6	45.0	50
Average (Ser. I)	C. I	0.700	1.10	15.7	1.15	15.2	31.9	48
	C. II	1.226	1.18	26.1	1.24	22.0	45.0	49

The above-mentioned corrected data for each individual were separately paired with the corresponding standard values for the same brain weight, quoted from my previous study (Sugita, '18 b) in table 8 a (unpublished) and from this latter table 8 was condensed, giving only the averages for each group.

Briefly stated, the area of the cortex in the sagittal section of the underfed is on the average greater by 1.4 per cent (average of all eight litters, T. groups only) than in the standard, while the controls are on the average about 1.9 per cent less than the standard.

The average area of the total frontal section is in the underfed greater than that of the standard by 2.4 per cent (average of all eight litters, T. groups only), while the controls are less by 3.8 per cent (average of Litters A to E, C. groups only) than the standard, and the area of the cortex in the frontal section is in the underfed greater on the average by 5.0 per cent, while in the controls less by 2.1 per cent, than the standard (table 8). From these observations, it may be easily concluded that in the underfed the proportion of the cortex to the total section is higher than in the standard or control, as shown by the percentage values directly calculated for each brain (table 7 b) and given in a condensed form in the last column of table 7, where the values are

TABLE 8

Giving for each litter group in this study the average brain weight, the corrected areas of the cortex in the sagittal and frontal sections, and the area of the entire frontal section, respectively, compared with the corresponding standard values for the same brain weight. The standard values are all entered according to my previous presentation (Sugita, '18b). This table was condensed from an original complete table 8a for each individual. The averages for the test and control groups are given at the end of the table.

SERIES, LITTER AND GROUP	AVERAGE BRAIN WEIGHT	SAGITTAL SECTION			FRONTAL SECTION				
		Area of cortex			Total area		Area of cortex		
		Corrected	Standard	Area	Corrected	Standard	Corrected	Standard	Area
				Thickness					Thickness
grams	mm. ²	mm. ²	mm.	mm. ²	mm. ²	mm. ²	mm. ²	mm.	
<i>Series I</i> A c, a, d, f h b, g i	0.584	14.6	13.8	11.4	28.8	28.3	13.4	12.9	8.9
	1.024	22.2	23.0	13.5	45.0	42.0	22.8	20.7	11.1
	0.688	17.4	16.0	12.6	31.9	31.8	15.2	15.0	10.1
	1.278	27.4	26.7	15.5	43.6	48.5	21.7	23.0	10.9
	0.644	16.9	15.4	12.5	31.6	30.4	15.0	14.2	9.6
	1.052	23.3	23.6	14.0	45.7	43.0	23.4	21.0	10.9
b, d g, h, j	0.543	13.1	13.0	11.0	25.1	28.3	11.6	11.9	8.6
	1.144	24.6	25.2	14.1	45.3	45.2	21.7	21.7	10.8
<i>Series I</i> C a, c, d b, e	1.105	24.5	24.4	14.0	43.6	44.1	22.0	21.5	10.6
	1.307	27.8	27.1	15.8	46.0	49.3	22.2	23.3	11.3
<i>Series I</i> D a, c, d e b f	0.778	19.4	18.9	12.6	36.1	34.8	17.9	17.0	9.5
	1.089	24.2	24.5	14.0	41.0	44.0	20.0	21.3	9.5
	0.870	20.6	20.5	13.3	38.8	38.0	18.7	18.8	10.0
	1.220	26.7	26.0	15.0	—	47.0	—	22.5	—
<i>Series I</i> E b, c, d g, h e, f	0.867	19.9	20.3	13.0	38.4	37.5	19.8	18.7	10.1
	1.122	25.9	25.0	14.3	45.9	44.5	23.4	21.5	10.9
	1.179	24.2	25.3	14.4	45.2	46.0	22.2	23.6	11.4

TABLE 8—Continued

SERIES, LITTER AND GROUP	AVERAGE BRAIN WEIGHT	SAGITTAL SECTION				FRONTAL SECTION				
		Area of cortex				Total area		Area of cortex		
		Cor- rected	Stand- ard	Area		Cor- rected	Stand- ard	Cor- rected	Stand- ard	Area
				Thick- ness						
grams	mm. ²	mm. ²	mm.	mm. ²	mm. ²	mm. ²	mm. ²	mm.		
<i>Series II</i>										
F a, b	0.832	20.8	19.4	13.2	38.0	36.5	18.6	17.9	9.9	
c-1	1.204	26.0	25.9	14.4	47.3	46.7	23.4	22.3	10.9	
<i>Series III</i>										
G a-g	0.844	20.1	19.8	13.0	38.5	36.9	19.2	18.2	10.2	
h-j	1.154	25.6	25.7	14.3	46.2	45.3	22.9	21.9	10.7	
Average } (T. I)	0.758	18.6	17.9	12.6	35.2	34.1	17.3	16.5	9.7	
(Ser. I-III) } (T.II)	1.107	24.5	24.6	14.1	45.0	44.2	22.6	21.5	10.7	
Average } (C. I)	0.700	15.7	16.5	12.3	31.9	32.7	15.2	15.2	9.6	
(Ser. I) } (C. II)	1.226	26.1	26.1	15.0	45.0	47.2	22.0	22.8	11.1	

higher on the average by 3 per cent (1 to 4 per cent in individual cases) than the standard or controls. These results fit with the observation that in the underfed the cortical thickness in the frontal section is 8.7 per cent greater than for the standard (chapter 7).

9. COMPUTED VOLUME OF THE CORTEX

In a former paper (Sugita, '18 b), it was assumed that, as the form of the cerebrum of the albino rat is relatively simple and nearly constant, the relative volumes occupied by the cortical cells could be computed, and compared among themselves, by reducing the data obtained by measurement to a simple geometrical form, since the cortical areas in the sagittal and frontal sections stand in fixed relations to the respective diameters $L.F$ and $W.D$ and to the cortical thickness of the sections from the same brain. These relations have been expressed as follows (Sugita, '18 b):

$\frac{\text{Cortical area (mm.}^2\text{) in sagittal section}}{\text{Cortical thickness (mm.) in the same}} \div L.F \text{ (mm.)} = \text{constant (1)}$

$\frac{\text{Cortical area (mm.}^2\text{) in frontal section}}{\text{Cortical thickness (mm.) in the same}} \div W.D \text{ (mm.)} = \text{constant (2)}$

And the computed volume of the cortex should be obtained simply by the following formula:

$$L.F \times W.D \times T \text{ (all in millimeters),} \quad (3)$$

where T gives the general average thickness of the cerebral cortex of the same brain.

As shown in table 9, which has been condensed from table 9 a (unpublished) for each individual, the constant ratios obtained by the above formulas (1) and (2) fall between 1.10 and 1.29 for the sagittal sections and between 0.80 and 0.95 for the frontal sections, throughout both the underfed and the control groups. The averages of the ratios for the sagittal and frontal sections of the underfed are, respectively, 1.18 and 0.88, and those of the controls are, respectively, 1.20 and 0.88. I have previously given the figures 1.22 and 0.91, respectively, as these ratios of the standard albino rat brains weighing more than 0.5 gram. So it may be assumed that the ratios are nearly the same in both the underfed and the controls; slight differences in the underfed from the standard may be regarded as due to the facts that the cerebrum of the underfed is slightly more elongated and the cortical thickness is somewhat greater than in the standard. As the product of the coefficients in the underfed (1.18×0.88) falls somewhat lower than that in the standard (1.22×0.91), the results of $L.F \times W.D \times T$ should be about 5 per cent higher in the underfed than in the standard.

The relative volumes of the cortex, obtained by the formula (3), are computed and given in table 11 (without any special correction), compared with the corresponding standard values for brains of the same age, instead of for brains of the same weight. The relative volume of the cortex in the underfed brains, which are considerably retarded in total weight development, is greater than for the standard brains of the same weight, which are necessarily younger and less developed as regards the cortical elements than the underfed brains of like weight.

Since in the underfed the average cortical thickness in the sagittal and frontal sections was used in place of the standard T , based on the thickness of the sagittal, frontal and horizontal sections (compare Sugita, '17 a), therefore corresponding values of T have been used in calculating the standard values for the present comparison.

For this comparison, the test animals may be considered in two groups, T. I and T. II. In T. I groups, in which all test rats have a brain weight less than 1.0 gram, the average computed volume of the cortex is less than the standard by 16 per cent, while in T. II groups, which contain the test rats with brains weighing above 1.0 gram, it is more than the standard on the average by 1 per cent. On the other hand, the cortical volume in C. I groups, which embraces the controls having brain weights less than 1.0 gram, is on the average 2.4 per cent less, and in C. II groups, the controls with brain weights above 1.0 gram, it is on the average 7.5 per cent more than the standard for the same age (table 11, last lines). As these comparisons are based on the numbers obtained by calculation and not on the direct measurement, slight discrepancies cannot be regarded as significant, and, as already noted, the results in the underfed are open to special correction of a few per cent for an accurate comparison.

The underfed brains are much retarded in the weight development and the brains weighing up to 1.0 gram include those of ages up to sixteen days, at which age the normal rats have a brain weight 10 per cent heavier than the test rats (chapter V). We conclude, therefore, that, calculated by the formula $L.F \times W.D \times T$, the relative volumes of the cortex in the underfed are nearly the same as in the standard in the brains weighing more than 1.0 gram (T. II groups), while, on the contrary, they are considerably smaller than the standard in the case of the brains weighing under 1.0 gram or under the age of sixteen days, if the age be taken as the standard of comparison.

It appears, therefore, that in rats underfed severely the cortical volume is considerably retarded in growth during the early period of development, but this is probably fairly compensated later when the brain attains a weight of more than 1.0 gram or an age

TABLE 9

Giving for each litter group in this study the average brain weight, the measurements *L.F* and *W.D*, the quotient of the cortical area divided by the cortical thickness (given also in table 8), and the ratio of the latter to the measurement *L.F* or *W.D*, for the sagittal and frontal sections. The width-length index which is obtained by $(W.D \times 100)/L.F$ is also given. This table was condensed from an unpublished table 9a for each individual. The averages for the test and control groups are given at the foot of the table. The ratios given in this table 9 are based on the average of the individual ratios and not on those obtained directly from the average *L.F* or *W.D* and the average quotients

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	<i>L. F</i>	CORT. AREA CORT. THICKN. IN SAGITTAL SECTION	RATIO	<i>W. D</i>	CORT. AREA CORT. THICKN. IN FRONTAL SECTION	RATIO	WIDTH-LENGTH INDEX
		days	grams	mm.	mm.		mm.	mm.		
<i>Series I</i> A c, a, d, f h	T. I	7-	0.584	9.28	11.4	1.23	9.88	8.9	0.89	106
	T. II	15	1.024	11.85	13.5	1.14	12.00	11.1	0.93	101
	C. I	8-	0.688	9.90	12.6	1.27	10.60	10.1	0.95	107
	C. II	17	1.278	12.95	15.5	1.20	12.85	10.9	0.84	99
<i>Series I</i> B a, c, e, f i	T. I	9-	0.644	9.70	12.5	1.29	10.46	9.6	0.92	108
	T. II	19	1.052	12.10	14.0	1.16	12.45	10.9	0.88	103
	C. I	6	0.543	8.78	11.0	1.24	9.85	8.6	0.88	112
	C. II	18-	1.144	12.28	14.1	1.16	12.40	10.8	0.87	101
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	12.32	14.0	1.14	12.17	10.6	0.87	99
	C. II	22-	1.307	13.30	15.8	1.19	12.98	11.3	0.87	98
<i>Series I</i> D a, c, d e	T. I	12-	0.778	10.90	12.6	1.15	10.77	9.5	0.88	99
	T. II	18	1.089	12.25	14.0	1.14	11.85	9.5	0.80	97
	C. I	9	0.870	10.95	13.3	1.21	11.45	10.0	0.82	104
	C. II	22	1.220	12.40	15.0	1.21	12.80	—	—	103
<i>Series I</i> E b, c, d g, h	T. I	12	0.867	10.65	13.0	1.22	11.30	10.1	0.90	106
	T. II	20	1.122	12.10	14.3	1.19	12.35	10.9	0.88	102
	C. II	17-	1.179	12.23	14.4	1.18	12.48	11.4	0.92	102

TABLE 9—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	L. F.	CORT. AREA	RATIO	W. D.	CORT. AREA	RATIO	WIDTH-LENGTH INDEX
					THICKN. IN SAGITTAL SECTION			THICKN. IN FRONTAL SECTION		
		days	grams	mm.	mm.		mm.	mm.		
<i>Series II</i> F a, b c-l	T. I	13-	0.832	11.18	13.2	1.19	11.23	9.9	0.88	101
	T. II	25+	1.204	12.66	14.4	1.14	12.30	10.9	0.88	97
<i>Series III</i> B a-g h-j	T. I	11+	0.844	10.99	13.0	1.18	11.22	10.2	0.90	102
	T. II	22-	1.154	12.58	14.3	1.14	12.20	10.7	0.87	97
Average (Ser. I-III)	T. I	11-	0.758	10.45	12.6	1.21	10.81	9.7	0.90	104
	T. II	20-	1.107	12.27	14.1	1.15	12.19	10.7	0.87	99
Average (Ser. I)	C. I	8-	0.700	9.88	12.3	1.24	10.63	9.6	0.88	108
	C. II	19+	1.226	12.63	15.0	1.19	12.70	11.1	0.88	101

of more than sixteen days, so that after this period there is no longer any significant difference in the cortical volumes between the test and the standard animals.

10. NUMBER OF NERVE CELLS IN THE CEREBRAL CORTEX

The actual number of nerve cells in the frontal cortex in a unit volume of 0.001 mm.³, or 0.1 mm.² in area on the slide by 10 micra in thickness, was counted in the lamina pyramidalis and in the lamina ganglionaris at locality VII, the middle part of the cortical band of the frontal section. The procedure for counting the cell number, adopted by me for the standard values and described in my previous paper (Sugita, '18 b), has been strictly followed here also. The number of cells in the lamina pyramidalis and the lamina ganglionaris and the number of the ganglion cells in a unit volume have been recorded and then converted into the number of cells in the same unit volume in the fresh condition of the brain by the use of the correction-coefficients based on observations. All the data have been tabulated in table 10 a (unpublished) and condensed in table 10 for each group. The

TABLE 10

Giving for each litter group in this study the average age, brain weight, correction-coefficient, and the corrected number of nerve cells in a unit volume (0.001 mm.³) in the lamina pyramidalis and the lamina ganglionaris and the corrected number of ganglion cells only in the same volume, measured at locality VII. This table was condensed from a detailed table, table 10a (unpublished), which gives the same data for the individual cases. The averages for the test and control groups are given at the foot of the table.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	CORRECTION COEFFICIENT	NUMBER OF CELLS IN 0.001 mm. ³		
					Lamina pyramidalis	Lamina ganglionaris	Ganglion cells in lam. gangl.
		<i>days</i>	<i>grams</i>				
<i>Series I</i> A c, a, d, f h b, g i	T. I	7-	0.584	1.18	271	167	47
	T. II	15	1.024	1.28	120	86	21
	C. I	8-	0.688	1.14	224	131	40
	C. II	17	1.278	1.26	107	75	20
<i>Series I</i> B a, c, e, f i b, d g, h, i	T. I	9-	0.644	1.17	232	132	39
	T. II	19	1.052	1.37	117	77	19
	C. I	6	0.543	1.09	268	177	58
	C. II	18-	1.144	1.31	109	76	21
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	1.25	109	73	20
	C. II	22-	1.307	1.16	109	79	26
<i>Series</i> D a, c, d e b f	T. I	12-	0.778	1.24	152	90	21
	T. II	18	1.089	1.28	118	81	18
	C. I	9	0.870	1.22	152	93	27
	C. II	22	1.220	1.14	111	75	22
<i>Series I</i> E a, b, c, d g, h e, f	T. I	12-	0.835	1.21	144	101	25
	T. II	20	1.122	1.26	116	79	21
	C. II	17-	1.179	1.21	116	79	23
<i>Series II</i> F a, b e-1	T. I	13-	0.832	1.21	162	98	29
	T. II	25+	1.204	1.32	105	74	19

TABLE 10—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	CORRECTION COEFFICIENT	NUMBER OF CELLS IN 0.001 mm. ³		
					Lamina pyramidalis	Lamina ganglionaris	Ganglion cells in lam.gangl
<i>Series III</i>	<i>days</i>	<i>grams</i>					
G a-g	T. I	11+	0.844	1.24	149	94	24
h-j	T. II	22-	1.154	1.26	108	80	20
Average } (Ser. I-III)	T. I	11-	0.753	1.21	185	114	31
	T. II	20-	1.107	1.29	113	79	20
Average } (Ser. I)	C. I	8-	0.700	1.15	215	134	42
	C. II	19+	1.226	1.24	110	77	22

sum of the cell numbers in the lamina pyramidalis and the lamina ganglionaris, which may be regarded as representing the average cell density in the cerebral cortex, are also given in table 11, as N , and compared with the corresponding standard values for the brains of the same age, taken from a former paper (Sugita, '18 b).

When compared in this way, it is seen that the observed cell number in a unit volume is generally higher than the standard in brains which weigh less than 1.0 gram (T. I groups). The excess in cell number in underfed brains weighing less than 1.0 gram (T. I groups) is on the average 17 per cent, and that of the control brains weighing less than 1.0 gram (C. I groups) is on the average about 7 per cent. On the other hand, the average cell number of the underfed brains weighing more than 1.0 gram (T. II groups) is almost equal to, while that of the control brains weighing more than 1.0 gram (C. II groups) is less by 4 per cent than, the standard for the same age. The underfed brains are underdeveloped in weight and the brains weighing less than 1.0 gram (T. I groups) contain those of ages up to sixteen days. These relations lead me to conclude that, in the underfed brains weighing less than 1.0 gram or under sixteen days in age, the cell density denoted by N (the average cell number in two unit volumes) is distinctly high, when compared with the normal brains of the same age, probably because the brain size or weight

or the cortical volume is relatively undeveloped in comparison with the cell number (see above). In older brains weighing more than 1.0 gram or of ages above sixteen days, these discrepancies have been somewhat balanced, but, when compared with the controls, the underfed brains remain generally slightly higher in the cell density even in rats of sixteen days or older.

Considered in relation to the facts presented in the previous chapter showing that the computed volume of the cortex is below the standard in the underfed brains weighing less than 1.0 gram, it may be inferred that the underfed brains, underdeveloped in weight and size, have a relatively higher cell density, because the normal number of cells is crowded into a cortex of smaller total volume.

11. RELATIVE VALUE OF THE COMPUTED NUMBER OF CELLS IN THE ENTIRE CORTEX

As previously shown (Sugita, '18 b), the computed number of nerve cells in the entire cortex may be obtained and the values compared among themselves by the use of the following formula:

$$N \times L.F \times W.D \times T \quad (L.F, W.D \text{ and } T, \text{ in millimeters}),$$

where N means the relative cell density represented by the sum of the cell numbers in the unit volume in the lamina pyramidalis and in the lamina ganglionaris (that is, the number in two unit volumes), given in table 11, based on table 9, and $L.F \times W.D \times T$ is the computed volume of the cortex, as already given in the foregoing chapter.

In table 11, these relative values for the volume of the cortex and for the cell number in the cortex in the underfed Albinos are given for each group, each paired with the corresponding standard values for brains of the same age, all condensed from table 11 a (unpublished), which gives the corresponding data for each individual. Every standard value was taken from my previous presentation (Sugita, '18 b). Throughout the underfed and the controls, these pairs of figures seem to be nearly in accord, showing on the average only 1.7 per cent excess in the underfed and 3.4 per cent excess in the control brains (average

of all groups), as compared with the standards. As already noted in chapter 9, the results obtained by the use of formulas are open to some error, and in addition the results in the underfed are subject to special correction of a few per cent for a fair comparison, so that the differences recorded may be regarded as probably insignificant and the computed cell number in the entire cortex of the underfed may presumably be considered as equal to the standard number for brains of the same age. If this is so, the process of the cell division in the cerebrum during early life must have been going on undisturbed even by the severe underfeeding, though both the size and the weight of the brain have been arrested in development by this, in some cases very considerably.

12. SIZE OF NERVE CELLS

The standard size of the pyramids (in the lamina pyramidalis) and the ganglion cells (in the lamina ganglionaris) in the cerebral cortex of the albino rats at different ages was presented in my sixth paper (Sugita, '18 c). In the present study on the influence of the severe underfeeding upon the growth of the cerebral cortex, the size of the nerve cells in the cortex was also determined by the measurement of the transverse and longitudinal diameters of the cell body and the nucleus in the pyramids (in the lamina pyramidalis) and in the ganglion cells (in the lamina ganglionaris) at locality VII in the frontal section, in the same manner as for the standard determinations (Sugita, '18 c). The results have been tabulated in table 12 a (unpublished) and condensed in table 12 for each group. The average diameters of the cell body and of the nucleus are obtained by extracting the square roots of the respective products of the transverse by the longitudinal diameters, and these have been corrected, by applying the correction-coefficient, to the fresh condition of the brain. The corrected average diameters have been tabulated in table 13 a (unpublished), compared respectively with the corresponding standard values for the brains of the same age, and condensed in table 13. The correction-coefficients which were used are given in table 12.

TABLE 11

Giving for each litter group in this study the average brain weight, the age, the computed cortical volume, the cell density and the computed number of cells in the entire cortex, as based on the observed measurements presented in this paper, each compared with the corresponding standard values for the same age. Standard values were taken from my previous presentation (Sugita, '18b). This table was condensed from an original full table 11a (unpublished), which gives the data for each individual. At the end of the table the averages for the test and control groups are given.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	CORTICAL VOLUME: $L.F. \times W.D \times T$		CELL DENSITY: N		CELL NUMBER: $N \times L.F. \times W.D \times T$		
				Starved and controls	Standard for the same age	Starved and controls	Standard for the same age	Starved and controls	Standard for the same age	
<i>Series I</i> A c, a, d, f h b, g i	T. I	7—	0.584	134.4	151.8	437	375	482.9	450.8	
	T. II	15	1.024	263.1	265.0	206	202	542.0	535.0	
	C. I	8—	0.688	159.9	165.0	355	354	452.4	467.5	
	C. II	17	1.278	314.5	275.0	182	198	572.4	545.0	
			days	grams	mm. ³	mm. ³				
<i>Series I</i> B a, c, e, f i b, d g, h, j	T. I	9—	0.644	151.6	187.0	364	298	489.1	479.2	
	T. II	19	1.052	287.7	285.0	194	191	558.1	544.0	
	C. I	6	0.543	112.4	126.5	445	388	457.8	448.5	
	C. II	18—	1.144	285.5	278.3	184	195	526.2	543.3	
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	287.3	284.7	182	191	521.6	542.0	
	C. II	22—	1.307	320.9	289.5	188	188	603.4	540.5	
<i>Series I</i> D a, c, d e b	T. I	12—	0.778	201.1	238.3	242	213	486.4	505.3	
	T. II	18	1.089	278.7	280.0	199	195	554.6	546.0	
	C. I	9	0.870	214.4	207.0	245	230	525.3	476.0	
<i>Series I</i> E b, c, d g, h e, f	T. I	12	0.867	210.3	249.3	238	207	497.1	516.7	
	T. II	20	1.122	295.9	290.0	194	188	574.0	545.0	
	C. II	17—	1.179	278.0	272.5	195	197	535.9	535.0	

TABLE 11—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	CORTICAL VOLUME $L.F \times W.D \times T$		CELL DENSITY: N		CELL NUMBER: $N \times L.F \times W.D \times T$	
				Starved and controls	Standard for the same age	Starved and controls	Standard for the same age	Starved and controls	Standard for the same age
<i>Series II</i>		<i>days</i>	<i>grams</i>	<i>mm.³</i>	<i>mm.³</i>				
F a, b	T. I	13—	0.832	218.7	252.5	260	206	550.4	520.0
c-l	T. II	25+	1.204	307.9	303.4	178	180	548.7	545.7
<i>Series III</i>									
G a-g	T. I	11+	0.844	213.2	229.1	248	225	520.4	504.1
h-j	T. II	22—	1.154	302.2	294.7	189	186	570.3	546.7
Average } (Ser. I-III)	T. I	11—	0.758	188.2	218.0	298	254	504.4	496.0
	T. II	20—	1.107	289.0	286.1	192	190	552.8	543.5
Average } (Ser. I)	C. I	8—	0.700	162.2	166.2	348	324	478.5	462.3
	C. II	19—	1.227	299.7	278.8	187	195	559.5	541.0

By comparing the corrected values in the underfed with the standard values, the average diameters of the cell body and of the nucleus in the underfed brains are found to be generally smaller, on the average, by 9.8 per cent (cell body by 8.6 per cent and nucleus by 11.0 per cent) than the standard value. At the end of the following table 13 appears a summary of the comparisons, arranged as in the earlier tables in this study.

As seen in this summary, both the pyramids and the ganglion cells are much retarded in development in size of the cell body in the underfed brains weighing less than 1.0 gram or of ages under sixteen days, the average diameters of the cell body being 11.5 per cent (in the pyramids 11.2 per cent and in the ganglion cells 11.8 per cent) smaller than the standard for the same age. But in the underfed brains weighing more than 1.0 gram, this arrest in size-development of nerve cells is no longer so notable, the average diameters of the cell body being smaller than the standard by only 5.7 per cent (in the pyramids by 8.3 per cent and in the ganglion cells by 3.1 per cent). The size of the

TABLE 12—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE BRAIN WEIGHT	CORRECTION COEFFICIENT	LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS				
				Cell body diameters		Nucleus diameters		Cell body diameters		Nucleus diameters		
				Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	Transv.	Longit.	
				μ	μ	μ	μ	μ	μ	μ	μ	
<i>Series II</i>		<i>grams</i>										
F a, b c-1	T. I	0.832	1.21	14.8	19.7	13.6	14.7	19.3	28.6	17.6	19.3	
	T. II	1.204	1.32	14.9	21.0	13.7	14.8	19.0	30.0	17.3	19.1	
<i>Series III</i>												
G a-g h-j	T. I	0.844	1.24	14.0	19.8	13.1	14.3	17.9	28.4	16.8	18.4	
	T. II	1.154	1.26	13.9	19.8	12.6	13.9	18.3	28.7	16.2	18.1	
Average (Ser. I-III)	T. I	0.753	1.21	13.6	19.1	12.5	13.6	17.5	26.8	15.8	17.7	
	T. II	1.107	1.29	14.2	20.4	13.1	14.6	19.1	29.4	16.9	19.1	
Average (Ser. I)	C. I	0.700	1.15	14.7	18.9	13.3	14.6	19.3	25.7	16.6	18.3	
	C. II	1.226	1.22	15.2	21.4	14.2	15.3	19.7	30.1	17.8	19.3	

nucleus is much more affected by the underfeeding than that of the cell body. In the underfed brains of T. I groups the average diameter of the nucleus is smaller by 13.9 per cent (in the pyramids by 15.3 per cent and in the ganglion cells by 12.5 per cent) and in those of T. II groups it is smaller by 8.0 per cent (in the pyramids by 11.0 per cent and in the ganglion cells by 5.1 per cent) than the standard for the same age. The deficiency in the average diameter of the cell body by 6 to 12 per cent and that of the nucleus by 8 to 14 per cent correspond to the inferiority in volume of about 20 to 45 per cent and 25 to 50 per cent, respectively.

On the other hand, in the control brains of all weights, the size of the cell body and of the nucleus have proved to be also somewhat smaller than the standards, but the deviations are not so much in comparison with the underfed, the deficiency in the average diameters of the cell body and the nucleus being on the average 5.3 per cent (table 13).

TABLE 13

Giving for each litter group in this study the average age, brain weight, the corrected average diameters of the cell body and the nucleus of the pyramids (in the lamina pyramidalis) and the ganglion cells (in the lamina ganglionaris), based on the condensed data in table 12, each compared with the corresponding standard values for the same age, taken from my former presentation (Sugita, '18c.) This table was condensed from table 13a (unpublished) for individual cases. The averages for the test and control groups and their percentage relations are given at the end of the table. (per. diff.) = percentage difference

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT		LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
					Cell body Aver. diameter		Nucleus Aver. diameter		Cell body Aver. diameter		Nucleus Aver. diameter	
					Corrected	Standard	Corrected	Standard	Corrected	Standard	Corrected	Standard
					μ	μ	μ	μ	μ	μ	μ	μ
<i>Series I</i> A c, a, d, f h	T. I	7-	0.584	16.6	19.4	13.3	16.6	21.6	25.9	16.8	20.7	
	T. II	15	1.024	21.1	23.7	18.1	19.8	30.6	31.3	23.6	24.4	
	C. I	8-	0.688	18.7	19.6	15.4	16.9	24.7	26.7	19.5	21.2	
	C. II	17	1.27	23.1	23.8	18.7	20.0	31.2	31.3	21.1	24.4	
<i>Series I</i> B a, c, e, f i	T. I	9-	0.644	18.4	20.7	14.8	17.8	24.3	27.9	19.4	22.1	
	T. II	19	1.052	23.2	24.0	19.8	20.0	32.1	31.4	25.1	24.5	
	C. I	6	0.543	17.4	18.5	14.3	15.8	23.3	24.9	17.8	19.8	
	C. II	18-	1.144	23.1	23.9	19.7	20.0	32.4	31.3	25.0	24.4	
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	22.1	23.9	17.6	20.0	29.7	31.4	22.9	24.4	
	C. II	22-	1.307	21.4	24.0	17.4	20.0	29.1	31.5	21.8	24.5	
<i>Series I</i> D a, c, d e	T. I	12-	0.778	20.6	22.9	16.6	19.5	27.4	30.1	20.2	23.8	
	T. II	18	1.089	21.4	23.9	16.8	20.0	29.5	31.3	22.8	24.4	
	C. I	9	0.870	21.8	22.1	18.4	18.8	29.3	28.4	23.2	23.0	
	C. II	22	1.220	22.4	24.1	18.2	20.1	29.5	31.6	22.1	24.5	
<i>Series I</i> E a, b, c, d g, h	T. I	12-	0.835	19.8	23.0	16.4	19.8	27.1	30.9	20.7	24.2	
	T. II	20	1.122	21.5	24.0	16.8	20.0	31.0	31.4	21.7	24.5	
	C. II	17-	1.179	22.0	23.7	17.7	19.9	29.5	31.3	22.4	24.5	

TABLE 13—Continued

SERIES, LITTER AND GROUP	TEST CON- TROL	AVERAGE BRAIN WEIGHT		LAMINA PYRAMIDALIS				LAMINA GANGLIONARIS			
		AVERAGE AGE		Cell body Aver. diameter		Nucleus Aver. diameter		Cell body Aver. diameter		Nucleus Aver. diameter	
				Corrected	Standard	Corrected	Standard	Corrected	Standard	Corrected	Standard
		days	grams	μ	μ	μ	μ	μ	μ	μ	μ
<i>Series II</i> F a, b c-l	T. I	13-	0.832	20.8	23.2	17.1	19.8	28.5	31.1	22.3	24.4
	T. II	25+	1.204	22.9	23.9	18.6	20.0	31.0	31.5	23.6	24.4
<i>Series III</i> F a-g h-j	T. I	11+	0.844	20.6	22.5	17.0	19.2	27.9	29.9	21.9	23.5
	T. II	22-	1.154	21.0	24.1	16.7	20.1	29.0	31.5	21.7	24.5
Average (Ser. I-III) (per. diff.)	T. I	11-	0.753	19.5	22.0 (-11.2)	15.9	18.8 (-15.3)	26.1	29.3 (-11.8)	20.2	23.1 (-12.5)
Average (Ser. I-III) (per. diff.)	T. II	20-	1.107	21.9	23.9 (- 8.3)	17.8	20.0 (-11.0)	30.4	31.4 (- 3.1)	23.1	24.4 (- 5.1)
Average (Ser. I) (per. diff.)	C. I	8-	0.700	19.3	20.1 (- 3.8)	16.0	17.2 (- 6.7)	25.8	26.7 (- 3.2)	20.2	21.3 (- 5.1)
Average (Ser. I) (per. diff.)	C. II	19+	1.226	22.4	23.9 (- 6.2)	18.3	20.0 (- 8.5)	30.3	31.4 (- 3.3)	23.1	24.5 (- 5.5)

It is also seen that by underfeeding the nucleus is more affected than the entire cell body both in the pyramids (deficiency in diameters; T. I groups: cell body 11.2 per cent and nucleus 15.3 per cent, T. II groups: cell body 8.3 per cent and nucleus 11.0 per cent) and in the ganglion cells (deficiency in diameters; T. I groups: cell body 11.8 per cent and nucleus 12.5 per cent, T. II groups: cell body 3.1 per cent and nucleus 5.1 per cent) of brains of all weights, while the pyramids are more markedly affected than the ganglion cells both in the cell body (deficiency in diameters on the average of T. I and T. II groups: pyramids 9.8 per cent and ganglion cells 7.5 per cent) and in the nucleus (deficiency

in diameters on the average of T. I and T. II groups: pyramids 13.2 per cent and ganglion cells 8.8 per cent). In young brains which weigh less than 1.0 gram, the influence of the underfeeding is considerable, while in brains weighing more than 1.0 gram or of ages more than sixteen days we can not detect any large arrest in the size-development, especially of the ganglion cells (the sizes of the cell body and the nucleus of the ganglion cells in the T. II groups are quite equal to the corresponding sizes in C. II groups) (tables 12 and 13). These observations are in agreement with the conclusions reached by Morgulis ('11).

13. PERCENTAGE OF WATER IN BRAIN

As stated earlier (in chapter III), Litter H in Series II, in which a young primipara mother was entrused with seventeen young in order to produce a series of underfed young, was used partly for the investigation of the percentage of water in the underfed brain and partly for a histological study of myelination (not considered at this time).

In this Series II the development in brain weight is not so greatly arrested, as compared with the arrest in body growth, as in Series I. As already shown, in Litter F, which was treated in a similar manner, the brain weight is on the average 9 per cent low, but in this Litter H it has been possible to arrest the brain-weight growth on the average by about 12 per cent, compared with the standard of the same age (compare table 4).

Table 14 gives for each individual examined in this litter the sex, the age, the brain weight, and percentage of water in the brain, each accompanied by the standard percentage of water contained in the brains of the same age and sex and also of the same weight and sex. The differences are given in special columns.

By obtaining averages, it is found that the underfed brain contains slightly (0.48 per cent) more water, when compared with the normal brain of the same age and somewhat (1.4 per cent) less water, when compared with the normal brain of the same weight. This means in terms of the percentage of water,

TABLE 14

Showing for each brain in litter H the sex, the age, the brain weight, and the percentage value of water in the brain, accompanied with the standard values of percentage of water in brain for the same age and for the same brain weight. The differences between the observed percentages and the corresponding standard values are given in special columns, with their averages.

NO.	SEX	AGE IN DAYS	BRAIN WEIGHT	PERCENTAGE OF WATER IN BRAIN OBSERVED	PERCENTAGE OF WATER STANDARD FOR THE		PERCENTAGE OF WATER STANDARD FOR THE	
					Same age	Difference in observed	Same brain weight	Difference in observed
			<i>grams</i>					
H a	f	13	0.880	86.39	85.40	+0.99	86.82	-0.43
b	f	17	1.024	84.15	83.82	+0.33	85.08	-0.93
c	f	23	1.135	82.00	81.93	+0.07	83.21	-1.21
d	f	28	1.166	80.83	80.74	+0.09	82.70	-1.87
e	m	32	1.215	80.31	80.04	+0.27	81.70	-1.39
f	f	37	1.101	80.12	79.55	+0.57	83.78	-3.66
g	m	43	1.295	80.24	79.32	+0.92	80.56	-0.32
Average.....						+0.48		-1.40

that the underfed brain is slightly underdeveloped for its age, but somewhat overdeveloped for its weight. Similar relations have been revealed by the comparisons already made. Normally about 0.5 per cent excess in percentage of water in the brain would mean at the early ages approximately one or two days' retardation in development (compare table 74 in 'The Rat,' Donaldson, '15).

From the same litter (Litter H) I took with each of the above individuals a second rat for the study of the myelination, because it is known that the percentage of water in the brain is correlated with its myelination. The brains under seventeen days of age showed no fibers in the frontal sections, as stained with Pal-Kultschitzky method. The twenty-eight-day brain showed only a few faintly stained fibers in the cortex, the fibers in the corona radiata (designated C. E. by Watson, '03) being already myelinated. Material above thirty-seven days was not examined. This passing examination of a small number of cases roughly indicates, therefore, that the first appearance of myelina-

tion in somewhat retarded, because, according to the investigation of Watson ('03), myelination in the corona radiata should have begun at eleven days and radiations into the cortex should have been recognized at twenty-four days. But a more detailed test for this process is required before any special use can be made of the results.

14. RELATIVE QUANTITIES OF THE ALCOHOL EXTRACTIVES

In my former paper (Sugita, '17 a) a chart, based on the data given in 'The Rat' (Donaldson, '15), was presented to show the absolute quantity of solids contained in the Albino brain according to the brain weight. For comparison with this, I calculated also the relative quantity of alcohol-extractive substances in the Albino brains, as shown by comparing the initial weight of the brain with its weight after extraction by 80 per cent alcohol (for twenty-four hours) and 90 per cent alcohol (for twenty-four hours) according to a uniform procedure. As the brains were treated uniformly throughout the investigation, the results are comparable among themselves.

The results from 120 normal albino rat brains, grouped in twenty brain-weight groups (Groups I to XX), are given here in table 15 and plotted also in chart 1, in which the smooth curve (in a dotted line) represents the percentage weight of the extracted brain on the fresh brain weight. In chart 1, the graph which presents the absolute amounts of solids (in grams) according to the brain weight is also given in a solid line based on the chart in my former paper (chart 12, Sugita, '17 a). It was remarked previously (Sugita, '17 a) that in the Albino brains weighing between 0.95 gram and 1.4 grams, that is, between ten and thirty-five days of age, the rate of increase in solids is somewhat higher than in the periods before and after that phase, and this fact was formerly interpreted as indicating that, during this phase, the myelination in the brain had been proceeding very actively. This interpretation is now supported by the graph which gives the percentage weight of the brain. This graph varies inversely to the amount of the alcohol-extractives

and, as it decreases relatively rapidly in the phase during which the brain grows in weight from 0.9 gram to 1.35 grams, or in the ages between nine and thirty-three days, it shows that during that phase the alcohol-extractives increased.

The turning points in the both graphs marked with crosses \times and $\times\times$) and asterisks (* and **), respectively, are in fair

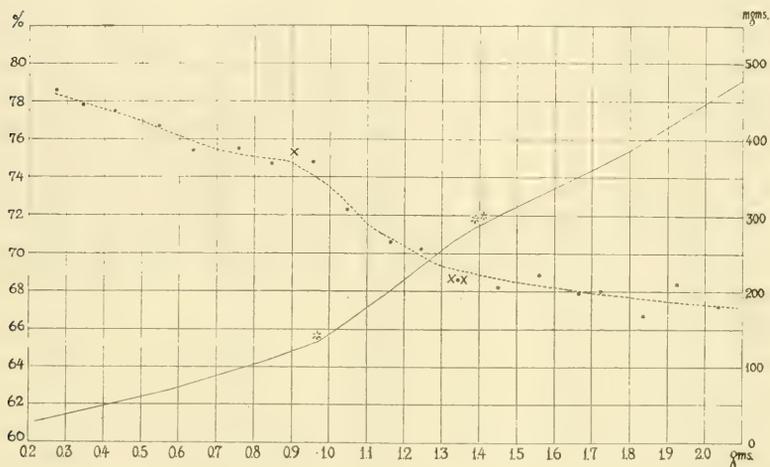


Chart 1 The dotted line shows the ratio between the initial brain weight and the weight after its dehydration and extraction in 80 per cent alcohol (for twenty-four hours) and 90 per cent alcohol (for twenty-four hours) according to a uniform procedure, plotted on the brain weight. The data were taken from table 15. The graph was drawn connecting the middle points of each pair of entries. * and ** indicate the turning points in the graph.

The solid line shows the absolute weight of the solids in the brain according to the brain weight. The data were taken from table 74 in 'The Rat' (Donaldson, '15) and calculated by me. * and ** indicate the turning points in the graph.

For the ratios of brain weight the scale is given on the left side of the chart and for the absolute weight of the solids the scale is given on the right side.

coincidence, so that it may be concluded that the mass of the alcohol-extractives would be in proportion to the grade of myelination in the brain, and by following the former the progress in myelination could be estimated roughly.

It must be emphatically stated that my figures given in table 15 do not represent the total quantity of the alcohol-extractives,

TABLE 15

Giving for each brain-weight group of the normal albino rat the average initial brain-weight in the fresh condition and the brain weight after dehydration and extraction in 80 per cent alcohol (for twenty-four hours) and 90 per cent (for twenty-four hours) by a uniform procedure. The ratio of the final brain weight to the initial weight is given in the last column as a percentage value. Based on observations on 120 albino rats, sexes combined.

BRAIN-WEIGHT GROUP	NUMBER OF CASES	BRAIN WEIGHT WHEN FRESH	BRAIN WEIGHT AFTER DEHYDRATION IN 80 AND 90 PER CENT ALCOHOL	RATIO TO THE INITIAL BRAIN WEIGHT
		<i>grams</i>	<i>grams</i>	<i>per cent</i>
II (birth)	6	0.271	0.213	78.6
III	8	0.343	0.267	77.8
IV	9	0.428	0.332	77.5
V	14	0.543	0.416	76.7
VI	5	0.636	0.479	75.4
VII	4	0.755	0.571	75.7
VIII	10	0.844	0.630	74.7
IX (10 days)	5	0.954	0.714	74.8
X	6	1.047	0.757	72.3
XI (20 days)	5	1.161	0.820	70.6
XII	5	1.245	0.874	70.2
XIII	8	1.341	0.921	68.6
XIV	5	1.449	0.989	68.2
XV	7	1.558	1.074	68.9
XVI	8	1.667	1.131	67.9
XVII	6	1.721	1.170	68.0
XVIII (90 days)	5	1.832	1.222	66.7
XIX	1	1.924	1.317	68.4
XX	3	2.037	1.369	67.2

because the extraction was not complete. My figures are only by-products in a study on histological technique, and to obtain the total quantity of the extractives the brain must have stayed much longer in alcohol of a higher concentration. My data therefore give merely the relative values for the quantity of the alcohol-extractives, but are comparable among themselves and with the values from the underfed brains treated in the same manner.

In giving the ratio of the brain weight after extraction in alcohol (by this method) to its initial weight, no correction was made for the weight of water replaced by alcohol, because my object was

only to compare the results among themselves and not to determine the exact quantity of the extractive substances.

Table 16 gives for each group in this study the ratio of the brain weight after dehydration in 80 per cent alcohol (for twenty-four hours) and in 90 per cent alcohol (for twenty-four hours) to its initial weight in the fresh condition, calculated in the same way as in table 15 and each paired with the standard ratio for the same age, quoted from table 15. Thus compared, the underfed brains show in general a higher ratio, the difference amounts to 1.0-4.3 per cent, on the average 1.9 per cent, while the difference in the control brains is generally low, on the average + 0.4 per cent.

This examination tells us roughly that in the underfed brains the alcohol-extractives are somewhat less in quantity than in the normal brain, if the age be taken as the standard of comparison, and, therefore, it may be concluded that they are somewhat retarded in the formation of alcohol-extractive substances and therefore in myelination. Reviewing tables 14 and 16 together, we see that during underfeeding the myelination process or the increase in the alcohol-extractives is retarded slightly, but is going on, not greatly affected by the outside influence, regularly according to its age. It is fair to say, however, that the differences thus determined by extraction are seemingly less than those shown by the histological tests.

15. A DISCUSSION ON THE RELATION BETWEEN THE BODY WEIGHT AND THE BRAIN WEIGHT IN THE UNDERFED ALBINO RATS

By examining table 4 it will be readily seen that under severe underfeeding at an early age, the increase in the body weight and the brain weight, according to the age, is notably reduced, and, as a consequence, the acutely underfed (Series I, chapter 5 and table 1) have lost, in the course of first twenty days after birth (during suckling period), about 29 per cent in body weight, but only 8 per cent in brain weight, when compared with the corresponding standard values for the same age. By chronic starvation, during which the young (excessive in number) were left

TABLE 16

Giving for each litter group in this study the average age, the initial brain weight in the fresh condition and the brain weight after extraction in 80 per cent alcohol (for twenty-four hours) and 90 per cent alcohol (for twenty-four hours) by a uniform procedure, and the ratio of the latter to the initial weight. The corresponding standard values for the same age were calculated on the basis of the data in table 15 and compared with each and the difference between them given as an average for each group. This table was condensed from table 16a (unpublished) for individual cases. The averages for the test and control groups are given at the end of the table.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	AFTER EXTRACTION IN 80 PER CENT AND 90 PER CENT ALCOHOL		Standard ratio for the brain of the same age	DIFFERENCE FROM THE STANDARD
				Final brain weight	Ratio to the initial brain weight		
		days	grams	grams	per cent	per cent	per cent
<i>Series I</i> A c, a, d, f h	T. I	7-	0.584	0.450	77.2	75.7	+1.5
	T. II	15	1.024	0.779	76.0	72.8	+3.2
	C. I	8-	0.688	0.517	75.7	75.4	+0.3
	C. II	17	1.278	0.928	72.7	72.3	+0.4
<i>Series I</i> B a, c, e, f i	T. I	9-	0.644	0.488	76.1	74.9	+1.2
	T. II	19	1.052	0.799	76.0	71.7	+4.3
	C. I	6	0.543	0.414	76.4	76.1	+0.3
	C. II	18-	1.144	0.826	72.2	72.1	+0.1
<i>Series I</i> C a, c, d b, e	T. II	20	1.105	0.816	73.9	72.9	+1.0
	C. II	22-	1.307	0.934	71.5	71.8	-0.3
<i>Series I</i> D a, c, d e	T. I	12-	0.778	0.584	75.1	73.7	+1.4
	T. II	18	1.089	0.795	73.0	72.0	+1.0
	C. I	9	0.870	0.656	75.4	74.5	+0.9
	C. II	22	1.220	0.863	70.8	71.0	+0.2
<i>Series I</i> E a, b, c, d e	T. I	12-	0.835	0.626	75.0	73.7	+1.3
	C. II	13	1.024	0.760	74.1	73.4	+0.7
<i>Series II</i> F a, b c-k	T. I	13-	0.832	0.636	76.7	73.4	+3.3
	T. II	25+	1.198	0.862	72.3	70.7	+1.6

TABLE 16—Continued

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	AVERAGE BRAIN WEIGHT	AFTER EXTRACTON IN 80 PER CENT AND 90 PER CENT ALCOHOL		Standard ratio for the brain of the same age	DIFFERENCE FROM THE STANDARD
				Final brain weight	Ratio to the initial brain weight		
		days	grams	grams	per cent	per cent	per cent
<i>Series III</i>							
G a-g h-j	T. I	11+	0.844	0.641	76.0	73.9	+2.1
	T. II	22-	1.154	0.833	72.2	71.2	+1.0
Average } (Ser. I-III)	T. I	11+	0.753	0.571	76.0	74.2	+1.8
	T. II	20+	1.104	0.814	73.9	71.9	+2.0
Average } (Ser. I)	C. I	8-	0.700	0.529	75.8	75.3	+0.5
	C. II	18+	1.195	0.862	72.3	72.1	+0.2

continuously with the mothers (Series II and III, chapter 2 and table 2), the loss in the brain weight is relatively less, in some individual cases nothing, while the body weight suffers much more, compared with the acutely underfed groups (Series I).

The observed body weight and the brain weight of each individual in this study are plotted separately for each litter in chart 2, A to H, according to the advancing age. Comparing the set of graphs both for the body weight and the brain weight within every litter, it is clearly seen at a glance that the courses of the graphs are similar, so that one, which advanced in age but has a smaller body weight, has also a relatively smaller brain weight, and vice versa. From this it is concluded that, though the brain, with a strong impulse to grow, regularly increases in weight with age and is only slightly affected by outside influence, yet it is controlled somewhat by the growth in the entire body. Thus, within certain limits, the brain weight may be said to be a function of the body weight: a rat reduced in body weight by starvation has a brain also reduced in weight and, on the other hand, a rat excessive in body weight for its age, through overfeeding, has an excess of brain weight for its age, as seen in the control groups shown in table 4. In the interrupted starvation tests (Series I), an average reduction of 29 per cent in the body weight

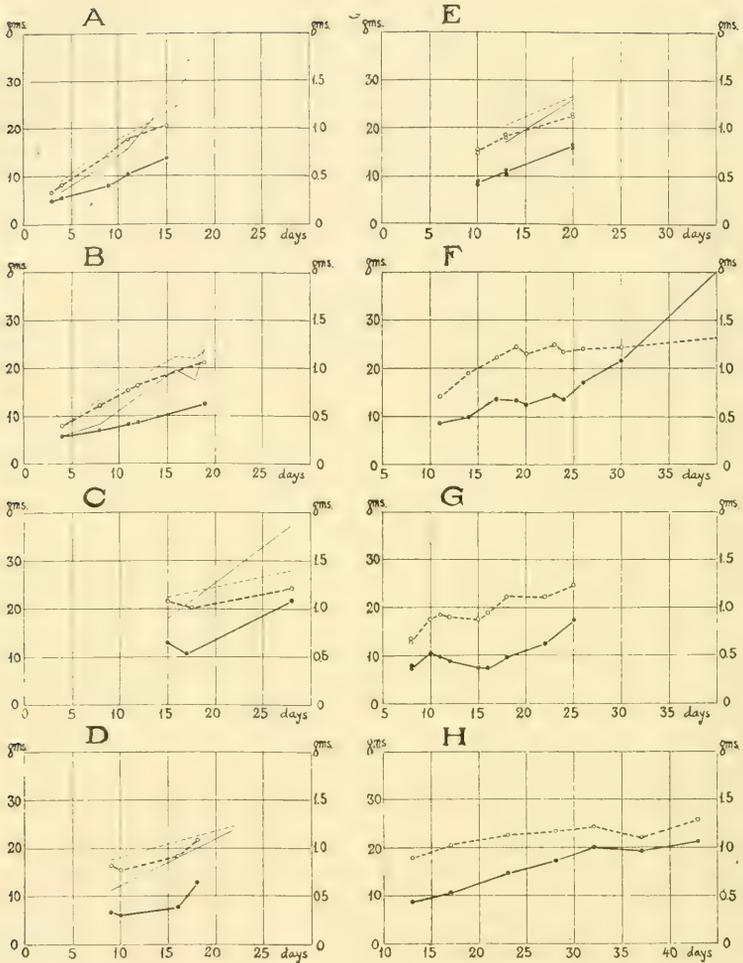


Chart 2 Giving for each litter in this study the relation between the body weight and the brain weight of the individuals. The capital letters for each small chart designate the litter. The data given in table 3 were plotted according to the advancing age in days.

- Observed body weight of the underfed, in grams.
- - -○ Observed brain weight of the underfed, in grams.
- Observed body weight of the controls, in grams.
- - - - - Observed brain weight of the controls, in grams.

For the body weight the scale is given on the left side and for the brain weight the scale is given on the right side of the chart.

is accompanied by 8 per cent reduction in the brain weight in the test rats, and an excess of 14 per cent in the body weight by an excess of 6 per cent in the brain weight in the controls. These relations indicate that the brain weight is affected in abnormal conditions of nutrition during early life so that its percentage is altered by about one-third the percentage of the change of the body weight, either plus or minus, as compared with the standard values. On the other hand, in chronic inanition (Series II and III) where the young rat is not disturbed, the brain-weight loss was also 8 per cent against a body weight loss of 39 per cent. It appears, therefore, that during the early helpless period the brain development is highly disturbed by the changes in the environmental conditions represented by removal from the nest, but that when the rats are not disturbed it is much less affected even by severe underfeeding.

Table 17 gives for each group in this study the brain weight—body weight ratio, in percentage value, paired with the ratio obtained from the corresponding standard values for the same age and sex, calculated on the data given in table 4. The complete data for each individual are contained in table 17 a (unpublished) from which table 17 was condensed. In the underfed the above ratios are all higher than the standard, as was to be expected, while in the controls lower ratios are sometimes seen, which, in turn, means an overgrowth of the body. The average differences for each litter and group are given and the values are indicative of the severity of starvation combined with the special characteristics of the litter. Within each litter the range of the differences is narrow but the evidence for this statement is furnished by the unpublished detailed table 17 a.

16. A DISCUSSION ON THE CHANGE IN SHAPE OF THE CEREBRUM

In my first paper (Sugita, '17) it was stated that the Albino cerebrum becomes relatively longer as the age advances. During starvation, the rate of increase in every dimension diminishes considerably, but the relations between the three dimensions remains nearly unchanged, so that, as a result, the underfed brain is somewhat elongated in shape in comparison with the standard

TABLE 17

Giving for each litter group in this study the average age, the sex, the brain weight—body weight ratio, compared with the same ratio for the standard rat of the same age and sex. The difference of the ratio for each group is given in the last column of the table. This table was condensed from table 17a (unpublished) for the individual cases. At the foot of the table the averages for the test and control groups are given.

SERIES, LITTER AND GROUP	TEST CONTROL	AVERAGE AGE	SEX	RATIO OF BRAIN WEIGHT TO BODY WEIGHT	<i>The same in standard rat of the same age</i>	DIFFERENCE FROM THE STANDARD
		<i>days</i>		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
<i>Series I</i> A c, a, d, f h	T. I	7—	1 m, 3 f	7.9	6.5	+1.4
	T. II	15	1 f	7.4	6.3	+1.1
b, e, g i	C. I	8	3 m	6.4	6.8	-0.4
	C. II	17	1 f	4.2	6.1	-1.9
<i>Series I</i> B a, c, e, f i	T. I	9—	3 m, 1 f	8.7	6.7	+2.0
	T. II	19	1 m	8.3	6.0	+2.3
b, d g, h, j	C. I	6	2 f	7.6	6.5	+1.1
	C. II	18—	3 f	5.7	6.0	-0.3
<i>Series I</i> C a, e, d b, e	T. II	20	2 m, 1 f	7.7	5.8	+1.9
	C. II	22	2 f	5.3	5.5	-0.2
<i>Series I</i> D a, c, d e	T. I	12—	1 m, 2 f	11.3	6.8	+4.5
	T. II	18	1 m	8.4	6.2	+2.2
b f	C. I	9	1 m	7.8	7.1	+0.7
	C. II	22	1 m	5.1	5.6	-0.5
<i>Series I</i> E a, b, c, d g, h e, f	T. I	12—	3 m, 1 f	8.6	6.8	+1.8
	T. II	20	2 f	7.0	5.6	+1.4
	C. II	17—	1 m, 1 f	5.6	6.4	-0.8
<i>Series II</i> F a, b c-l	T. I	13—	1 m, 1 f	9.1	6.8	+2.3
	T. II	25+	4 m, 6 f	7.5	5.1	+2.4
<i>Series III</i> G a-g h-j	T. I	11+	4 m, 3 f	10.3	6.9	+3.4
	T. II	22—	2 m, 1 f	9.3	5.5	+3.8
Average } (Ser. I-III)	T. I	11—		9.3	6.8	+2.5
	T. II	21+		7.9	5.8	+2.1
Average } (Ser. I)	C. I	8—		7.3	6.8	+0.5
	C. II	19+		5.2	5.9	-0.7

brain, which is the same in weight but younger. As shown in table 5, in the underfed brains the measurement *L.G* (the sagittal diameter) is on the average nearly 2 per cent (about 0.25 mm. in a brain weighing 1.0 gram) greater than the standard, while, on the other hand, as shown in table 6 a (unpublished), in the underfed the cortical thickness at the frontal pole (locality I) which was measured almost in the same direction with *L.G* is also greater by 10 per cent (about 0.25 mm. in a brain weighing 1.0 gram) than the standard for the same brain weight, while the cortex at the occipital pole (locality V) is nearly equal to the standard in thickness. Considering together the above facts, the sagittal length of the central nuclei only, if measured between the frontal and occipital poles, would be supposedly about the same in both the underfed and the standard brains weighing alike. On the other hand, the width *W.B* is, in the underfed, less by nearly 2 per cent (about 0.3 mm. for 1.0 gram brain) than in the standard, and the cortical thickness at locality VII, which was measured at the side of the cerebrum, is thicker in the underfed by nearly 10 per cent (about 0.4 mm. for the both hemispheres in a 1.0 gram brain (based on the unpublished table 6 b for each locality), and therefore the central nuclei in the underfed are less in width by about 0.7 mm. (for a 1.0 gram brain) than the standard for the same brain weight. In short the central nuclei are notably elongated in shape in the underfed brain compared with the normal brain of like weight.

17. A DISCUSSION ON THE THICKNESS OF THE CORTEX IN THE UNDERFED

As described in Chapter 7, the cortical thickness in the starved brain is on the average markedly greater than the standard for the same brain weight. In the sagittal sections, the locality I surpasses the standard most, the localities II and III are the next, while the localities IV and V are almost equal in thickness to the standard (these statements are based on the unpublished table 6 a for each locality). This order in which the localities surpass the standard in thickness is the same as the order in rate of increase in the cortical thickness during the post-

natal growth (Sugita, '17 a). The same statement is true for the localities VI, VII, and VIII in the frontal sections (based on the unpublished table 6 b). The order in the rate of increase in the cortical thickness is an index of the grade of intensity in cell migration to those localities and of the growth impulse of the elements there. From previous studies (Sugita, '17 a), it was found that, as a rule, the cortical thickness decreases from the frontal to the occipital pole and from the dorsal to the ventral aspect, and the nearer a locality is to the ventricular wall or the matrix the more rapid the rate of increase in the thickness of the cortex. In underfed brains, the localities which show normally the higher rate of increase in thickness are also greater in the cortical thickness when compared with the standard. So, in the underfed, the cerebral cortex is generally thicker than the standard for the same brain weight and thicker in each locality in proportion to the rate of increase in the thickness of that locality under normal conditions.

In short, the growth in the cortical thickness in the case of the underfed is more advanced than that of the normal brain of the same weight, which is, of course, younger.

18. A DISCUSSION ON THE RELATION BETWEEN CELL DENSITY AND THE COMPUTED VOLUME OF THE CEREBRAL CORTEX

As stated earlier, the cell density of the cerebral cortex, represented by the number of nerve cells in two unit volumes (N), is, in the underfed Albino brain, under sixteen days in age, considerably higher than the standard for the same age, and accordingly the cell size in the underfed must be smaller than the standard size and, by inference, the cell attachments also underdeveloped for the age. The relations between these data will be examined now according to my measurements as presented in this paper.

The cortical area as measured in the sections from the underfed brains proves to be slightly greater than the standard values for the same brain weight, but on the other hand, it is distinctly less in brains under sixteen days of age than the standard values

for the same age, which belong to brain weights higher by about 10 per cent.

Let us take as an example an underfed brain which weighs less than 1.0 gram for examination. The computed volume of the cerebral cortex is in the underfed smaller on the average by 16 per cent than the standard for the same age (chapter 9). As shown by calculation, the computed number of nerve cells in the entire cortex is almost the same in both the standard and the underfed, throughout all ages, so that the process of cell division appears to have been going on undisturbed by the condition of underfeeding. The cell density, the cell size, and the cortical volume must therefore be regulated so as to provide the cerebral cortex with the number of cells fixed according to the age, regardless of the starvation.

To present the relation, the formula $N \times L.F \times W.D \times T$ was used. The value of $N \times L.F \times W.D \times T$ has proved in my present material from the underfed to have been 1.7 per cent higher than the standard, but as this is open to some correction, it may be regarded as approximately the same in both the underfed and the corresponding standard. To be less in the cortical volume, which was computed by the formula $L.F \times W.D \times T$, by about 16 per cent or more, the cell density must be increased by about 19 per cent or less theoretically. This latter figure is fairly in accord with that obtained in my direct observation; that is, 17 per cent excess in the number of cells in a unit volume in the underfed brains (chapter 10). To be reduced in cortical volume by 16 per cent or more, the individual cell must theoretically be reduced in volume also in the same ratio, in order not to be reduced in total number. My results in cell-size measurement showed that the individual cells measured are reduced in average diameter by about 12 per cent, and accordingly in average volume by about 30 per cent or more. These figures appear somewhat higher than was to be expected, but it must be recalled that these figures apply only to the largest cells found in the measured locality, and this class of cells may suffer a disproportionate arrest, so that the figures do not indicate what has taken place in the small cells and those of average size. Furthermore, in the

cerebral cortex the neuroglia, the intercellular tissue and the blood-vessels occupy considerable space and these may not be reduced in volume in the same proportion as the large nerve cells. These facts combined seem to furnish an explanation why the largest nerve cells, which have been here studied, deviate somewhat in size from the figures theoretically to be expected.

The data here presented show, I think, that the relations between the cell density and the cortical volume in the underfed fit with the formulas presented earlier and which represent the relations in the normal Albino brains.

19. A DISCUSSION ON THE PROCESS OF MYELINATION

Tables 14 and 16 supply the data on which the myelination process in the underfed Albino brain may be tentatively discussed.

In Donaldson's series ('11), which consisted of twenty-two litters of albino rats in which the underfeeding was begun at 30 days of age and in which all were killed after three weeks and compared with the controls from the same litter, the average brain weight of the underfed was 1.402 grams and the percentage of water 79.28, while the average brain weight of the controls was 1.519 grams and the percentage of water 79.39. Here the underfed had 0.11 per cent less water. By examining the sections from the underfed and the controls, the author could not discover any recognizable difference in myelination between them. Hatai ('04) made a partial starvation experiment, extending over three weeks, using the albino rats in the growing stage, about thirty days old. In this series, the final average brain weight was 1.341 grams and the percentage of water 79.15 or 0.21 per cent less than in the controls from the same litter and killed at the same age and in which the final brain weight was 1.508 grams and the percentage of water 79.36. In the same series, the solids extracted with alcohol and ether were determined. The average amount of the extractives in the test brains was 46.7 per cent, or 0.9 per cent more than in the controls, in which it was 45.8 per cent. Though higher in percentage in the underfed,

the absolute mass of the extractive substances is 0.065 gram (about 5 per cent of the brain weight) less than in the controls of the same age. The absolute weights were in the underfed 0.626 gram and in the controls 0.691 gram. These extractives represent mainly the myelin which is contained in the sheaths of the nerve fibers, and the above results mean that the extractive substances are increasing at the same rate or slightly slower in the underfed than in the controls.

In my material as seen in table 14, the underfed brains contain slightly more water (by 0.48 per cent on the average) than the standard of like age, and, as presented above (chapter 13), the frontal section showed a higher percentage in area of the cortex against the area of the central nuclei, which latter contain the bulk of the myelin sheaths. On the other hand, the underfed brains contain less water (by 1.4 per cent on the average) than the standards of the same brain weight. Comparisons of the absolute weight of the solids in the underfed brain with the corresponding standard value for the same brain weight and for the same age, based on data in 'The Rat' (Donaldson, '15), are given in table 18. The underfed has shown as a rule considerably less in total solids than the standard for the same age, though it proved to be only slightly higher in percentage of water than the standard (also table 14).

From the above, the absolute mass of the solids in the underfed brain seems to be more than in the standard for the same brain weight, but less than in the standard for the same age. So the increase in solid mass is somewhat retarded by starvation. It will be noted that in my series of rats the percentage of water in the underfed was 0.48 per cent above that in the standards of like age and this is the reverse of the results reported by Donaldson and by Hatai in the studies just cited. This discrepancy probably depends on the fact that my rats are absolutely much younger than those studied by the other authors, but the explanation must await further study.

Since, as shown in chart 1, the relative values of the quantity of the alcohol-extractives has a fixed relation to the absolute weight of the solids in the brain, the above statement may be also

TABLE 18

Giving for each individual in Litter H (Series II) the sex, the age, the observed brain weight, percentage of water, and the calculated absolute weight of the solids in the brain, compared with the standards for the percentage of water and the mass of solids for the brains of the same weight and of the same age. Averages are given in the last line.

STARVED						STANDARD				
No.	Sex	Age	Brain weight	Percent- age of water	Mass of solids	For the same brain weight		For the same age		
						Percent- age of water	Mass of solids	Brain weight	Percent- age of water	Mass of solids
			<i>grams</i>	<i>per cent</i>	<i>grams</i>	<i>per cent</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>	<i>grams</i>
H a	f	13	0.880	86.39	0.120	87.45	0.110	1.003	85.40	0.146
b	f	17	1.024	84.15	0.162	85.08	0.153	1.099	83.82	0.178
c	f	23	1.135	82.00	0.204	83.21	0.191	1.208	81.93	0.218
d	f	28	1.166	80.83	0.224	82.60	0.203	1.282	80.74	0.247
e	m	32	1.215	80.31	0.239	81.70	0.222	1.338	80.04	0.267
f	f	37	1.101	80.12	0.219	83.78	0.179	1.391	79.55	0.285
g	m	43	1.295	80.24	0.256	80.51	0.252	1.468	79.32	0.304
Average		28—	1.117	82.01	0.203	83.48	0.187	1.256	81.54	0.235

confirmed by the data given in table 16, in which it is clearly shown that in the underfed the alcohol-extractives are slightly less developed as compared with the standards for the same age.

20. SUMMARY

1. Young albino rats were experimentally starved throughout the suckling period, by one of the following methods:

Series I. Separation of the young from the nursing mother for the maximum time each day.

Series II. Entrusting one mother with an excessive number of young (over seventeen) at the same time and thus reducing the amount of milk for each young one.

Series III. Starving the nursing mother and thus reducing the quantity of milk secreted.

I employed five litters for Series I, two litters for Series II, and one litter for Series III; in all forty-six individuals were subjected to experiment and there were fourteen controls.

2. The underfed and the controls were killed at different ages (between three and forty days) and the body measurements and the brain weights recorded. The brain was fixed, sectioned, stained, and examined according to the standard procedure previously adopted for these studies (Sugita, '17, '17 a, '18 b, '18 c) and the size of the cerebrum, the thickness of the cerebral cortex, the area of the cortex in the sections, the number of nerve cells in a unit volume of the cortex, and the size of the pyramidal and the ganglion cells, were all determined and then corrected to the values for the fresh condition of the material, by the use of the correction-coefficients devised for these purposes.

Using these data, the relative volume of the cerebral cortex and the number of nerve cells in the entire cerebral cortex were computed, employing the formulas already devised by me (Sugita, '18 b). All the observed and computed data were compared with the corresponding respective standard values for the normal Albino brain of the same weight or of the same age, as given in my previous papers (tables 3, 4, 5, 6, 8, 11 and 13).

3. In Series I the underfed rats were found to be 29 per cent less in the body weight and 8 per cent less in the brain weight, than the standards for the same ages (between three and forty days). In Series II and III the underfed rats were 39 per cent less in the body weight while 8 per cent less in the brain weight. It appears from this that starvation without removal from the nest, and the corresponding disturbance to the young, retards the growth of the brain relatively less, despite the greater arrest in the body growth.

The underfed brain weight was found on the average 24 per cent higher than the standard for the same body weight. The brain weights in the underfed have values between the standards for the same age and those for the same body weight, but generally fall nearer to the former.

The brain weight is a function of the body weight: a rat which is more reduced in body weight by starvation has a more reduced brain weight. The brain weight—body weight ratio is always higher in the underfed than in the standard for the same age, and the difference between the ratios roughly indicates the severity of

the starvation. Thus in those severely underfed the difference is higher than in those less severely underfed.

4. The shape of the cerebrum in the underfed is slightly elongated as compared with that of the standard with the same brain weight and approximates that for the same age. As the result of underfeeding, the growth of the central nuclei seems to be more arrested in width than in length and the changes in the growth in the cortex in thickness matter little for the shape of the cerebrum.

5. The thickness of the cortex is on the average 10 per cent greater in the underfed in the localities I, II, VI, and VII than in the standards for the same brain weight. By averaging according to the entire section, the average thickness in the sagittal section of the underfed exceeds that of the standard by 5.3 per cent and in the frontal section by 8.7 per cent. The general average thickness of the cortex in the underfed is consequently greater by about 7 per cent than the standard for the brain of the same weight. The localities which normally show the higher rate of increase in thickness during the postnatal growth are those which are notably greater in the cortical thickness in the underfed brains.

6. The relative volume of the cerebral cortex, computed by the formula $L.F \times W.D \times T$, is generally smaller in the underfed than in the standard for the same age. In the underfed brains weighing up to 1.0 gram (that is, under sixteen days of age), it is on the average less by 16 per cent or more, while in the underfed brains weighing more than 1.0 gram it is 6 per cent greater than the standard. So it may be said that, in rats underfed severely, the cortical volume is considerably retarded in growth in early period of development, but this is somewhat compensated or overcompensated later when the brains attain the weight of more than 1.0 gram or in age of more than sixteen days.

7. The cell density in the cerebral cortex, represented by the sum of the number of pyramids in the lamina pyramidalis and the number of nerve cells in the lamina ganglionaris in two unit volumes of 0.001 mm.³, is considerably higher in the underfed than in the standard rat for the same age. The excess in cell

density in underfed brains weighing less than 1.0 gram is on the average 17 per cent, and that in underfed brains weighing more than 1.0 gram is almost equal to the standard for the same age. As in the underfed brains weighing less than 1.0 gram, the relative volume of the cortex is smaller than in the standard, it follows that the underfed brains, if they contain the same number of cells, must have a relatively higher cell density in a unit volume to balance the smaller total volume of the cortex.

8. The relative value of the computed number of the nerve cells in the entire cortex, calculated by the formula $N \times L.F \times W.D \times T$, in the underfed was compared with the corresponding standard value for the same age and the former was found to be only slightly higher than the latter, so that they may be regarded as practically the same. If so, the process of the cell division in the cerebrum must have progressed according to the advancing age, in spite of the starvation.

9. The size of the nerve cells was studied on the pyramids in the lamina pyramidalis and on the ganglion cells in the lamina ganglionaris. The cell body of the pyramids in the underfed brains weighing less than 1.0 gram is smaller by 11.2 per cent in average diameter and that in brains weighing more than 1.0 gram smaller by 8.3 per cent than the standards for the same age. The corresponding figures for the nuclei of the pyramids are 15.3 per cent and 11.0 per cent.

The cell body of the ganglion cells in the underfed brains weighing less than 1.0 gram is smaller in average diameter by 11.8 per cent, and that in the underfed brains weighing more than 1.0 gram is smaller by 3.1 per cent than the standards for the same age. The corresponding values for the nuclei of the ganglion cells are less by 12.5 per cent and 5.1 per cent, respectively. So, on the average, the nerve cells in the cortex of the underfed of all weights are smaller in average diameter by about 9 per cent (for the underfed brains weighing less than 1.0 gram by about 12 per cent and for those weighing more than 1.0 gram only by about 6 per cent), and consequently smaller in volume by about 25 per cent than the standard cells of the same age. These determinations apply only to the largest cells found at the measured locality.

10. The underfed brains (Series II) contain on the average slightly (0.48 per cent) more water, if compared with the normal brain of the same age, and somewhat (1.4 per cent) less water, if compared with the normal brain of the same weight. This means probably that, in terms of the percentage of water, the underfed brain is slightly underdeveloped for its age and somewhat overdeveloped for its weight. If the absolute weight of the solid mass be calculated and compared with the standard for the same brain weight and sex, the solids are found to be somewhat more in the underfed and if the same compared with the standard for the same age and sex the solids are always less in the underfed. The relative value of the alcohol-extractives, obtained by comparing the initial brain weight with its weight after dehydration and extraction in 80 per cent alcohol (for twenty-four hours) and 90 per cent alcohol (for twenty-four hours) according to a uniform procedure, shows that in the underfed brains the amount of the alcohol-extractives is somewhat smaller than in the normal of the same age.

The above observations indicate that in the underfed the myelination process in the brain is somewhat retarded for the age. This assumption was supported in a general way by the direct examination on the sections obtained from the underfed brains.

11. Briefly, we conclude that by starvation in the early days the brain suffers much in its development in toto, but the cell division is going on quite normally according to its age. The growth of the cells in size is retarded and the formation of myelinated fibers somewhat diminished by inanition. So the smaller weight and size of the underfed brain is due to an arrest in the growth and development of the constituent neurons and not to a decrease in their number.

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COMPARATIVE STUDIES ON THE GROWTH OF THE CEREBRAL CORTEX

VIII. GENERAL REVIEW OF DATA FOR THE THICKNESS OF THE
CEREBRAL CORTEX AND THE SIZE OF THE CORTICAL CELLS IN
SEVERAL MAMMALS, TOGETHER WITH SOME POSTNATAL GROWTH
CHANGES IN THESE STRUCTURES

NAOKI SUGITA

From The Wistar Institute of Anatomy and Biology

THREE FIGURES AND TWO CHARTS

I. INTRODUCTION

Years ago Schwalbe ('81) pointed out as characteristic somatic expressions, which might be taken to indicate the grade of intelligence of a species of animals, the following four measurements on the brain: 1) total weight of the brain; 2) total number of nerve cells in the brain; 3) total area of the surface of the hemispheres of the brain, and 4) the thickness of the cerebral cortex. Since then he and many other neurologists have endeavored to gather data on the morphological evidence for the development of mental ability. Donaldson and Hatai ('The Rat,' Donaldson, '15) have made systematic observations on the growth changes in the central nervous system as well as in other organs and systems, using exclusively the albino rat. As a result of their investigations, the postnatal growth of the brain and the spinal cord, in gross measurements, and the relations of these to the other systems during growth have been determined. In line with these studies, I also made further researches on the growth in the thickness of the cerebral cortex, the size and shape of the cortical nerve cells and the relative number of the cortical cells in both the Norway and albino rats. The results of these researches have been already presented (Sugita, '17, '17 a, '18, '18 a, '18 b, '18 c, '18 d), with references

to some similar studies by other authors. These data give us a general idea of the postnatal development of the cerebral cortex in a representative mammal (albino rat), and we may fairly infer that similar changes occur in other mammals during the growth of the brain. To test how far my conclusions on the mode of the development of the cerebral elements during postnatal life may be extended, I shall review and summarize in the present paper the results obtained by several authors on the development of the cortex in other mammals and make a comparison of their results with the data obtained by me.

II. THICKNESS OF THE CEREBRAL CORTEX IN THE ALBINO RAT

The results obtained by me regarding the cortical thickness in the brain of the albino rat may be summarized as follows (Sugita, '17 a):

1. The cortex at the frontal pole of the hemisphere is the thickest and that at the occipital pole is the thinnest. Speaking in general terms, the cortex diminishes in thickness from the frontal to the occipital pole and from the dorsal to the ventral aspect.

2. After birth, the general average of the cortical thickness increases very rapidly during the first ten days, thickening from 0.74 mm. at birth to 1.73 mm. at ten days, more than twice the thickness at birth, while the brain weight increases from 0.25 gram to 0.95 gram during the same period. This is designated by me the first phase of the cortical development.

3. Between the tenth and the twentieth day after birth, the cortical thickness increases more slowly, attaining at twenty days to within 4 per cent of the full thickness of the cortex, namely, 1.84 mm., or about 2.5 times the thickness at birth, while the brain weight increases to 1.15 grams. This is designated the second phase of the cortical development.

4. From the twentieth to the ninetieth day, the cortical thickness increases but little on the average, attaining at ninety days the thickness of 1.93 mm., or 2.6 times the thickness at birth, while the brain weight has increased to about 1.80 grams. This is designated the third phase of the cortical development.

After the ninetieth day, there is no significant change in the thickness of the cortex, but the area of the cortex increases as the brain weight rises and at 2.0 grams is greater than at 1.15 grams (20 days) by about 45 per cent.

5. In the first phase the cortex increases its thickness by receiving some newly formed cells from the matrix and many already formed from the transitional layers and at the same time by the general enlargement of the neurons, especially the cell bodies; in the second phase, however, it grows main'y by the enlargement of the cell bodies and the growth of the axons and dendrites; while during the third phase it thickens only slightly, but extends in area as the result of the ingrowing axons and the formation of the myelin sheaths and non-nervous structures.

6. The cortex at the frontal pole increases its thickness very rapidly and steadily, continuing to do this even after the end of the second phase, while at all the other localities the cortex thickens in the same proportion, so that at the end of the second phase all the localities reach nearly the full thickness, but maintain their initial relations. The localities heterogeneous in their cell lamination show in the course of thickening some deviation from the localities which are typical.

7. The cortex generally attains nearly its full thickness before myelination, as shown by the Weigert staining method, occurs in it. In the Albino, the cortex has nearly its mature thickness at twenty days, just before the young rat is weaned and when the brain has attained only a trifle more than half its final weight. The growth of the cortex in thickness is therefore precocious.

III. INCREASE IN CORTICAL THICKNESS DURING GROWTH OF THE BRAINS OF THE MOUSE AND THE GUINEA-PIG

Mouse. Isenschmid ('11) has made a study of the cortical cell lamination in the brain of the mouse and given a map of the topographic localization in the hemisphere, which is reproduced here as figure 1. De Vries ('12) and Rose ('12) have also presented a brain map of the mouse according to their studies on the cell architecture of the cortex; a map which resembles that

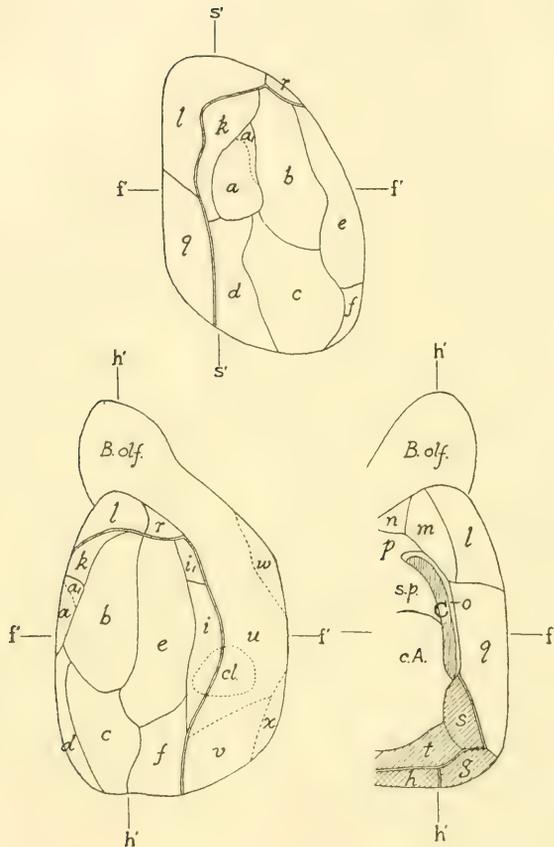


Fig. 1 Cortical area of the mouse (*Mus musculus*)—reproduced from the original by Isenschmid ('11); the thickness of the cortex at each area designated on the map is tabulated in table 1 of this paper. Double lines show borders of three—the dorsolateral, the frontomedial, and the suboccipital—regions of the neopallium. Shaded parts (areas *t*, *s*, and *h*) do not lie in the same (median) plane as the other areas. *A* = Dorsal view of the right hemisphere; *B* = Lateral view of the right hemisphere; *C* = Medial view of the right hemisphere. *B.olf.* = Bulbus olfactorius; *C* = Corpus callosum; *c.A.* = Cornu Ammonis; *cl.* = Clastrum; *s.p.* = Septum pellucidum. *s-s'* = the level corresponding to that from which the sagittal sections of the Albino brain were taken by me; *f-f'* = the level corresponding to that from which the frontal sections of the Albino brain were taken by me; *h-h'* = the level corresponding to that from which the horizontal sections of the Albino were taken by me.

TABLE 1

Giving for each locality of the brain of the adult mouse the characteristics of the cell lamination, the thickness of the cortex on the slide as determined from the photograms given by Isenschmid ('11), and the relative thickness of the outer and inner layers as presented by the same author. For the localities consult figure 1 in this paper, which was reproduced from the original of Isenschmid ('11)

AREA (FIG. 1)	CHARACTERISTICS OF THE AREA IN CELL-LAMINATION	THICKNESS OF THE CORTEX	RELATIVE THICKNESS OF THE OUTER AND INNER LAYERS OF THE CORTEX OUTER: INNER ²
		<i>mm.</i>	
a	Largest ganglion cells contained ($18 \times 20 \mu$)...	0.73	48: 52
a ¹	Not so large cells.....		
b	IV layer thick.....	0.86	45: 55
c	0.50	45: 55
d	0.53	45: 55
g	Transitional part.....		
h	Paleopallium.....		
e	IV layer not so well developed.....		42: 58
f	Adjoins to fovea limbica, cell lamination not clear.....	0.62	
i	0.44	
k	Transitional part (ganglion cells: $13 \times 15 \mu$)..	0.81	34: 66
l	At the corner (ganglion cells: $12 \times 14 \mu$).....	0.78	23: 77
m	0.71-0.61	
r	1.20 ¹	22: 78
q	(Ganglion cells: $15 \times 18 \mu$).....	0.56	28: 72
s	Similar to area q.....	0.26	
t	0.34	

¹ Section cut obliquely.

² The outer layer = the lamina granularis externa plus the lamina pyramidalis plus the lamina granularis interna. The inner layer = the lamina ganglionaris plus the lamina multiformis.

of Isenschmid. Isenschmid ('11) has recorded the thickness of the cerebral cortex of the mouse on the slide at every locality mapped in his figure (fig. 1). But the actual thickness not being given explicitly for each locality, I calculated the values from the direct measurements made on the photograms. The brain was fixed in alcohol, imbedded in paraffine and cut in 10-micra sections and stained with kresyl-violet. The thicknesses of the cortex on the slide as thus obtained are given for each locality in table 1 and also are condensed in table 2, in which the data

TABLE 2

A comparison of the thicknesses of the cerebral cortex at several corresponding localities in the albino rat and in the mouse. The data for the albino rat were taken from table 11 in my previous paper (Sugita, '17 a, p. 578) and the data for the mouse were taken from a paper by Isenschmid ('11). The order of increasing thickness is the same in both animals

ALBINO RAT		MOUSE		
Locality	Average thickness of cortex by locality	Corresponding locality	Thickness of cortex at each of the localities	Average thickness of cortex by locality
	<i>mm.</i>		<i>mm.</i>	<i>mm.</i>
V and XIII	1.24	c	0.50	0.50
IV	1.42	d	0.53	0.53
XII and VIII	1.67	e and i	0.65 and 0.44	0.55
III and XI	1.91	a and e	0.73 and 0.65	0.69
VI	2.01	l (corner)	0.78	0.78
II and X	2.03	k and b	0.81 and 0.86	0.84
VII	2.29	b	0.86	0.86
I and IX	2.99	frontal pole	1.00	1.00
Average.....	1.94	Average.....		0.72

for the Albino are so entered that the cortical thicknesses at the corresponding localities in the two forms may be compared. The order of the localities is arranged according to the increasing thickness in the Albino (taken from table 11, Sugita, '17 a, p. 578). The average value of the cortical thickness in the mouse is, on the slide, 0.72 mm., and if corrected to the fresh condition would probably be somewhat thinner than one-half the average thickness of the Albino cortex. The order of the thickness according to localities is quite the same, so that in both forms the cortical thickness decreases from the frontal to the occipital pole and from the dorsal to the ventral aspect. Moreover, the cortex at the frontal pole is the thickest and has double the thickness of that at the occipital pole.

As seen in figure 1, the cerebral hemisphere is divided by Isenschmid into three main regions—the dorsolateral, frontomedial and suboccipital regions—separated by the double line in figure 1.

The average cortical thickness in the dorsolateral region (fig. 1 a) is 0.56 mm. at its hinder-medial part and 0.90 mm.

at its fore-lateral part, and in this region the lamina zonalis is about one-twelfth, the main outer layers (the lamina granularis externa plus the lamina pyramidalis plus the lamina granularis interna) about two-fifths and the main inner layers (the lamina ganglionaris plus the lamina multiformis) about one-half the total thickness of the cortex. In the frontomedial region (fig. 1 c) the cortical thickness at the frontal pole is 1.00 mm. and that at the caudal part is 0.35 mm., while in the suboccipital region the cortical thickness ranges between 0.2 and 0.3 mm.

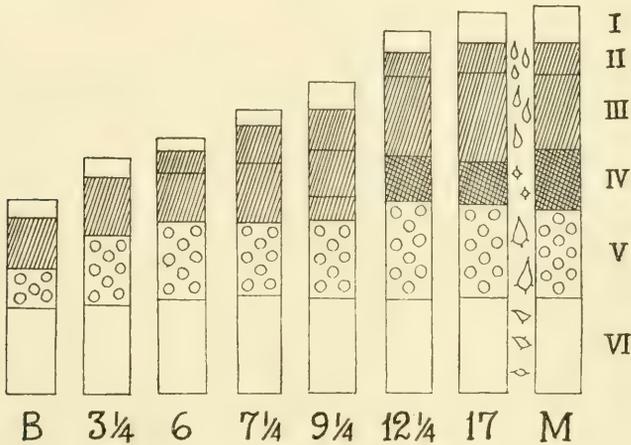


Fig. 2 Showing diagrammatically the thickness of the cerebral cortex at locality *a* in the mouse at different ages. Reproduced from the original given by Isenschmid ('11). B = at birth. M = at maturity. The other arabic numbers show the age in days. I = lamina zonalis; II = lamina granularis externa; III = lamina pyramidalis; IV = lamina granularis interna; V = lamina ganglionaris; VI = lamina multiformis. The cell outlines found between the last two diagrams indicate the relative size and shape of the cells in each cortical layer.

Isenschmid has given also diagrams illustrating the growth in cortical thickness at locality 'a' (fig. 1 a, corresponding approximately to locality III in my study, fig. 2, Sugita, '17 a, p. 525), sampled from material at several different ages and magnified uniformly. These are also reproduced here as figure 2. The diagrams show that as age advances the lamina pyramidalis (II and III) thickens steadily and continuously while the lamina

ganglionaris (V) and especially the lamina multiformis (VI) grow much less rapidly. Chart 1 gives a comparison of the increase in the cortical thickness at corresponding localities (locality 'a' of the mouse and locality III of the albino rat) in the albino rat and the mouse, the data being from Isenschmid ('11) and Sugita ('17 a). In the Albino the cortex attains nearly its full thickness at twenty days (weaning time), while in the mouse this stage was reached between twelve and seventeen days of age, very closely corresponding to the weaning time of

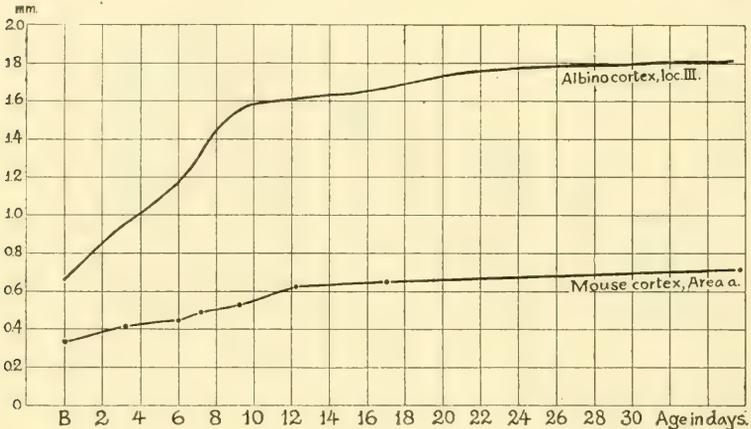


Chart 1 Giving the cortical thickness of the albino rat and of the mouse according to age. The data for the albino rat are taken from Sugita ('17 a) at locality III measured on the sagittal section and the data for the mouse are taken from Isenschmid ('11) at locality 'a.' These two localities approximately correspond.

the mouse, which is fifteen days. The remarkable phase during which the rapid increase in cortical thickness takes place in the Albino (first ten days after birth) cannot be clearly identified on the graph for the mouse cortex. It must be recalled, however, that data on the mouse cortex have not been corrected for the action of the reagents, while the data for the rat have been so corrected. The outstanding fact, however, is that the cerebral cortex in both forms attains nearly its full thickness just before the weaning time.

Guinea-pig. I have had the opportunity at The Wistar Institute to examine the sections of the guinea-pig brains prepared by Allen ('04) for her study on the myelination of the nervous system of that animal. The sections were cut in series in the frontal plane from material fixed in Müller's fluid, imbedded in celloidin and stained by Weigert's method for the myelin sheaths. The thickness of the cerebral cortex in the adult guinea-pig (body weight, 618 grams; brain weight not recorded) is on the average 1.90 mm. (1.80 mm., 1.88 mm., and 2.01 mm., respectively, at the localities corresponding to localities VI, VII, and VIII examined by me on the frontal section of the Albino brain at the level of the commissura anterior). The corresponding measurements at birth (body weight, 108 grams) are 1.71 mm. (and 1.51 mm., 1.75 mm., and 1.86 mm., respectively) and those at thirty-five days (body weight, 250 grams) are 1.85 mm. (and 1.77 mm., 1.86 mm., and 1.92 mm., respectively). So, from birth on to the maturity, the cortical thickness has on the average increased only 11 per cent. According to Allen, the guinea-pig at birth is covered with hair, has complete muscular development, and is almost independent of the mother, the central nervous system being practically completely myelinated, whereas, by contrast, the albino rat is born quite naked, extremely helpless and undeveloped, and myelination in the brain has not begun. The guinea-pig is psychically mature soon after birth (three days after birth); the degree of development of the central nervous system of the new-born guinea-pig corresponds to that of the albino rat at twenty-three to twenty-seven days or its period of first psychical maturity. A new-born guinea-pig is found to have a cerebral cortex in which the myelination is going on.

Comparing the sections from the guinea-pig brain with those from the albino rat brain, it appears that the new-born guinea-pig corresponds to the albino rat of about ten days in cortical thickness, but seems to be older when judged by the myelination of the cortex. This coincides with observation that the guinea-pig is, almost from the start, relatively independent of the mother.

IV. THE CORTICAL THICKNESS AT SEVERAL LOCALITIES IN THE
BRAINS OF SOME MAMMALS OTHER THAN THE RAT

Few papers have been published regarding the differences in the thickness of the cerebral cortex at given localities of the brain in mammals other than the rat, except for man. Yet even in these cases, the techniques of hardening, imbedding, and staining used by the different authors are dissimilar and their results are accordingly not precisely comparable. Despite this, however, it has seemed worth while to make a survey of the data at hand.

Rabbit. Bevan Lewis ('81) has given as the natural thickness¹ of the cerebral cortex of the adult rabbit the following figures (table 3) according to localities. For the localities, the map made by him and reproduced by me in a previous paper (Sugita, '17 a, fig. 10, p. 544) should be here consulted. He has presented the thicknesses of every layer of the cortex separately, but here only the total cortical thicknesses, as computed by me from his data, are given in round numbers.

Pig. Lewis ('79) has also determined the cortical thickness at several localities in the pig brain (the names of the localities

TABLE 3

The thickness of the cerebral cortex of the rabbit, quoted from Bevan Lewis ('81)

Depth of cortex on a plane with genu of corpus callosum:	
Gyrus fornicatus.....	<i>mm.</i> 1.72
Sagittal angle.....	2.23
Extra-limbic.....	2.81
Near limbic sulcus.....	2.31
Depth of cortex on a plane with posterior border of corpus callosum:	
Gyrus fornicatus.....	1.70
Sagittal angle.....	1.91
Extra-limbic.....	2.46
Depth of cortex of the modified lower limbic type.....	2.23 to 2.47
Depth of cortex in the cornu Ammonis:	
Anterior regions.....	2.27
Average at six different sites.....	2.23

¹ Lewis measured the cortical thickness on sections cut by the freezing microtome from fresh material and then hardened by osmic acid, stained by aniline black and mounted in Canada balsam. According to his statement we obtain, by this method, the natural depth of the cortex, no shrinkage occurring if the preparations have been carefully made (Lewis, '78).

TABLE 4

The thickness of the cerebral cortex of the pig, quoted from Bevan Lewis ('79)

Depth of cortex from before backward:

	<i>mm.</i>
	4.97
	4.48
Limbic lobe.....	3.70
	4.98
	3.53
	3.77
Average.....	4.22
	3.28
	2.65
Upper parietal convolutions.....	3.08
	3.91
	4.23
	3.44
Average.....	3.50
	3.44
	3.91
Lower parietal convolutions.....	3.95
	3.35
	3.02
	3.67
Average.....	3.64

are analogous to those given for the rabbit brain, loc. cit.). His results are summarized in table 4. These values are distinctly high compared with those for other mammals, as shown in the various tables in this paper. These results taken together with those for the rabbit just given, which are also noticeably high, suggest that the determination by Lewis are for some reason systematically too high.

Marsupials to man. Table 5 is quoted (slightly modified) from Brodmann ('09) and gives for several species of mammals, including man, the cortical thickness at six localities (areae precentralis, frontalis, parietalis, occipitalis, hippocampica et retrosplenialis) in the brain of each animal. The sections were made by hardening the material in 4 per cent formaldehyde, imbedding in paraffine, and staining by the modified Nissl's method, and the cortical thickness was measured by the micrometer directly on the slide. The average thickness was calculated by me for the four areas, excluding the areae hippocampica et retrosplenialis which are heterogeneous in cell lamination.

TABLE 5

The cortical thickness at the corresponding parts of the cerebral hemisphere in different mammals, quoted from Brodmann ('09). According to his nomenclature, area precentralis = type 4, area frontalis agranularis = type 6, area parietalis = type 7, area occipitalis = type 17, area hippocampica = type 28, and area retrosplenialis = type 29, as given in his 'Hirnkarte' (Brodmann, '09)

SPECIES	BODY WEIGHT	BRAIN WEIGHT	AREA PRECENTRALIS	AREA FRONTALIS AGRANULARIS	AREA PARIETALIS	AREA OCCIPITALIS	AREA HIPPOCAMPICA	AREA RETROSPLENIALIS	AVERAGE OF THE FIRST FOUR LOCALITIES
	grams	grams	mm.	mm.	mm.	mm.	mm.	mm.	mm.
Homo sapiens (man)	60,000	1,400	3.0-4.5	3.0-3.8	3.08	2.3-2.6	2.5	2.3	3.0
Cercopithecus (long-tailed ape)	2,500	85	3.0	2.5	2.0	1.7	1.6	1.1	1.95
Lemur	1,800	23	2.3	2.3	1.67	1.55	1.35	1.19	1.73
Hapale (marmoset)	200	8	2.15	2.17	1.73	1.26	1.14	1.07	1.59
Pteropus edwardsii (vampire bat)	375	7	1.9	1.6	1.7	1.76	1.52	1.4-1.76	1.66
Erinaceus europaeus (hedgehog)	700	3.5	1.87	2.1	1.78	1.5	1.6	0.8	1.61
Cerculeptes caudivolvulus (kinkajou)	2,000		2.17	2.0	1.7	1.9	1.9	1.67	1.89
Lepus cuniculus (rabbit)	2,200	10	2.7	2.33	2.2	1.8	1.2	0.8-1.5	1.79
Spermophilus citillus (ground squirrel)	200	2.2	2.1	2.18	1.73	1.37	1.13	0.75	1.54
Macropus giganteus (kangaroo)	5,000	25	2.8-3.1		2.2	1.9	1.7	1.2	2.15

Reviewing this table, it is readily seen that, within each order, the animal which has a greater brain weight shows also a greater cortical thickness, but a fixed relation between the brain weight and the cortical thickness has not been here revealed. In different orders, this relation is not true; the lemur and the kangaroo have a similar brain weight (23 to 25 grams),

while the cortical thickness in the latter is much greater (by about 25 per cent).

Prosimiae and primates. The following table (table 6) is summarized from a paper by Marburg ('12) and shows for some species of the prosimiae and primates the total cortical thickness measured at four representative localities (gyri centralis, frontalis, temporalis et occipitalis). The average values were taken by me.

TABLE 6

Thickness of the cerebral cortex at several localities in monkeys, as presented by Marburg ('12). Averages are calculated by me

SPECIES	CENTRAL GYRUS	FRON- TAL GYRUS	TEM- PORAL GYRUS	OCCI- PITAL GYRUS	AVERAGE	
					Of the four locali- ties	Of the three locali- ties
	mm.	mm.	mm.	mm.	mm.	mm.
<i>Simia satyrus</i>	3.11	2.97	2.43			2.84
<i>Hylobates</i> (sp.?).....	3.78	3.24	2.51	1.78	2.83	3.18
<i>Semnopithecus nasicus</i>	3.78	2.43	2.43	1.35	2.50	2.88
<i>Macacus rhesus</i>	2.84	2.70	2.15	1.49	2.30	2.56
<i>Cynocephalus hamadryas</i>	2.97	2.70	2.03	1.35	2.26	2.57
<i>Ateles niger</i>	2.97	2.84	2.43			2.75
<i>Lemur varius</i>	1.30	1.76	1.76	1.67	1.62	1.61

This table also suggests that, in the order of monkeys, the average thickness of the cortex varies so that those which have the greater brain weight have also the greater thickness of the cerebral cortex, but the brain weights are not available for comparison.

V. THE THICKNESS OF THE CEREBRAL CORTEX IN MAN

Man. There are scores of papers giving the measurements of the thickness of the cerebral cortex in man, but they are diverse in the techniques used for preparing the material, in the localities selected for measurement, and also in the manner of measurement. The results published before 1891 were all summarized by Donaldson ('91), but the table is not reproduced here as, owing to the lack of the information necessary for the interpretation of the values found, it has mainly an historical interest.

Donaldson ('91) measured also the thickness of the cerebral cortex at fourteen localities from each hemisphere of nine normal brains (six males and three females), as shown in figure 3 reproduced from his original paper, in order to obtain control

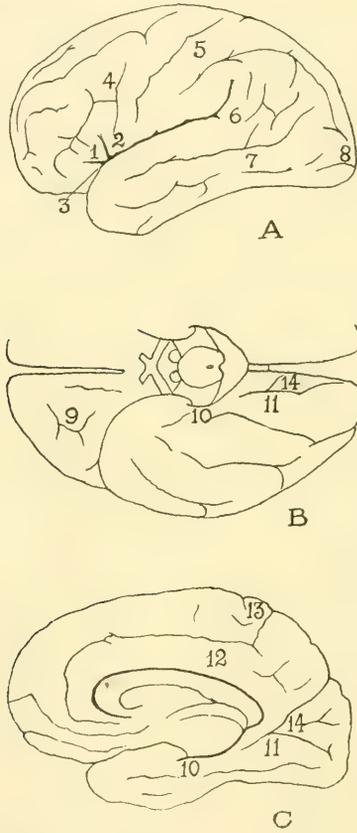


Fig. 3 This figure shows the localities on the hemispheres from which the samples of cortex were taken by Donaldson ('91). For the thickness of cortex at each locality see table 8 and chart 2. A = Lateral aspect. 3 is used to designate the insula, here not exposed. B = Ventral aspect; C = Mesial aspect.

values for the study of the brain of a blind deaf-mute, Laura Bridgeman. The technique employed by Donaldson was fixation in bichromate and alcohol (potassium bichromate $2\frac{1}{2}$ per cent plus $\frac{1}{6}$ its volume of 95 per cent alcohol) for six to eight

TABLE 7

Giving the average cortical thickness of man, arranged according to age and sex, together with the brain weight. Quoted from Donaldson ('91)

AGE	BRAIN WEIGHT	AVERAGE CORTICAL THICKNESS
<i>Males</i>		
<i>years</i>	<i>grams</i>	<i>mm.</i>
35	1419	2.81
35	1443	2.98
39	1393	2.82
45	1367	2.92
57	1464	2.94
?	1210	3.11
<i>Females</i>		
40	1196	2.74
45	1173	2.90
?	1312	3.07
<i>Average</i>		
	1331	2.92

weeks, washing in water for twenty-four hours, 95 per cent alcohol for two days, final preservation in 80 per cent alcohol, and imbedding in celloidin. The sections were cut about 100 micra thick and measured unstained under a low magnifying power with a micrometer eyepiece, at the summit of the gyrus and at the side, midway between the summit and the bottom of the bounding sulcus. To obtain the average thickness at the locality, the smaller figure was multiplied by 2, added to the larger figure, and the sum divided by 3.

Table 7 shows the average thickness of the cortex (taken from the fourteen localities) arranged according to sex and age, quoted from Donaldson ('91). If we take the nine cases in this table as the basis for computation, we find the mean thickness of the cortex to be 2.92 mm., with a probable error of the mean equal to ± 0.026 mm.

I wish to cite also the average thickness of the cortex, as thus obtained by Donaldson ('91), according to locality (table 8). These localities are shown in figure 3 and the relative thickness

of the cortex at each is graphically presented in chart 2. Generally summarized, the average thickness of the cortex of the adult man is 2.92 mm.; females have a slightly thinner cortex than males (differences less than 1 per cent, or 0.02 mm.) and the right hemisphere usually has a cortex a few per cent less thick than the left (maximum difference 7 per cent).

With the foregoing determinations are to be compared the measurements by three other observers.

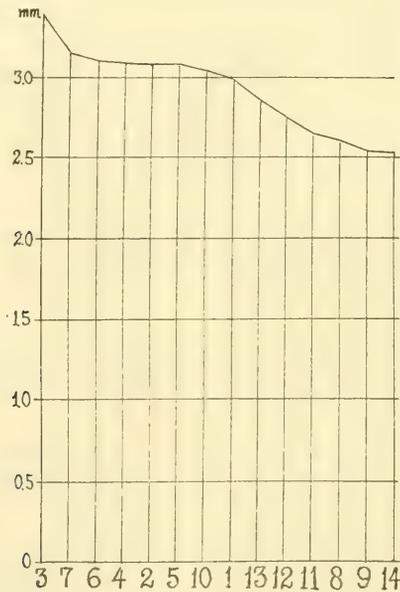


Chart 2. The curve was plotted according to table 8 to show the cortical thickness at each locality as measured by Donaldson ('91). The numbers placed by the ordinates indicate the thickness of the cortex in millimeters. The numbers for the localities are given below, and correspond to those in figure 3, A, B and C.

In accordance with this plan, the results obtained in a careful study by Hammarberg ('95) are tabulated in table 8. The material used for this study was a brain of a male, twenty-eight years old, mentally normal, and who died of typhoid fever. The technique employed was fixation in 95 per cent alcohol, imbedding in paraffine by means of xylol, sections 10 micra in

TABLE 8

Giving for several localities on the hemisphere of the adult human brain the thickness of the cortex, as measured by different authors. The general average thickness was taken, averaging all measurements presented by each author. For reasons given in the text, these averages as they stand are by no means comparable with each other. The data were taken from Donaldson ('91), Hammarberg ('95), Campbell ('05), and Brodmann ('08)

Locality	Author		Donaldson	Hammarberg	Campbell		Brodmann		
	Kind of section	Unit	Cell mm.	Cell mm.	Cell mm.	Fiber mm.	Cell mm.	Fiber mm.	
Regio Rolandica	Gyrus centralis	anterior		2.97	2.50	2.62	3.94	4.05	
	Gyrus centralis posterior	oral side	3.08	2.70	2.20	2.12	1.86	1.98	
		intermediate part					2.93	3.16	
		caudal side					2.60	1.90	2.43
	Lower end of sulcus Rolandi						2.53		
Lobulus paracentralis			2.86						
Lobus frontalis	Gyrus frontalis superior	hinder part		3.10		2.62	2.52	3.82	3.84
		middle part						3.93	
		fore part			2.60				3.45
	Gyrus frontalis medius		3.09	3.40	2.40	2.10		3.57	
	Gyrus frontalis inferior	Pars opercularis	3.08	2.50				3.52	
		Pars triangularis	2.98	3.00				3.34	
		Pars orbitalis						3.60	
Gyrus rectus		2.53					3.17		
Frontal pole					2.37	1.82	3.07		
Lobus parietalis	Gyrus parietalis superior				2.37	2.25	3.08	3.20	
		extreme fore part					2.93	2.85	
	Gyrus parietalis inferior	Gyrus angularis		2.43	2.50	2.00	3.35	3.17	
		Gyrus subramarginalis						3.31	3.25
Lobus occipitalis	Gyrus occipitalis lateralis	fore part	2.61	1.80	2.50	2.52	2.68	2.83	
		polar part					2.34	2.33	
	Cuneus		2.52	2.38	1.82	1.40	2.38	2.47	
		Gyrus lingualis	2.65						
Lobus temporalis	Gyrus Temporalis superior		3.10	2.64	2.60	2.40	3.81	3.83	
		in fissura Sylvii			2.61	1.90	3.35	3.80	
		do. external part					3.57	3.92	
	Pole of Temporal lobe					3.70	3.87		
	Gyrus Temporalis medius		3.15			3.52	3.64		
	Gyrus Temporalis inferior				2.68	2.25	3.47	3.42	
		extreme hinder part					2.97		
Insula		3.38	2.34	2.67	2.62				
Gyrus hippocampi		perirhinal part	3.04				2.07		
		ectorrhinal part					2.93		
		presubicular part					2.25	2.70	
		Ilncus					2.53	3.10	
		Subiculum					2.33	2.60	
Gyrus cinguli		- posterior ventralis	2.75				2.97	2.94	
		- posterior dorsalis					3.10	3.03	
		- anterior ventralis					3.05	3.17	
		- anterior dorsalis					3.48	3.44	
		Pregenual part					1.80		
		subgenual part					2.35		
		retrosplenial part					1.95		
	2.30								
	2.97								
General average			2.92	2.57	2.46	2.17	3.00	3.17	

thickness and staining with methyleneblue. Hammarberg claims that after twenty-four hours in 95 per cent alcohol the brain piece shrinks about 20.5 per cent in volume and the cortical thickness diminishes by 0.1 to 0.2 mm., but that during the subsequent procedures no significant size changes occur. According to his results, the gyri frontales have the thickest cortex (about 3.0 mm.) and the lobus centralis or insula is the thinnest among localities typical in cell lamination. This latter part as measured by Donaldson shows the thickest cortex.

Campbell ('05) gave two series of determinations of the cortical lamination of the human brain, after cell staining and after fiber staining, represented by uniformly magnified illustrations of the sections at the several localities. Making use of his illustrations, I obtained a series of cortical thicknesses at different localities (table 8), reduced to the actual thickness on the slide, by dividing the direct measurement on the illustration by the magnification. His sections were taken from the material fixed in Müller's or Orth's fluid and imbedded in celloidin, cut at 25 micra, and stained with thionine. The general average thickness thus obtained, the two series combined, is about 2.3 mm.

Brodmann ('08) also has measured the thickness of the cortex on the human brains at forty-two different localities on sections prepared by two different methods: one set was fixed in 4 per cent formaldehyde, imbedded in paraffine, and stained by Nissl's method for cell study, and the other, fixed in Müller's fluid, imbedded in celloidin, and stained by Weigert's method for the myelin sheaths. His results, which are the averages from brains between seventeen and forty-five years in age, are also tabulated in table 8 for a comparison. The general average thickness given by Brodmann is about 3.09 mm.

Kaes ('07) also studied the growth in thickness of the human cerebral cortex, measured at twelve different localities on the hemisphere, using sections fixed in Müller's fluid and stained by Weigert's method. His results are remarkably high, giving 4.9 mm. on the general average. His method of measuring the cortex is so arbitrary and peculiar, however, that his results are not included in this table 8.

Bevan Lewis ('79) has given as the average depth of the human cortex the figures as high as 4.84 to 5.70 mm., a higher value even than that of Kaes. His results for both the pig and rabbit cortex were also very high, compared with those obtained for other mammals. These results suggest that his technique, which he claims gives the natural depth of the cortex, is likely to produce very high values.

Reviewing the table (table 8), the values for the cortical thickness given for a fixed part of the hemisphere by different authors are by no means in accord; the results by Brodmann stand close to the results by Donaldson, while those given by Campbell are the lowest, less than one-half the values given by Lewis. These differences are probably due mainly to differences in technique and are not to be attributed to variations within the same species, as the series of Donaldson (table 7) and my previous study (Sugita, '17 a) both have shown that individual variations in cortical thickness, obtained by the use of the same technique, are low as compared with the variations for other body measurements.

On the average, the figures given by Donaldson and Brodmann are fairly close and the former being somewhat lower, probably because Donaldson took the average from the values at the summit and at the sides of the gyrus, while Brodmann has measured the thickness at the summit only. The figures given by Hammarberg and Campbell are low, probably owing to the shrinkage of the material during preparation, as may be inferred from the descriptions by the authors and from the studies on the effects of fixing fluids by King ('10) and by me (Sugita, '17 a, '18 b, '18 c).

Despite the apparent irregularity among the figures given for the cortical thickness at different localities by the several authors, as shown in table 8, there are some general relations which are fairly clear. If we examine table 9 in which has been entered for each region the average thickness obtained by each author, it may be safely said that this table (and also table 6 for the monkeys) shows that in man (and the primates) the cerebral cortex differs normally according to locality. The

TABLE 9

Giving the average cortical thickness for several lobes and regions (with typical cell lamination) of the cerebral hemisphere as given by different authors, and the order of localities according to the cortical thickness, together with the difference in thickness between the temporal and occipital regions. R = regio Rolandica, F = lobus frontalis, P = lobus parietalis, O = lobus occipitalis, T = lobus temporalis. Based on table 8 in this paper

LOCALITY	DONALDSON (91) (Cell)	HAMMAR- BERG (95) (Cell)	CAMPBELL (05) (Cell)	CAMPBELL (05) (Fiber)	BRODMANN (08) (Cell)	BRODMANN (08) (Fiber)
	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>	<i>mm.</i>
Regio Rolan- dica.....	2.92	2.34	2.43	2.21	2.74	2.93
Lobus frontalis	2.92	2.92	2.46	2.15	3.50	3.84
Lobus parietal- lis.....		2.43	2.44	2.13	3.17	3.12
Lobus occipita- lis.....	2.59	2.09	2.16	1.96	2.47	2.54
Lobus tempora- lis.....	3.21	2.49	2.64	2.29	3.48	3.75
Average.....	2.91	2.45	2.43	2.15	2.92	3.16
Order of the above five localities as to the thick- ness.....	TFRO?	FTPRO	TFPRO	TRFPO	FTPRO	FTPRO
Difference be- tween T and O.....	0.62	0.40	0.48	0.33	1.01	1.21

frontal and temporal regions have in all cases the thickest cortex and the occipital region is the thinnest, while the position for the cortex of the parietal and Rolandic regions is less fixed. These thickness relations support the earlier statement made by me for the rat cortex that the thickness diminishes from the frontal to the occipital pole and from the dorsal to the ventral aspect.

Brodmann ('08) has concluded from his careful study that regional characteristics for the cortical thickness clearly exist. "Diese sind in allen normalen Gehirnen gesetzmässig und kon-

stant und bilden ein Hauptmerkmal der strukturellen Verschiedenheiten der Gehirnoberfläche; jedes Strukturfeld besitzt demnach eine bestimmte, mittlere Durchschnittsbreite, durch welche es sich von den Nachbarfeldern auszeichnet." On the other hand, local variations within a fixed area are small, while individual differences between different brains for each locality may run sometimes as high as 0.5 mm. or more.

VI. INCREASE IN CORTICAL THICKNESS DURING THE GROWTH OF THE BRAIN OF THE MAN

From the point of view of the growth changes, there have been only few studies on the human cerebral cortex ever published.²

Kaes ('05, '07, '09), employing forty-one human brains (twenty-eight males and thirteen females, normal and pathological combined) of different ages and of different grades of intelligence, studied the cerebral cortex for the purpose of following the growth changes in it. He took his sections from twelve localities in each hemisphere, stained the fibers by Weigert's method and measured the so-called cortical thickness from the ectal border of the Meynert's arcuate fibers (or *fibrae propriae*) to the ectal border of the zonal layer. His conclusions on the growth

² His ('04) has given the following values as the cortical thicknesses measured at different localities of the hemisphere of the human embryos in early months, at different stages of intrauterine development—measured directly on the sections imbedded in paraffine.

AGE OF EMBRYOS	AT CORPUS STRIATUM	AT LATERAL WALL OF THALAMUS	AT LATERAL WALL OF HEMISPHERE (BASAL PART)	AT LATERAL WALL OF HEMISPHERE (MID PART)	AT MEDIAN WALL OF HEMISPHERE	AT BOTTOM OF SULCUS CINGULI
	μ	μ	μ	μ	μ	μ
<i>weeks</i>						
1			50-55			
2			65-75			
4	150	130		110		60
5	360	160		120		50
6	800	300		130	90	40
7	1300	600	300	170	110	30
8	2000	900	400	200	130	30

changes, briefly stated, are as follows: The average thickness of the cortex diminishes rapidly from his first entry (three months old, 5.58 mm.) to the twenty-third year (4.44 mm.) and is followed by an increase up to the forty-fifth year (5.71 mm.), where it is to be noted that the thickness attained is even greater than that at birth. Then it undergoes a second thinning up to the old age (at ninety-seventh year, his last entry, 4.62 mm.).

These conclusions have been disputed by Donaldson ('08) and by Brodmann ('09), and I am in agreement with these critics that Kaes' results cannot be taken seriously.

Brodmann ('08), in his paper on the cortical measurement, has noted only in a general way the average cortical thickness at the lateral surface of the hemisphere at several ages, as shown in table 10 (columns A and C). Nevertheless, these data can be used for a comparison.

Donaldson ('08) has compared the albino rat with man in respect to the growth of the brain and reached the conclusion that man and the rat show growth curves for the brain which are similar in form when the data are compared at equivalent ages, and the condition of the brain of the rat at five days of age is taken as like that of the human brain at birth. The relative growth rates of the rat and man are as 30 to 1 and the brain of the child at one year corresponds to that of the albino rat at seventeen days of age in its stage of development (Donaldson, MS.). These statements are also confirmed by me for the cortical thickness, as shown in table 10 (see below), and I have already noted that the transitional cortical cell layers, which are no longer to be seen in a new-born child, do not disappear in the albino rat until after four days of age (Sugita, '17 a, p. 539).

From these relations, we conclude that the course of growth in the thickness of the cerebral cortex in man and the albino rat would probably be similar, if the brains were compared at the equivalent ages. Such a comparison is attempted in table 10. Here the increase in cortical thickness in man and in the albino rat is compared, employing data given by Brodmann ('08) and by me (Sugita, '17 a). From the age (column A) given by Brodmann, the approximate brain weight (column B) was de-

TABLE 10

Giving a comparison in the course of increase in cortical thickness in man and in the albino rat, according to data given by Brodmann ('08) and by Sugita ('17 a). Approximate brain weight in man and in the Albino for the equivalent ages were assumed in round numbers according, respectively, to Vierordt ('90) and Donaldson ('08)

A	B	C	D	E	F	G
MAN			ALBINO RAT			
Age	Approximate brain weight	Observed thickness of the cortex, Brodmann ('08)	Approximate brain weight, at the equivalent (observed) ages (Donaldson)	Equivalent (observed) age	Thickness of the cortex at ages given in Column E	Corresponding cortical thickness in human brain, when the adult values in the both are taken as the standards
	grams	mm.	grams	days	mm.	mm.
Fetus						
8-9 months		1.0-1.5		Birth	0.80	1.25
Birth	380	1.5-2.0	0.50	5	1.10	1.75
1 year	950	2.0-3.0	1.10	17	1.75	2.76
Adult	1400	2.0-4.0	1.90	Adult	1.90	3.00

terminated according to Vierordt ('90) and then the final weight (1400 grams) was entered corresponding to the adult brain weight of the albino rat (1.9 grams). The other corresponding brain weights of the Albino of the equivalent ages were entered also according to Donaldson ('08) (column D). The cortical thickness (column F) for the given brain weights of the Albino were then entered according to my former determination (Sugita, '17 a). If the cortical thickness of the adult man be assumed as 3.00 mm. (the mean value of 2.0 to 4.0 mm.) and the corresponding thickness at each age be calculated on the basis of the course of increase in cortical thickness in the Albino (given in column F), the results given in column G—a mere inference, to be sure—are fairly in accord with the figures presented by Brodmann (column C).

In this connection, I had the opportunity, through the courtesy of Dr. W. H. F. Addison, to prepare sections and examine the cortical thickness at the dorsal part of the gyrus centralis anterior (regio Rolandica) from a child thirteen months old (material hardened in 4 per cent formaldehyde, imbedded in paraf-

fine, and stained by Nissl's method). The mean value of the cortical thickness at the summit of the gyrus was 3.55 mm., or within 10 per cent the value obtained by Brodmann at the same locality *in the adult brain* and on a section similarly prepared and measured (table 8). So far, then, as this observation goes, it helps to support my conclusion presented earlier that the human cortex has attained nearly its full thickness at the age of fifteen months (Sugita, '17 a).³

VII. THE BRAIN WEIGHT, THE CORTICAL VOLUME, AND THE BODY WEIGHT

Dhéré and Lapicque ('98) and DuBois ('98 a, '98 b), working independently, found several important relations existing between the body and the brain weights in man and a number of other vertebrates. Recently DuBois ('13) has obtained results which he has formulated in following terms:

1) In species of vertebrates that are alike in organization of their nervous system and their shape, but differ in size, and also in the two sexes of one and the same species, the quantity of the brain increases; A) as the quotient of the superficial dimension divided by the cube root of the longitudinal dimension. B) as the product of the longitudinal dimension by the square of its cube root.

2) In individuals of one and the same species and of the same sex, but differing in size, the quantity of brain increases as the square of the cube root of the longitudinal dimension of the body.

So, briefly stated, 1) reads: in any species of vertebrates that are equal in organization, in form of activity and in shape, the weights of the respective brains are proportional to the 0.55 power

³ According to a study by Fuchs ('83), the child is born without any myelinated fibers in the cerebral cortex. In the lamina zonalis the first myelination appears at five months, in the lamina pyramidalis at the end of the first year, while in the innermost layers we see some faintly stained fibers at two months. The *fibrae arcuate* (association fibers) appear clearly at seven months. Later the myelinated fibers increase in caliber and number as the age advances, and at eight years they attain nearly the appearance which they have in the adult cortex.

of the weights of bodies, and 2) the exponent of correlation within the same species is for all vertebrates the 0.22 power.

These relations were based on a series of observations, and this illuminating idea is now generally accepted as true.

The brain in general consists of the white and the gray matter, and in higher animals the gray matter as represented by the cerebral cortex occupies a relatively large part of the entire cerebrum. This cortex is the seat of a complex series of physiological nerve centers, and the possibility that it has definite quantitative relations with the body as a whole is suggested by the following statement made by Du Bois ('13):

If the quantity of brain does not increase proportionally to the volume of the body, expressed by the weight, it might be that this is really the case with regard to the superficial dimension, as being proportional with the receptive sensitive surfaces and with the sections of the muscles, thus measuring the passive and active relations of the animal to the outer world, for which in this way the quantity of brain can be a measure.

This statement, to be sure, is applied by DuBois to the weight or volume of the entire brain, but if the volume of the cortex stands in some definite relation to the volume of the entire brain, then the cortical volume should be also in a definite relation to the size or weight of the body.

The cortical volume is determined by the area of surface of the cerebral hemisphere and the thickness of the cortex. The former factor is not easy to determine exactly, even in lissencephala, while in higher animals the hemispheres have many convolutions which increase still further the difficulty of this determination. In lissencephala, the surface area of the hemispheres in two brains, which are nearly similar in the form of cerebrum, are approximately comparable with squares of the corresponding diameters of the cerebra.

The cortical thickness, on the other hand, is not so hard to determine exactly. The average thickness of the cortex in different mammals is given in table 11, quoted from various sources, and, as seen from this table, it is not directly related to the size or weight of the brain, since, as Marburg's ('12) table shows, the

cortical thickness in several primates ranges within rather narrow limits (2.3 mm. to 2.8 mm.), while the brain weight shows a distinctly wider range (82 grams to 400 grams) (table 11). In some cases indeed the smaller brain has a thicker cortex, even in the same family (e.g., the smaller hapale has a thicker cortex than the larger lemur). But in general we may conclude with Brodmann ('09) that, within one and the same order or family of mammals, the large brain tends to have a larger average value for the cortical thickness.

The relative cortical volume has been formerly computed by me, employing the formula especially devised for this purpose, in the albino and the Norway rat brains, so that the two forms may be compared directly (Sugita, '18 b). The ratio of the cortical volumes in the adult Albino (brain weight, 2.0 grams) and the Norway (brain weight, 2.3 grams) is 1.31, as the relative cortical volumes are, respectively, 393 and 517 (Sugita, '18 b, table 15), and the ratio of the body surfaces in the two animals amounts also to 1.30, when the body weights of the adult albino and the Norway rats are taken as 300 grams and 450 grams, respectively. Moreover, the ratio of cortical volumes in the two forms at any given age will prove to be almost equal to the ratio of body surfaces of the two at the same age.⁴

As above tested, the body weight and the cortical volume of the animals in the same family stand in a definite relation, at least in this instance. But, as we cannot compute the volume of the cortex in other mammals from the data given in table 11, the relation can not be tested further.

⁴ For example, according to my former presentation (Sugita, '18 b), the computed cortical volume in the Albino Group XV (brain weight, 1.54 grams) is about 346 and that in the Norway Group N XVIII (brain weight, 1.83 grams) is about 423, and according to another determination (Sugita, '18 a) these two groups may be regarded nearly equal in age, as the Albino brain weight would be about 18 per cent less than the Norway brain weight of the like age. The ratio in cortical volume of the above two is 1.22. The body weight corresponding to the brain weight of 1.54 grams in the albino rat is 64 grams and that corresponding to the brain weight of 1.83 grams in the Norway rat is 90 grams ('The Rat,' Donaldson, '15). The ratio of the body surface in the above two, therefore, is about 1.25, quite near to the ratio in cortical volume.

TABLE 11

Giving for several species of mammals the adult body weight and brain weight, the average cortical thickness and the name of author from whom the data for the cortical thickness or for the brain and body weights were cited, arranged in the order of decreasing body weight within each family of mammals. The abbreviations of the names of authors are as follows: B = Brodmann ('09), I = Isenschmid ('11), L = Lewis ('79), M = Marburg, ('12), S = Sugita ('17 a, '18 a, MS.)

OF MAMMALIA	NAME OF SPECIES	BODY WEIGHT ¹	BRAIN WEIGHT ¹	AVERAGE CORTICAL THICKNESS	REFERRED AUTHOR
		grams	grams	mm.	
Primates	Simia satyrus (orang-outang).....	7,350	400.0	2.8	M
	Hylobates.....	950	130.0	2.8	M
	Cynocephalus hamadryas.....	920	142.0	2.3	M
	Macacus rhesus (macaques)....	356	82.0	2.3	M
Prosimiae	Cercopithecus (long-tailed ape)	2,500	85.0	2.3	B
	Lemur varius.....	2,170	28.7	1.6	M
	Lemur.....	1,800	23.0	1.7	B
	Hapale (marmoset).....	200	8.0	2.0	B
	Microcebus.....	62	1.9	1.5	B
Artiodactyla et Carnivora	Ovis musimon (sheep).....	23,000	100.0	1.6 (2.6) ²	L
	Felis domestica (cat).....	3,000	30.0	1.5 (2.6) ²	L
Insectivora	Erinaceus europaeus (hedgehog).....	700	3.5	1.8	B
	Talpa europaea (mole).....	75	1.3	1.0	B
Rodentia	Lepus cuniculus (rabbit).....	2,200	10.0	2.2	B
	Cavia cobaya (guinea-pig)....	600	4.5	1.9	S
	Mus norvegicus (Norway rat).....	450	2.5	2.1	S
	Mus norv. albinus (albino rat)	300	2.0	1.9	S
	Spermophilus citillus (ground-squirrel).....	200	2.2	1.8	B
	Mus musculus (mouse).....	20	0.4	0.8	I
Chiroptera	Pteropus edwardsii (vampire bat).....	375	7.0	1.7	B
	Vespertilio murinus (bat).....	23	0.3	0.4	B
Marsupialia	Macropus giganteus (kangaroo).....	5,000	25.0	2.3	B
	Didelphys.....	1,100	5.5	1.2	B

¹ The body and brain weights of some animals were not given by the author who has given the cortical thickness. In such cases the body and brain weights were taken from the list given by Weber ('96).

² According to Lewis ('79), the values given here without brackets were taken from Meynert and show the value measured on the slide and the values given within brackets were obtained by his own observation and represent the natural depth of the cortex.

VIII. SIZE AND GROWTH CHANGES IN SOME NERVE CELLS IN THE MAMMALIAN BRAIN

Albino rat. The results obtained by me regarding the size and the growth changes of the pyramidal cells and of the ganglion cells in the cerebral cortex of the albino rat were summarized in a previous study (Sugita, '18 c). Four of the conclusions are here quoted:

1. The full size of the pyramids in the lamina pyramidalis is cell body $21 \times 27 \mu$ and nucleus $18 \times 20 \mu$ in the fresh condition (on the slide, respectively, $16 \times 21 \mu$ and $14 \times 15 \mu$). The full size of the ganglion cells in the lamina ganglionaris is cell body $27 \times 37 \mu$ and nucleus $23 \times 25 \mu$ in the fresh condition (on the slide, respectively, $21 \times 29 \mu$ and $18 \times 19 \mu$).

2. The cell body and the nucleus of the pyramids attain their maximum size at twenty to thirty days in age. Up to ten days they still retain their fetal morphology. After having passed the maximum size at about twenty-five days, they diminish somewhat in size, but the internal structure differentiates as the age advances.

3. The cell body and the nucleus of the ganglion cells attain nearly their maximum size at ten days, when they remain still in fetal form. After this stage, the size of the cell body still increases slowly but steadily as the age advances, while the nucleus remains nearly unchanged in size throughout life.

4. Taking a general view of the data already presented in this series of studies, it is very interesting to observe that the thickness of the cortex, the total number of the cortical nerve cells, and the size of the cortical cells, all attain nearly their full values at the same age of twenty days; that is, at the weaning time of the albino rat.

For comparison with these results on the cells of the cerebral cortex, there are some observations by Addison ('11) on the post-natal growth of the Purkinje cells in the cerebellar cortex of the albino rat. His material was also obtained from the rat colony at The Wistar Institute and the cerebellum was fixed in Ohlmacher's solution, imbedded in paraffine, and stained with

carbol-thionine and acid fuchsin. A part of his results on the Purkinje cells is here quoted:

The Purkinje cells are easily distinguishable at birth along the inner boundary of the molecular layer by their relatively large size and lightly staining nucleus. These cells measure $12 \times 7 \mu$ and nuclei $8 \times 6.3 \mu$. During the first week, there is great increase in size of both nucleus and cytoplasm. The main bulk of the latter is at the ectal pole and from it several fine processes radiate into the molecular layer. At eight days the cells measure $18 \times 12 \mu$ and nuclei $10 \times 8 \mu$ to $12 \times 9 \mu$. At eight to ten days there is definite change in form by the elongation of the cytoplasm of the ectal pole to form the main dendrite, the previously existing fine processes becoming its branches. At the same time all the dendrites become arranged in one plane, and this plane is parallel to sections directed across the folia. Nissl granules appear in the cytoplasm at eight to ten days. The arrangement of Purkinje cells changes with the increase in the surface area of the cortex. At birth they are arranged in two to three irregular rows; at three days in one to two irregular rows, and at five days in one continuous row. As growth of the cortex continues, the space intervening between the Purkinje cells becomes greater. Some nuclei reach their maximum size of $12 \times 9 \mu$ at eight days, while the cell bodies usually continue to grow, reaching a maximum size of $24 \times 19 \mu$ at twenty days. The dendrites reach the outer limiting membrane when all the outer granule cells have migrated (twenty-one to twenty-five days), and continue to develop new branches until a much later period as is shown by a comparison of cells from a 31 day with cells from a 110-day cerebellum.

From this it is plain that the Purkinje cells (cell bodies) of the albino rat cerebellum have also reached full size at about the weaning time (twenty days of age).

From the foregoing, we see that the functional cortical cells both in the cerebrum and in the cerebellum reach their full size at an early age—before the weaning time—and though they continue to mature after that they change only slightly in size, sometimes even diminishing. Thus the cortical nerve elements are all precocious in their growth, which is nearly complete when the young become independent of the mother and their education begins. Addison ('11) has stated also that the development of motor control in the young rat is closely correlated with the completion of the cerebellum and the rat attains its full motor control when the cerebellum has attained structural

maturity at twenty-one to twenty-five days of age. At that age the cells are nearly full size. We may conclude, therefore, at least regarding some of the nerve cells, that the beginning of functional education of the cells at twenty days is preceded by the attainment of nearly full size, and after this period there is very little change in size, though the internal structures mature as the age advances.

Mouse. A study in this field was made by Stefanowska ('98) on the cortical cells of the mouse. She stained the cells by the method of silver impregnation and studied mainly the development of the cell attachments. Her conclusions may be condensed as follows:

1. In the new-born mouse most of the cortical nerve cells have a simple morphology.
2. The cells are usually arranged in chains, disposed perpendicularly to the surface of the cortex.
3. Besides these, there are some groups of cells more advanced in development and having many dendrites, and cells which have the adult form having many, long, ramified dendrites.
4. The different parts of the cortex do not attain the same degree of development at the same time. Some cell groups are more precocious.
5. In the lamina multiformis and in the lamina ganglionaris, we find always the most advanced cells in large numbers.
6. In the lamina pyramidalis the development of the cells is very slow. On the ectal surface, near the pia mater, many cells not at all differentiated are often found.
7. At one day after birth, the dendrites of cortical cells are covered with varicosities. The axis-cylinders have also many nodal swellings.
8. As the neurons develop, the varicosities become more and more rare. At fifteen days, varicosities are no longer seen on the dendrites and the neurons at this age have completed their development.
9. The appearance of the piriform appendices on the dendrites is somewhat delayed. At ten days all pyramidal cells show these appendices. These latter are the constant feature of the neuron, while the varicosities are only a temporary formation. The piriform appendices may be the terminal apparatus of the dendrites.
10. The piriform appendices are the last element which appears on the cortical cells during growth. This fact seems to suggest the high importance of these appendices for this nerve function.

As seen from the foregoing, the morphological completeness in respect of the dendrites and the axis-cylinder of the cortical cells is attained at fifteen days or at the weaning time of the mouse also.

TABLE 12

Giving for man and other mammals the size of the largest ganglion cells in the lamina ganglionaris of the cerebral cortex as presented by different authors. Data are arranged according to the order of the average diameters

NAME OF SPECIES	MAXIMUM SIZE REPORTED IN MICRA		Author
	Linear diameters	Average diameter or square root of the product	
Homo sapiens (man).....	60×120	85	Betz
Homo sapiens (man).....	55×126	83	Lewis
Homo sapiens (man).....	53×106	75	Brodmann
Homo sapiens (man).....	40× 80	57	Hammarberg
Felis leo (lion).....	60×133	90	Brodmann
Felis tigris (tiger).....	60×100	78	Brodmann
Cerculeptus caudivolvulus (kinkajou).....	50×110	74	Brodmann
Ursus syriacus (bear).....	53×100	73	Brodmann
Indris (babakoto).....	44× 80	59	Brodmann
Felis domestica (cat).....	32×106	58	Lewis
Cercopithecus mona (African monkey).....	40× 72	54	Brodmann
Elephas (elephant).....	35× 60	46	Brodmann
Lemur.....	30× 70	46	Brodmann
Mus norvegicus (Norway rat).....	33× 48	40	Sugita
Ovis musimon (sheep).....	23× 65	39	Lewis
Sus (pig).....	27× 48	36	Lewis
Mus norvegicus albinus (albino rat).....	30× 42	36	Sugita
Lepus cuniculus (rabbit).....	18× 60	33	Lewis
Lepus cuniculus (rabbit).....	18× 40	27	Brodmann
Pteropus edwardsii (vampire bat).....	16× 36	24	Brodmann
Mus musculus (mouse).....	18× 20	19	Isenschmid

There are no other systematic investigations on the postnatal development of the cortical nerve cells in mammals, although there are some studies on the growth of nerve cells in the fetus, among which the researches by His ('04) (see footnote 2), Koelliker ('96), and Vignal ('89) are the most important.

Table 12 was compiled by me in order to compare the size of the largest ganglion cells in the lamina ganglionaris (the fifth layer of Brodmann) of the cerebral cortex of man and some other mammals. The tabulated data were taken from Brodmann ('09), Lewis ('79, '82), Hammarberg ('95), and others.

The results obtained by me (Sugita, '18 c) in the albino and the Norway rats have been also entered.

IX. THE SIZE OF THE LARGEST CORTICAL CELLS IN MAN AND SOME OTHER MAMMALS

From table 12 we can draw only very general conclusions as to the significance of the size of the largest cortical cells. The giant Betz cells even in man vary rather widely in size according to the different authors, probably owing largely to the different technical methods used, as has been pointed out repeatedly in the course of this paper.

From time to time attempts have been made to formulate a general interpretation of the size of the Betz cells and of the nerve cells in general. From the examination of table 12, it is seen that the values for the mean diameters do not, except in the very most general way, follow the size of the animal, but that the Felidae, even the cat, stand high in the series.

We are not able to contribute any general explanation for the size of these cells, although it may not be out of place to repeat that in the Norway rat with the heavier brain these cells are larger than in the albino rat with the lighter brain (Sugita, '18 c), and so will merely call attention to the various authors who have had something to say in the matter: Lewis ('79), Hughlings Jackson ('90), Schwalbe ('81), Barratt ('01), Dunn ('00, '02), Herrick ('02), Donaldson ('03), Campbell ('05), Boughton ('06), Johnston ('08), and Kidd ('15).

X. SUMMARY

1. In the present paper I have attempted to compare my conclusions regarding the development of the cortical elements in the brains of the albino and the Norway rats with the corresponding changes in other mammals. The data used for these comparisons were taken from various sources, but the comparisons are in many instances hampered by differences in technique or the lack of essential information.

2. The relations of the cortical thickness at different locali-

ties in the cerebrum are quite the same in the mouse and rabbit as in the rat. The development of the cortical thickness has proved to be similar in the mouse and guinea-pig; it attains nearly its full value at the weaning time of the animal.

3. The statement that the cortical thickness diminishes from the frontal to the occipital pole and from the dorsal to the ventral aspect probably holds true throughout mammals, including man.

4. The results given by different authors for the cortical thickness of human brain (averages or for each locality) are by no means in accord. Even for the same locality there are wide deviations. The best data indicate that the average cortical thickness of the adult human brain is about 3 mm.

5. The mode of increase in cortical thickness in man according to age appears to be similar to that in the albino rat, if the brains are compared at equivalent ages. The developmental stage of the brain of a new-born child corresponds to that of an albino rat of five days of age, and throughout the postnatal life the relative growth rate of the rat and man are as 30 to 1. The span of life 30 for man corresponds to 1 for the rat and the equivalent ages are represented by like fractions of the span of life. The human cortex probably attains nearly its full thickness at fifteen months, equivalent to twenty days of rat age.

6. The relative cortical volumes of the albino and the Norway rat brains, computed formerly by me (Sugita, '18 b), appear to be proportional to the surface areas of the entire bodies at the like age. This relation may be generally applicable within a given order of mammalia. The cortical thickness or the brain weight is in general only loosely correlated with the body weight or size of the animal.

7. The cortical nerve cells in the cerebrum and in the cerebellum of the albino rat are precocious in their growth, attaining almost the full size at twenty days, the weaning time. The maturation of the intracellular structures probably continues after the size is apparently completed. This process is shown also in the mouse.

8. The size of the Betz giant cells in the adult human cortex

(found in the gyrus centralis anterior) is reported differently by different authors. The mean value is about 75 micra in average diameter.

9. The size of the cortical cells, especially the Betz motor ganglion cells, of adult animals has no clear relationship to brain size or body size. These cells are notably large in the Felidae.

10. As a general conclusion to this series of studies the following statement may be made:

The morphological organization of the cerebral cortex is generally precocious. The size of individual cortical nerve cells, the total number of cortical cells, and the thickness of the cortex, all attain nearly their full values at the same time and very early in life (corresponding to the weaning time in some rodents), after which the maturation of internal structures of the cell body and the nucleus continues. The brain weight and the cortical volume continue to increase even after this stage throughout the postnatal life, though not so rapidly as during the early period. This later growth is due principally to the development of the cell attachments, intercellular tissues (neuroglia tissue and blood-vessels), the ingrowth of axons into the cortex and their myelination, which together separate the cells from each other, and cause an increase in cortical volume. The cortical volume is primarily dependent on the size of individual cortical cells and their total number and it appears in animals belonging to a given zoological order to have a definite relationship to the size (or area of surface) of the body of the animal.

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THE PERIPHERAL TERMINATIONS OF THE NERVUS LATERALIS IN SQUALUS SUCKLI

SYDNEY E. JOHNSON

From the Anatomical Laboratory of Northwestern University Medical School¹

TEN FIGURES

The observations set forth below supplement the writer's previous paper on the structure and development of the lateral canal sense organs of *Squalus acanthias* and *Mustelus canis*.² In the investigation referred to the peripheral terminations of the lateral nerve were demonstrated in *Mustelus canis*, but not in *Squalus acanthias*, as fresh specimens of the latter species were unobtainable at that time. Last summer (July, '17), while at the Puget Sound Biological Station, I secured a number of living specimens of the Pacific coast dogfish, *Squalus sucklii*, which appears to be practically identical to the Atlantic form, *Squalus acanthias*. The histological structure of the lateral sense organs of these specimens was examined and the peripheral terminations of the lateral nerve were demonstrated by the pyridine silver method and also with methylene blue. These observations supply the omission which was necessitated in the paper referred to above.

The papers which deal specifically with the peripheral terminations of the nervus lateralis and which are of more than historic value are those of Retzius '92, v. Lenhossék '92, Bunker '97, Heilig '12, and Pfüller '14. They are discussed briefly in the writer's previous paper and need no further comment except to say that most attempts to stain the peripheral terminations of the lateral nerve have heretofore yielded rather meagre results.

¹ Contribution No. 60.

² Jour. Comp. Neur., Vol. 28, No. 1.

In comparing the lateral sensory canals of *Mustelus canis* and *Squalus sucklii* there are a number of differences to be noted. Perhaps the most striking is the difference in calibre of the sensory tubes. The sensory tubes (or canals) of *Squalus* are much smaller than would be found in a *Mustelus* specimen of the same size. The column of sensory epithelium is proportionately narrower in *Squalus*. A slight but apparently constant difference in the course of the lateral canals of the two species is seen in the slight elevation of the canal above the anal fin in *Mustelus*. There are other differences in the distribution of the canals, but they are less striking and have not been carefully examined. The lateral canals of both species lie chiefly in the dermis and their tubules pass directly ventrad for a short distance before making a sharp bend laterally to open on the surface of the integument. The surface tubules correspond in number with the ramuli of the lateral nerve and there are approximately five tubules for every four segments of the vertebral column.

The lateral nerve lies at a considerable depth from the sensory canal, especially in the anterior region, and its ramuli pass obliquely to the basilar membrane of the sensory column, where their fibers diverge caudad and cephalad to form a continuous longitudinal fiber zone just outside of the basilar membrane. This fiber zone differs from that described for *Mustelus* only in the fact that it contains a considerably smaller number of nerve fibers.

The sensory epithelium of Squalus sucklii differs considerably from that of *Mustelus canis*. It is much less extensive and the sensory cells are aggregated in smaller groups. This can be seen readily in transverse and longitudinal sections. In the former one to three sensory cells can ordinarily be seen in the cell clusters (fig. 1), and in the latter, usually three to six (figs. 2 and 10). The groups of sensory cells are somewhat more widely separated from each other than they are in *Mustelus*, and the sensory column appears to show a stronger tendency towards segmentation. This apparent segmentation of the column of sensory epithelium, however, bears no relationship to the normal body segments for there are usually more than ten

clusters of these cells between adjacent surface tubules, and the tubules, in turn, are more numerous than the segments of the vertebral column. Nor is there any marked regularity in the number and size of the individual clusters of sensory cells. While the sensory column is thus essentially continuous throughout the entire length of the sensory canal it shows considerable

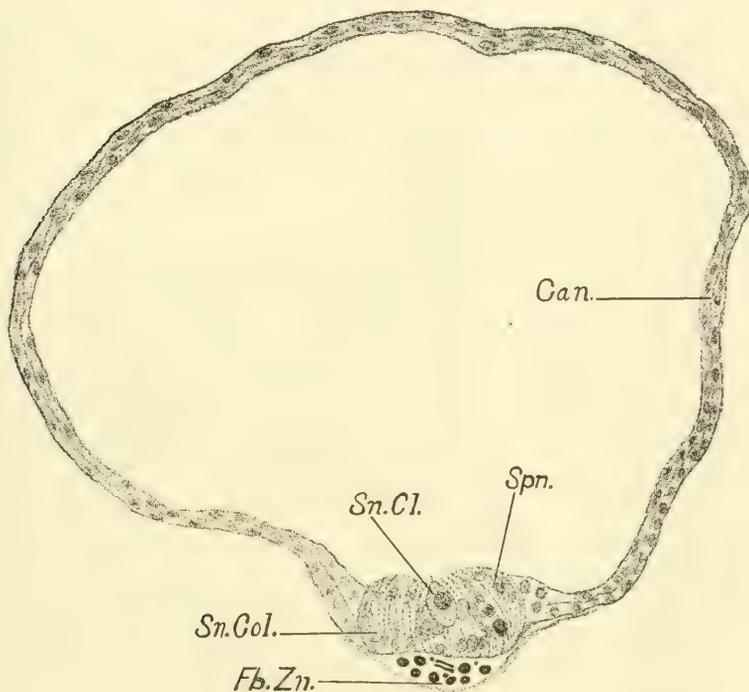


Fig. 1 Transverse section of the entire sensory canal of a *Squalus sucklii* garter. Camera lucida sketch. Iron haem. tech. $\times 432$, $\frac{2}{3}$ off. *Can.*, canal wall; *Fb.Zn.*, longitudinal fiber zone; *Sn.Cl.*, secondary sensory cell; *Sn.Col.*, sensory column; *Spn.*, spindle cells.

variation in thickness. It becomes gradually thinner posteriorly and, as in *Mustelus*, it is usually thinner between adjacent ramuli of the lateral nerve. The base of the column of sensory cells is limited by a continuous basilar membrane.

The same types of cells can be distinguished in the lateral sensory epithelium of *Squalus sucklii* as were found in the sensory

column of *Mustelus* and of *Squalus acanthias*. The hair cells or secondary sense cells are large, pear-shaped, and have centrally placed nuclei. In many specimens hair-like processes could be seen at their distal ends, but whether one or more for each cell has not been determined. The relative length of the cells is usually one-half to two-thirds the thickness of the sensory

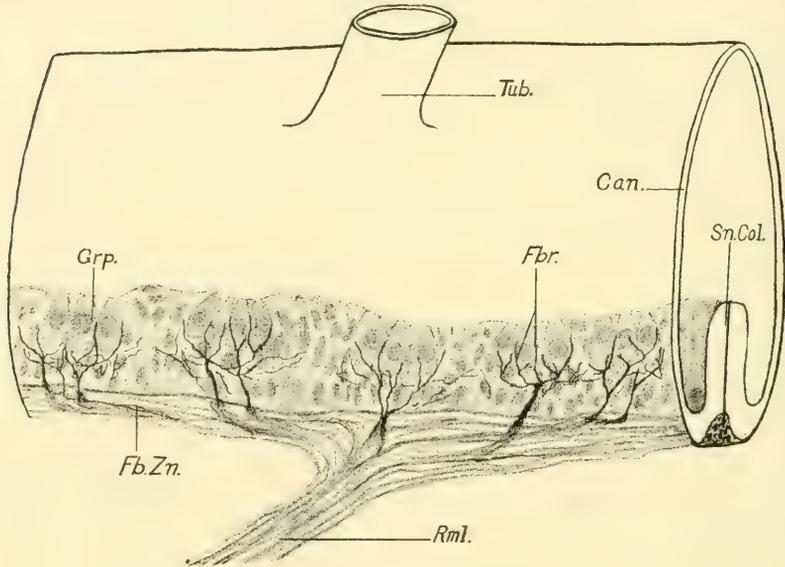


Fig. 2 Longitudinal section of the lateral sensory column (*Sn. Col.*) of *Squalus sucklii* (adult). The sensory epithelium was drawn with the aid of a camera lucida from an iron haematoxylin preparation, and the nerve fibers were put in free hand from pyridine silver sections. The outlines of the canal wall (*Can.*) and the surface tubule (*Tub.*) are not drawn to scale but are greatly reduced in order to conserve space. For correct proportions, see figure 1. Sensory column, $\times 650$, $\frac{1}{2}$ off. *Fbr.*, terminal fibrillae; *Fb.Zn.*, longitudinal fiber zone; *Grp.*, one group of secondary sensory cells (hair cells).

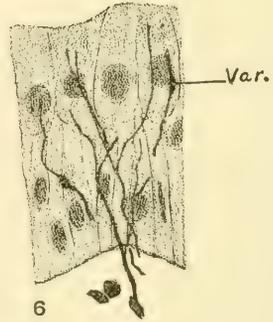
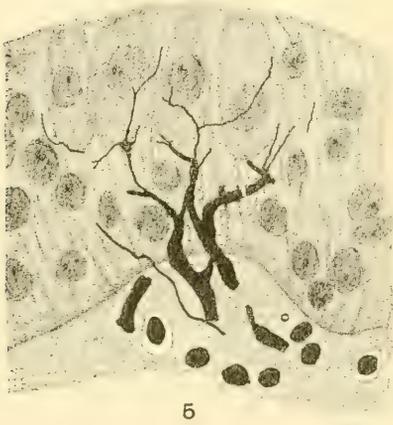
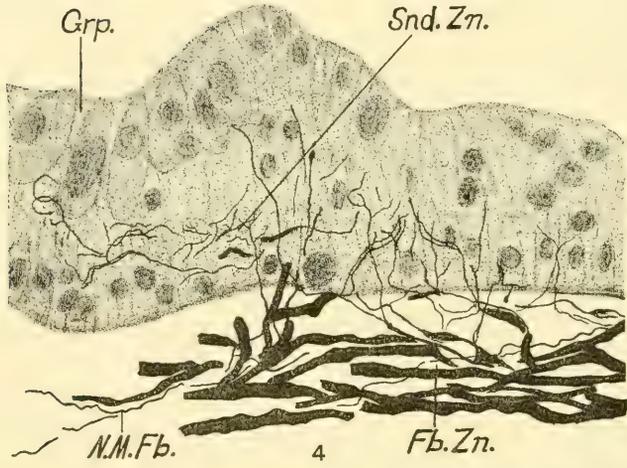
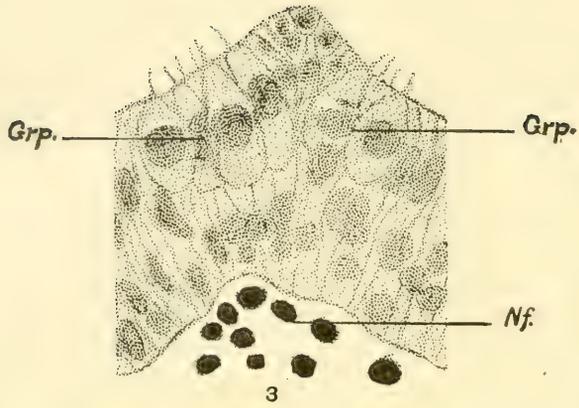
column. Spindle-shaped cells, basilar cells, and columnar cells constitute the supporting elements (see figs. 1, 2, 3 and 10). The rest of the canal wall is formed by a double layer of epithelial cells, both layers of which are continuous with the walls of the surface tubules and also with the columnar and stratified layers of the epidermis.

The peripheral terminations of the lateral nerve. On reaching the base of the sensory column the fibers of the lateral ramuli diverge caudad and cephalad in the subbasilar fiber zone. This fiber zone is shown in longitudinal section in figures 2 and 4, and in transverse section in figures 1 and 3. The majority of the fibers are medullated but a few non-medullated fibers can be found. These can be traced back through the ramulus to the lateral nerve, which indicates that they are not simply non-medullated branches of the large medullated fibers.

Two zones of distribution or branching of the nerve fibers appear well marked. Primary distribution takes place from the longitudinal fiber zone and the branching is almost entirely subbasilar (figs. 4 and 10), while a secondary zone of distribution or branching is located roughly between the limits marked by the nuclei of the basilar cells and the proximal ends of the hair cells. It is from this zone that the fine fibrillae arise which pass out freely between the hair cells.

The primary branches are large and coarse as a rule (fig. 7), although many fine branches arise from this zone also (fig. 4). Branching of the fibers appears frequently to be dichotomous but not uncommonly three or more branches arise at the same level. This statement holds for both zones of distribution. Enlargements of considerable size are commonly seen at the level of branching of the nerve fibers (fig. 9), but it seems likely that the majority of these extra large "varicosities" are caused by an over-deposit of silver at the points of branching. One or more fibers may rise from the subbasilar fiber zone to supply a single cluster of hair cells, and occasionally the fibrillae of a given fiber ramify in adjacent groups of hair cells (fig. 10). The medullary sheath is usually lost just outside of the basilar membrane.

The primary branches rise to a considerable height in the sensory epithelium—usually beyond the nuclei of the basal cells—where they form a rather rich plexiform network (figs. 4, 7, and 10). This network forms the secondary zone of distribution and it is from it that the ultimate distribution of fibrillae to the hair cells takes place. While this secondary zone of distribution is present in the lateral sensory epithelium of *Mustelus canis*, it is



not as uniformly developed and is much less conspicuous than it is in *Squalus sucklii*.

The fine fibrillae which arise from the secondary zone of distribution rise to various levels in the sensory epithelium. In many instances they can be traced to within a short distance of the outside limiting membrane (figs. 8 and 9). Varicosities of various sizes and shapes appear on the fibrillae at practically all levels and not infrequently at their distal extremities. In many cases the fibrillae appear to surround the bases of the hair cells (figs. 8 and 9), and in others, to pass out freely and separately between the hair cells.

The observations set forth above corroborate the results obtained on *Mustelus canis*. Only minor differences exist in the structure and innervation of the sensory epithelium of the two species. In *Squalus sucklii* the sensory epithelium is less extensive, there is a stronger suggestion of segmentation, and in nerve supply there is a more definite and conspicuously secondary zone of distribution.

A number of features which stand out in the embryonic and adult structure of the lateral canal system of *Squalus* and *Mustelus* appear to me to reflect doubt on the theory that this system of sense organs has a phylogenetic relationship with the segmental sense organs of certain invertebrates and that the system itself is segmental in the sense suggested by John Beard³ and W. H. Gaskell.⁴ The evidence, in part, against such a view may be

Fig. 3 Transverse section of the sensory column, showing the peculiar condition of two groups of hair cells (*Grp.*) existing side by side. Camera sketch, $\times 650$. *Nf.*, nerve fibers of the subbasilar fiber zone.

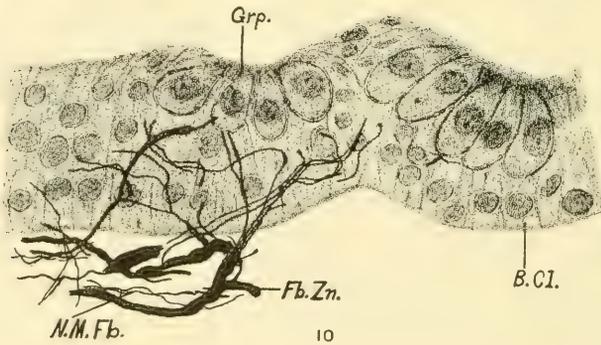
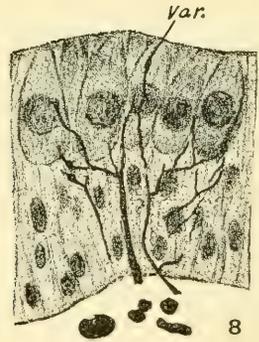
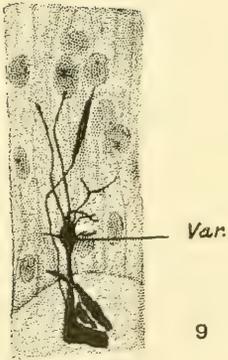
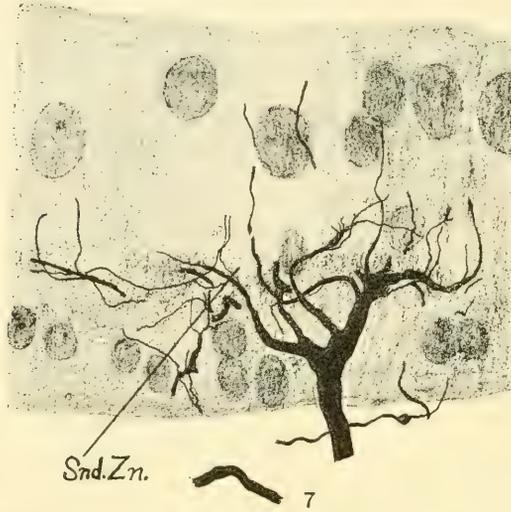
Fig. 4 Longitudinal section of the lateral sensory column and the subbasilar fiber zone (*Fb.Zn.*). The secondary zone of distribution (*Snd.Zn.*) is also shown. Camera sketch. Pyridine silver tech. $\times 650$, $\frac{2}{3}$ off. *Grp.*, group or cluster of hair cells; *N.M.Fb.*, non-medullated nerve fibers.

Fig. 5 Transverse section of the sensory column showing large fibers, and fibrillae diverging at a large varicosity. Pyridine silver tech. $\times 1525$, $\frac{1}{2}$ off.

Fig. 6 Transverse section of sensory epithelium showing long, fine fibers, and varicosities. Pyridine silver. $\times 650$, $\frac{1}{3}$ off.

³ See Zool. Anz., Bd. 7, 1884, p. 125 et seq., and also Bd. 8.

⁴ The Origin of Vertebrates, 1908.



summarized briefly. The lateral sense organs do not develop in situ from successive or segmental patches of ectoderm along the side of the body, but each lateral sensory column arises from a thickened area of ectoderm located on the side of the head; this invades the posterior segments of the body not as a segmental structure, but in the form of a continuous column of epithelial cells. The grouping of the sensory cells in small clusters occurs comparatively late in the development of the embryo. It has been pointed out that these groups, when they do appear, are not segmental in the sense of the term as here employed. It is only in a degenerating or breaking down condition of the sensory ridges that isolated groups (pit-organs) of hair cells are found (e.g., dorsal series of sense organs in *Squalus acanthias*). These so called pit-organs show no relationship to the body segments either in their number or in their innervation. Further, their early development is identical with that of the lateral sense organs, the separated organs simply representing parts of what was earlier a continuous ridge of epithelium. So much for the developmental aspect.

The opinion has already been expressed that the slight tendency towards segmentation as seen in the lateral sensory column of the adult is probably of no significance as an argument for the segmentation theory. This is one of the anatomical features, however, which might be considered as pointing in that direction. Another one is seen in the innervation of the sensory epithelium by separate and successive ramuli (of the lateral nerve) which correspond in number and level with the surface tubules. The first condition named loses segmental significance when one remembers

Fig. 7 Longitudinal section of lateral sensory epithelium showing the extensive branching of a single large nerve fiber. Pyridine silver. $\times 1525$, $\frac{2}{3}$ off.

Fig. 8 Longitudinal section of a group of hair cells, showing various relations of the terminal fibrillae. Pyridine silver. $\times 650$, $\frac{1}{3}$ off. Var., varicosity.

Fig. 9 Section showing several slender fibrillae diverging from a large varicosity (*Var.*). Pyridine silver. $\times 650$, $\frac{1}{3}$ off.

Fig. 10 Longitudinal section of the lateral sensory column, showing two groups of hair cells (*Grp.*), and a network of fibers arising from the subbasilar fiber zone (*Fb.Zn.*). Pyridine silver. $\times 650$, $\frac{1}{3}$ off. *B.Cl.*, basal cell; *N.M.Fb.*, non-medullated nerve fibers.

that there are from fifteen to twenty clusters of hair cells for every vertebral segment. Evidence based on the arrangement of the lateral ramuli and the surface tubules is unsatisfactory partly for the same reason and partly for other reasons. As shown above, the lateral ramuli and the surface tubules are considerably more numerous than the vertebral segments and a constant ratio between the number of vertebrae and ramuli of the lateral nerve is wanting. Furthermore, these ramuli are merely the branches of distribution of a cranial nerve which differs from other cranial nerves only because of the fact that it supplies this remarkable type of sense organ and extends from the head to the caudal fin. In this connection it must be remembered that the fibers of the ramuli diverge at the base of the sensory epithelium to form a *continuous* fiber zone from which the ultimate distribution takes place.

Further difficulty is met in attempting to relate the numerous organs of the head canals and of the cross-commissures to a corresponding number of ancestral segments.

In view of these considerations it seems improbable to me that the organs of the sensory canals have a phylogenetic history which would relate them either to the segmental sense organs of certain invertebrates, as claimed by Beard, Gaskell, and others, or to the posterior (body) segments of primitive vertebrates. To assume that the lateral sense organs have had such a past history involves the necessity of explaining why the innervation of the body organs should change from a segmental spinal nerve supply to a cranial nerve supply, and also, why the organs do not arise in situ on each segment of the body rather than from cephalic ectoderm which invades the posterior segments and carries with it its own nerve supply, probably from a corresponding primitive cephalic segment. It appears to me more likely that if the lateral sensory apparatus is segmental it is so only in relation to a limited number of cephalic segments. The several lines of organs, then, would represent simply an invasion or extension of a primitive cephalic sensory apparatus into other segments of the body.

Clearly the evidence at hand is not sufficient to warrant dogmatic statements or conclusions. The need is emphasized

for further histological and embryological work, to be conducted on a comparative basis. The amphibia, especially, need further investigation along this line.

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ON THE DEVELOPMENT OF THE NERVE ENDORGANS IN THE EAR OF TRIGONOCEPHALUS JAPONICUS

TOKUYASU KUDO

Anatomical Institute, Medical High School, Nūgata, Echigo, Japan

ONE PLATE

The endorgans of the auditory nerve in reptiles have been investigated morphologically with considerable thoroughness. Many authors have interested themselves particularly in the macula neglecta (described for the Amphibia by Deiters in 1862 and given the name now in common use by Retzius) and this endorgan has been studied in various vertebrates, especially in the fishes, the Sauropsida, the mammals and even in man.

Relatively few embryological investigations, however, have been published on this subject. Concerning the genesis of the macula neglecta, Retzius and Alexander concluded that this organ originates from the crista acustica posterior, the former basing his opinion on its comparative anatomy and the latter on observations of its innervation. In Hertwig's *Handbuch* Krause briefly states that a small region of common neuroepithelium differentiates upon the separation of the saccular from the utricular portions. Fleissig, who, working on reptiles (Gecko), was the first to investigate extensively the development of the macula neglecta, disagrees with both of these statements and is of the opinion that the organ arises from the macula sacculi. The same conclusion is reached by Okagima in the case of *Hynobius*; but this author remarks that because in the Amphibia the macula neglecta lies within the sacculus, its origin in these forms is easier to determine than in the reptiles, where the macula is found in the utriculus. Corroboration of this view, according to which the macula neglecta arises from the neuroepithelium of the pars inferior, is found in Okagima's study of the salmon embryo and Wenig's recent work on *Pelobates fuscus*.

This simple interpretation of the genesis of the macula neglecta has been considerably complicated by the studies of P. and F. Sarasin, who claim to have found a second endorgan in the Caeciliidae, for they distinguish two different maculae, one of which lies in a small evagination of the sacculus (macula neglecta of Retzius), the other in the floor of the utriculus (macula neglecta fundi utriculi). The existence of the latter was, however, denied by Retzius, in which opinion he is joined by Ayers. Retzius states: "Es geht nicht hervor, dass die am Boden des Utriculus der Caeciliiden gefundene Nervendstelle einer neu entdeckten Nervendstelle entspricht. Denn gerade am Boden des Utriculus liegt die von mir bei vielen Fischen, Reptilien und Vögeln entdeckte Nervendstelle, Welche von mir schon längst 'Macula neglecta' genannt wurde. Es ist deshalb ganz unrichtig, wenn die Herren Sarasin die von ihnen bei Ichthyophis am Boden des Utriculus beschriebene Nervendstelle als von ihnen neu entdeckt bet achten und sie als eine 'Macula fundi utriculi' aufführen. Die echte 'Macula neglecta' liegt am Boden des Utriculus oder Öffnung des Canalis utriculo-saccularis, oder auch nach meiner Ansicht—bei den niederen Amphibien in der eigentümlichen Ausstülpung dieses Canalis, welches ich 'Pars neglecta' genannt habe, bei den höheren aber in einer von ihm abgetrennten Ausstülpung der Sacculuswand." He adds that it would be interesting to know whether both of the endorgans as described by P. and F. Sarasin really do occur, in view of the fact that in all Amphibia that have been thoroughly studied a single macula neglecta occurs. Ayers contends that the new endorgan of the Sarasins is probably none other than the macula neglecta of Retzius. But Fleissig, from his study on the development of the labyrinth in Gecko, was able to demonstrate a transitional condition between the two described above. According to this author the macula neglecta of Retzius is to be regarded as a persisting organ in the sinus inferior, while only traces of the macula neglecta of the Sarasins occurs in adult individuals; and these traces may well be regarded as vestiges of Sarasin's macula, which is present as a developing organ only at a certain stage.

To this much mooted and interesting question, then, I wish to contribute the modest results which I have been able to obtain from my study of *Trigonocephalus japonicus*.

The viperid embryos which were placed at my disposal comprise more than 27 stages¹ (Suzuki-Okajimas series), of which I have employed four for the present study. The embryos were fixed in formol-alcohol, potassium bichromate-acetic and corrosive sublimate-acetic and were stored in alcohol until stained and imbedded in paraffin. Mainly frontal sections 10–15 μ thick were made through the heads of the embryos. These were stained in toto with alcoholic borax carmine and Weigert's iron haematoxylin, and in the latter case orange G was employed as a counter stain. The two adult specimens were fixed in potassium bichromate, imbedded in celoidin and cut vertically through the head. These sections, 30 μ thick, were stained in haematoxylin-eosin and orange G.

Stage 1 (fig. 1). The embryo is coiled up in 4½ turns. Olfactory pit very deep. Wall of optic cup thickened anteriorly; lens solid. Fixation: corrosive-acetic. Stain: Weigert's iron haematoxylin; sections 15 μ . Frontal sections of head and body.

The auditory vesicle, which is distended into a sac-like structure, is already oval in shape and, since it runs through 47 sections, is about 0.705 mm. in antero-posterior diameter. It lies some distance removed from the brain. Differentiation in the epithelial lining of the wall of the auditory vesicle is already apparent. Laterally the epithelium is flattened, while the medial and lower walls are stratified several cells deep and show here and there a mitotic figure. This thickened portion represents the common neuroepithelium which will later separate into the pars superior and the pars inferior. The ductus endolymphaticus is already tubular in form, with the dilated saccus endolymphaticus at the end.

Stage 2 (fig. 2) The embryo consists of 3½ coils. The parietal elevation is prominent. The lens is approximately as in the preceding stage; the retina moderately pigmented. The

¹ The number includes 7 sectioned by the writer.

pocket-shaped olfactory pit is deep and the oral sinus deeply cleft. Fixation: formol-alcohol. Stain: alcoholic borax carmine. Sections 15μ in thickness cut frontally through head and entire body. The antero-posterior diameter of the auditory vesicle is calculated to be 0.48 mm., since it runs through 32 sections.

The auditory vesicle has at this stage undergone considerable development. The pars superior and the pars inferior are distinctly separated. The anterior and the posterior semicircular canals are now completely constricted off; but this is not the case with the lateral canal; i.e., this canal is not yet independent of, but still broadly in communication with the main lumen of the vesicle. The pars inferior is well differentiated and possesses an elongated oval swelling on the ventro-medial wall of the vesicle. The ductus endolymphaticus appears as a long slender tube.

In correspondence with the external change in form the epithelial lining is also well differentiated. The anterior canal, which is flattened in a medio-lateral (partly dorso-ventral) direction, widens out at its anterior end into an ampulla, and the crista acustica anterior is here represented by high epithelium which is continuous, without any decrease in thickness, with the macula utriculi. The same holds true for the crista lateralis, the epithelium of which is somewhat lower than that of the anterior crista. The medial and ventral walls of the utriculus are made up of especially high stratified epithelium, which, bending upon itself at the entrance of the pars inferior, passes over into this without any sharp boundary line. The tallest epithelium of the medial wall decreases somewhat in thickness as it passes over into the medial wall of the endolymphatic duct. The flattened lateral wall of the utriculus presents no points of especial interest. The crista posterior has moved back some distance and appears as a thickened zone of cells in several layers at the ventro-medial portion of the semicircular canal.

Stage 3 (fig. 3) The embryo consists of about $2\frac{1}{2}$ coils. On the surface of the body striations are observed which are transverse on the ventral and crossed on the dorsal surface. Fixation: Corrosive-acetic. Stain: alcoholic borax carmine.

The 15 sections cut frontally through head and body. The membranous labyrinth runs through 102 sections and hence has an antero-posterior diameter of 1.53 mm.

The utriculus and the sacculus communicate by a narrow foramen, the canalis utriculo-saccularis; the lateral semicircular canal is now an independent structure. Each nerve endorgan is well developed. The crista anterior is mound-shaped; the crista lateralis is a thick cell mass which appears as a crescent in the sections. Both structures still maintain their connection with the crista utriculi.

The tall epithelium of the utricular foor, which diminishes in thickness as it passes upward, doubtless represents the first anlage of the macula neglecta Retzii. It is continuous with the macula partis inferioris through the still cylindrical epithelium of the canalis utriculo-saccularis. The macula partis inferior consists in this stage of an extended zone of neuroepithelium on the medial wall of the pars inferior and already there is to be seen on its margin several minimal though unmistakable points devoid of nuclei. The fine nerve-fiber bundles that arise from the ganglion acusticum show excellent mitotic figures where the fibers enter the macula. The low cylindrical epithelium of the ductus endolymphaticus is continuous with the tall neuroepithelium of the medial wall of the sacculus.

Stage 4 (fig. 4). The embryo, which is made up of $2\frac{1}{2}$ coils, has the appearance of a fully developed individual. Its peculiar dermal spots are prominently displayed over the entire body. Fixation: formol. Stain: Alcoholic borax carmine. Sections: $15\ \mu$ in thickness, cut frontally through the head.

The nerve endorgans are nearly all differentiated and on each the marginal zone free of nuclei may be recognized. The cristae anterior and posterior are separated from the macula utriculi by a low epithelium.

It is worthy of notice that the thick epithelium of the utricular wall shows clearly a border without nuclei and that it is differentiated from the epithelium of the canal by its greater thickness. It soon becomes thinner as it passes gradually over into the undifferentiated epithelium lining the vesicle. This thickening just

referred to may well be considered as the first anlage of the macula neglecta Retzii. In the wall of the canal there is no zone marked out by a cell-free border, although the epithelium is still rather thick, and this in turn is continuous with the mound-shaped swelling, the macula sacculi.

Corresponding to the external changes in form, the macula partis inferioris is now separated into the papillae basilaris and lagenae, which are still united by cubical epithelium. The crista posterior is quite separated from the macula sacculi by an unspecialized epithelium.

Stage 5. The embryo consists of $2\frac{1}{2}$ coils. The external characters are quite comparable to those of the preceding stage. Fixation: potassium bichromate. Stain: alcoholic borax carmine. The $15\ \mu$ sections are cut frontally through the head.

The macula neglecta Retzii, which lies closely adjoining the canalis utriculo-saccularis, is mound-shaped and consists of two or three layers of cells. The maculae neglecta and sacculi are united by means of cubical epithelium except in the wall of the canal, where the epithelial cells are still tall.

The Adult Animal (fig. 5). Fixation in potassium bichromate-acetic. Stain: haematoxylin-eosin and haematoxylin-orange G. The section are cut frontally through the head.

Among the endorgans the cristae anterior and posterior are composed of two- to three-layered epithelium and project as rounded protuberances into the lumen. The macula utriculi lies on the anterior-medial wall of the utriculus and is composed of auditory and supporting cells. The macula neglecta appears as a swelling in the proximity of the canalis utriculo-saccularis on the floor of the utriculus; its vesicular auditory cells rest upon one or two layers of supporting cells. The macula diminishes in thickness as it passes over into the simple cylindrical epithelium which makes up the wall of the canal and which is continued beyond in the wall of the sacculus. The tall epithelium found on the medial wall of the canal is also to be seen on and near the lateral wall. In several places within and near the canal the lining is thrown up into wave-like folds.

DISCUSSION

The results of my studies, as presented above, agree on the origin of the macula neglecta with the view of Fleissig, for it has been shown that this macula is derived directly from the macula partis inferioris. Even after the neuroepithelium has been completely separated by the undifferentiated epithelium from the pars inferioris, the macula neglecta remains for a long time in connection with the macula sacculi.

The common neuroepithelium on the ventro-medial wall of the auditory vesicle of stage 1 begins to divide into the utricular and the saccular portions (stage 2), the histological changes in the epithelium keeping pace with the external changes in form. The more strictly utricular portion swells to form the crista anterior, crista lateralis and macula utriculi, which are united by means of a tall epithelium. The more strictly saccular portion, separated from the utricular portion by flattened epithelium (stage 3) still extends from the medial wall of the canalis utriculo-saccularis upwards further into the floor of the utriculus.

After the macula saccularis has been differentiated (stage 3) the macula neglecta gradually protrudes more and more into the lumen and in stage 4 discloses a border free of nuclei, but is still connected by means of a cubical epithelial layer with the macula sacculi. Furthermore, the crista ampullaris posterior becomes entirely free from the saccular portion, while the papillae basilaris and lagenae still maintain their connection with the macula saccularis by means of a bridge of cubical epithelium. In stage 5 the well developed macula neglecta may be seen as a mound-shaped structure as in adult specimens.

The existence of two maculae neglectae I have failed to demonstrate in my *Trigonocephalus* material, although I have minutely examined the rather comprehensive series of the different stages. Fleissig says: "1) die macula sacculi, welche nicht mehr die ganze mediale Sacculuswand, sondern nur mehr deren untersten Abschnitt einnimmt. Ein Epithel, das etwas höher ist als das indifferente Wandepithel und ganz typisch in der Umgebung der Nervendstellen vorkommt, erstreckte sich von der Macula

sacculi nach aufwärts zum Foramen Utr.-Sacc., wo es zu einer zweiten Neuroepithelstelle—2) Macula neglecta Sarasinian-schwillt, die im Foramen Utr.-sacc. (an dessen hinterem Rand) gelegen, zum kleineren Teil in den Sacculus, zum grösseren in den Utriculus hineinragt. Von dieser erstreckt sich wieder ein niedriges Epithel in den Sinus inferior hinein zu persistierenden 3) Macula neglecta (Retzii). Beide Maculae neglectae stehen auf derselben Entwicklungsstufe.”

Now even if the bulging endorgan found in the floor of the utriculus of stages 4 and 5 were not to be regarded as the macula neglecta Sarasini but rather as the macula neglecta Retzii, I would not feel justified in interpreting the thickened epithelium which extends through the canalis utriculo-saccularis to the macula saccularis as the macula Sarasini. The further the development progresses the thinner does the epithelium of the inner wall of the alveus become as compared with the early stage of the auditory vesicle. One may readily see that the medial wall of the alveus communis is lined with relatively taller epithelial cells in stage 2 than in stage 3. From this it is apparent that the neuroepithelium, except where it progressively develops into nerve endorgans, is destined to be reduced to indifferent epithelium, even though the time when it retrogresses be very variable.

According to my opinion, therefore, the tall epithelium of medial wall of the canal and its proximity represents a developmental stage in the neuroepithelium which later retrogresses. If this epithelium were to be interpreted as a nerve endorgan, the tall epithelium of other regions, as e.g., of the lateral wall of the canal and the medial wall of the utriculus and the ductus endolymphaticus, would have to be regarded as neuroepithelium, since these latter regions are quite similar in structure and arrangement of their epithelial cells to those in the medial wall of the canal. At any rate, the macula neglecta does not occur in my material as it has been pictured by Fleissig in his work. But it should be noted that in the adult snake the epithelium of the canalis utriculo-saccularis and its immediate environs is relatively much thicker as compared with the medial and lateral walls.

From the above it appears, then, that the macula neglecta Retzii, which comes to lie in the floor of the utriculus, arises from the neuroepithelium of the pars inferior, as was first established by Fleissig in the case of Gecko; but, as stated above, I am unable to demonstrate in my material any progressively developing endorgan which could represent the macula neglecta Sarasini.

Alexander has suggested that in the embryo of *Echidna* the tall epithelium at the mouth of the ductus endolymphaticus may represent the vestige of the Amphibian macula neglecta Sarasini. This tall epithelium, which is continuous with the neuroepithelium of the medial utricular wall, Fleissig has also observed in the embryo of Gecko, but his interpretation is a totally different one, for he does not consider it remarkable that the mouth of the ductus endolymphaticus, which is still in active growth, should possess tall epithelium where it passes suddenly into the neuroepithelial anlage of the medial utricular wall.

In conclusion I desire to record the observation that the three semicircular canals of *Trigonocephalus japonicus* do not develop synchronously, the medial and posterior canals anticipating the lateral canal in their development.

SUMMARY

1. The macula neglecta arises directly from the macula partis inferioris.
2. The occurrence of two maculae neglectae is not to be observed in my material: while the macula neglecta Retzii is well developed, there does not form a persistent macula Sarasini nor does this endorgan even develop temporarily as in Gecko (Fleissig).
3. The anterior and the posterior semicircular canals are separated off much earlier than the lateral canal.

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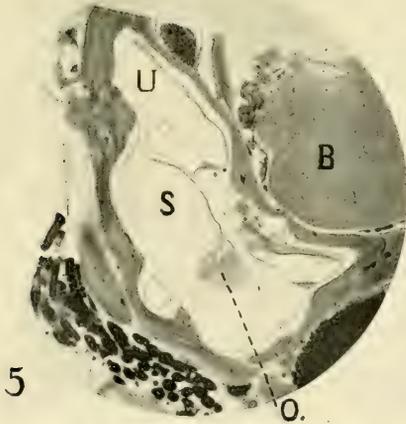
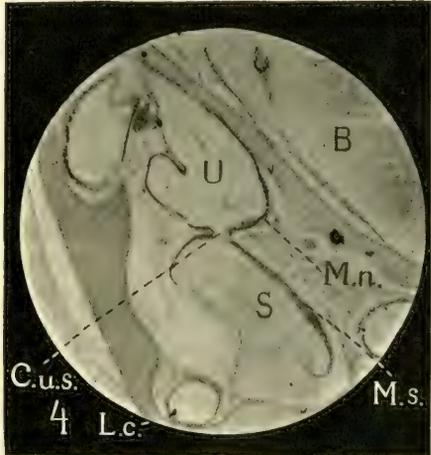
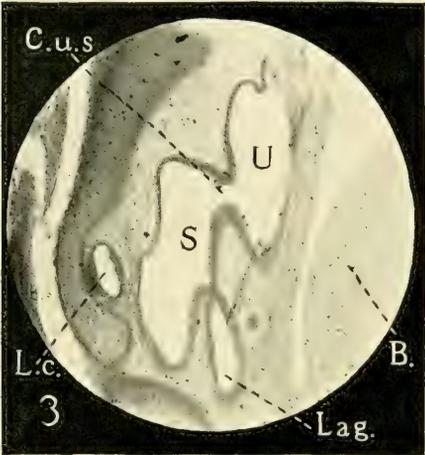
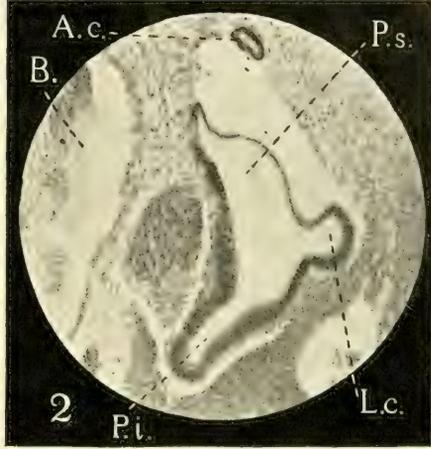
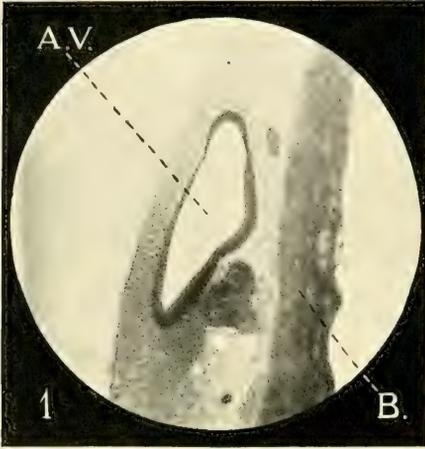
PLATE

PLATE 1

- 1 Stage 1. Stain: Weigert's Iron haematoxylin, Leitz Achromat 6; Ocular I.
- 2 Stage 2. Stain: Boraxcarmine. 3XI.
- 3 Stage 3. Stain: Boraxcarmine. 3XI.
- 4 Stage 4. Stain: Boraxcarmine. 3XI.
- 5 Adult. Stain: Haematoxylin-eosin. 1XI.

ABBREVIATIONS

<i>C.u.s.</i> , Canalis utriculo-saccularis	<i>M.n.</i> , Macula neglecta
<i>B.</i> , Brain	<i>M.s.</i> , Macula sacculi
<i>A.v.</i> , Auditory vesicle	<i>O.</i> , Otolith
<i>Lag.</i> , Lagena	<i>P.i.</i> , Pars inferior
<i>L.c.</i> , Lateral semicircular canal	<i>P.s.</i> , Pars superior
<i>A.c.</i> , Anterior semicircular canal	<i>S.</i> , Sacculus
<i>U.</i> , Utriculus	



AN INTRODUCTION TO A SERIES OF STUDIES ON THE SYMPATHETIC NERVOUS SYSTEM

S. W. RANSON

From the Northwestern University Medical School¹

ONE FIGURE

Anatomists have devoted little thought to the functional pathways within the sympathetic nervous system. Yet it is obvious that no account of the structure of any part of the nervous system is complete which does not include an analysis of the more important conduction paths. Such an analysis cannot, as a rule, be made by purely morphological methods, but requires the aid of physiological procedures including degeneration experiments. Above all, the investigator must approach his subject from the right point of view; he must regard the structures to be analyzed as parts of a functional mechanism and strive to understand how it works.

While histologists have given us many details concerning the structure of the ganglia, they have ignored the composition of the various nerves and plexuses in the sympathetic system and have made little effort to analyze what seemed to them a hopeless confusion of interconnected elements. In the anatomical and histological texts we find no hint that the sympathetic nervous system is made up of definite functional groups and chains of neurones as distinct and sharply limited as are any of the conduction systems of the brain and spinal cord. Nevertheless, such is the case; it is even probable that the functional groups and chains of neurones are more sharply limited in the sympathetic than in the central nervous system. The latter is provided with a mechanism for the widest possible diffusion of incoming impulses, while such diffusion does not occur in the former. Strong stimulation of a single small cutaneous nerve will give

¹ Contribution No. 53, February 15, 1918.

rise to nerve impulses which are distributed throughout the brain and spinal cord and may call into action any part of the smooth or striated musculature of the body. Nothing in any way comparable to this occurs in the sympathetic system.

Excluding the terminal ganglionated plexuses which require further study, we may say that there is probably no more opportunity for diffusion of nerve impulses in the sympathetic nervous system than there is in an ordinary spinal nerve. This can

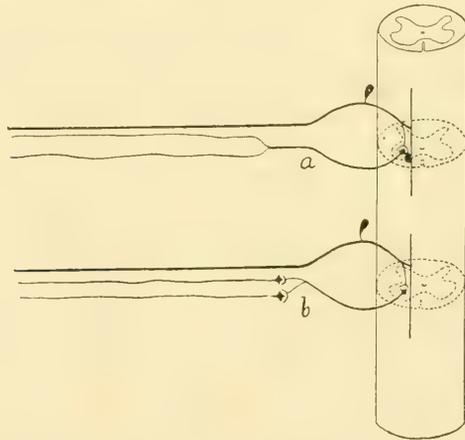


Fig. 1 Diagram of two conduction paths from which all purely topographic details, such as spinal nerves, rami communicantes, and sympathetic trunk, have been omitted: *a*, somatic path with branching efferent fiber; *b*, autonomic path with branching preganglionic efferent fiber, the branches ending in relation to two postganglionic neurones.

be made clear by a diagram (fig. 1). So far as the possibility for diffusion of nerve impulses is concerned, it is immaterial whether the efferent fiber branches in the course of a nerve or within a ganglion and whether its branches come in contact with the innervated structure directly or through the mediation of a second neurone, provided there is in the ganglion no other type of synapse than that indicated in the diagram.

Thanks to the work of Langley, we have reason to believe that the sympathetic system, with the probable exception of the terminal ganglionated plexuses, is built up on the simple lines

indicated in the diagram; and, if so, the working out of conduction pathways should not be as difficult as we had supposed. In fact, a great deal along this line has already been accomplished by the physiologists; but there yet remains a large amount of work to be done before the course of nerve impulses through the sympathetic nervous system can be mapped with accuracy.

Since there is considerable confusion in the use of terms referring to this division of the nervous system, we wish at the outset to define those which we shall have occasion to use.

The sympathetic nervous system is an aggregation of ganglia, plexuses, and nerves through which the glands, heart, and all smooth muscle receive their innervation. It is a term belonging primarily to descriptive anatomy and includes the ganglionated plexuses associated with the fifth nerve and the vagal plexuses of the thorax, as well as the sympathetic trunk and the parts more directly associated with the latter. Since it is connected at many points with the cerebrospinal nerves, it is necessary to decide what shall be included in it. The logical point of separation is that at which the cerebrospinal nerves give off branches which run exclusively to the sympathetic system. These branches of the cerebrospinal nerves form an integral part of this system. This is well recognized in the case of the rami communicantes; but the principle has never been carried through systematically. On this basis it would include the radix brevis of the ciliary ganglion, the cardiac and pulmonary rami of the vagus, and the visceral rami of the second, third, and fourth sacral nerves. We pass now to a consideration of the terms selected from the vocabulary of the physiologists.

The autonomic nervous system is that functional division of the nervous system which supplies the glands, heart, and all smooth muscle with their efferent innervation. It is the sum total of all general visceral efferent neurones both pre- and post-ganglionic.

The preganglionic visceral efferent neurones have their cells located in the cerebrospinal axis, and their fibers make their exit from this axis in three streams: 1) cranial—via the III, VII, IX, X, XI cranial nerves; 2) thoracolumbar—via the white

rami communicantes from the thoracic and upper lumbar spinal nerves; 3) sacral—via the visceral rami of the II, III, and IV sacral nerves. The fibers of the thoracolumbar stream run to the sympathetic trunk and are distributed through it to ganglia at higher and lower levels. The fibers of the cranial and sacral streams make no connection with the sympathetic trunk, but run directly to the various plexuses. While the fibers of the thoracolumbar stream end in the ganglia of the trunk or in collateral ganglia, those of the cranial and sacral streams end in terminal ganglia. In these two respects the cranial and sacral streams agree with each other and differ from the thoracolumbar stream. Also physiologically and pharmacologically the two former agree with each other and differ from the latter. It is therefore desirable to divide the autonomic nervous system into two divisions:

1. The thoracolumbar autonomic system (called by many physiologists the sympathetic nervous system).

2. The craniosacral autonomic system (called by many physiologists the parasympathetic system).

The importance of this division is further emphasized by the fact that most of the structures innervated by the autonomic system receive a double nerve supply, being furnished with fibers from both divisions of that system. The thoracolumbar fibers are accompanied in most peripheral plexuses by craniosacral fibers of opposite function, so that an analysis of these plexuses is greatly facilitated by subdividing the autonomic system in this way. These statements may be summarized in the form of three definitions:

The autonomic nervous system is that functional division of the nervous system which supplies the glands, the heart, and all smooth muscle, with their efferent innervation and includes all general visceral efferent neurones both pre- and postganglionic.

The thoracolumbar autonomic system is that division of the autonomic system, the preganglionic fibers of which make their exit from the spinal cord through the thoracic and upper lumbar spinal nerves.

The craniosacral autonomic system is that division of the autonomic system, the preganglionic fibers of which make their exit from the cerebrospinal axis through the III, VII, IX, X, and XI cranial nerves and the II, III, and IV sacral nerves.

The preganglionic neurones are those, the cell bodies of which lie in the brain or spinal cord and whose axons run through the cerebrospinal nerves to enter the sympathetic system and end in its ganglia. The autonomic nervous system therefore includes certain cells in the brain and spinal cord and certain fibers in the cerebrospinal nerves and is not contained exclusively in the sympathetic system. The postganglionic neurones are those whose cellbodies lie in the sympathetic ganglia and whose axons run to end on cardiac or smooth muscle or in glandular tissue.

In order to show how these terms will aid in the presentation of the facts of visceral innervation, we may give a few examples. While some points are still obscure, the outlines given below are as nearly correct as our present knowledge enables us to make them. They are given not as an ultimate statement of fact, but as an illustration of the sort of information which we should strive to perfect.

IMPORTANT FUNCTIONAL PATHS IN THE AUTONOMIC SYSTEM

1. Paths for the efferent innervation of the eye.

a. Ocular craniosacral pathway.

Preganglionic neurones. Cells in the oculomotor nucleus, fibers by way of the III cranial nerve to end in the ciliary ganglion.

Postganglionic neurones. Cells in the ciliary ganglion, fibers by way of the short ciliary nerves to the ciliary muscle and the circular fibers of the iris.

Function—accommodation and contraction of the pupil.

b. Ocular thoracolumbar pathway.

Preganglionic neurones. Cells in the intermediolateral column of the spinal cord, fibers by way of the upper white rami and sympathetic trunk to end in the superior cervical ganglion.

Postganglionic neurones. Cells in the superior cervical ganglion, fibers by way of the internal carotid plexus to the ophthalmic division of the Vth nerve, the nasociliary and long ciliary nerves to the eyeball: other fibers pass from the internal carotid plexus through the ciliary ganglion, without interruption, into the short ciliary nerves and to the eyeball.

Function—dilation of the pupil by the radial muscle fibers of the iris.

2. Paths for the efferent innervation of the submaxillary gland.

a. Submaxillary craniosacral pathway.

Preganglionic neurones. Cells in the nucleus salivatorius superior, fibers by way of the seventh cranial nerve, chorda tympani and lingual nerve to end in the submaxillary ganglion on the submaxillary duct.

Postganglionic neurones. Cells in a number of groups along the chorda tympani fibers as they follow the submaxillary duct, fibers distributed in branches to the submaxillary gland.

Function—increases secretion.

b. Submaxillary thoracicolumbar pathway.

Preganglionic neurones. Cells in the intermediolateral column of the spinal cord, fibers by way of the upper white rami, and the sympathetic trunk to end in the superior cervical ganglion.

Postganglionic neurones. Cells in the superior cervical ganglion, fibers by way of the plexuses on the external carotid and external maxillary arteries to the submaxillary gland.

Function—increases secretion.

3. Paths for the efferent innervation of the heart.

a. Cardiac craniosacral pathway.

Preganglionic neurones. Cells in the dorsal motor nucleus of the vagus, fibers through the vagus nerve to the intrinsic ganglia of the heart in which they end.

Postganglionic neurones. Cells in the intrinsic cardiac ganglia, fibers to the cardiac muscle.

Function—cardiac inhibition.

b. Cardiac thoracolumbar pathway.

Preganglionic neurones. Cells in the intermediolateral column of the spinal cord, fibers by way of the upper white rami and the sympathetic trunk to the superior, middle, and inferior cervical ganglia.

Postganglionic neurones. Cells in the cervical ganglia of the sympathetic trunk, fibers by way of the corresponding cardiac nerves to the musculature of the heart.

Function—cardiac acceleration.

4. Paths for the efferent innervation of the musculature of the stomach exclusive of the sphincters.

a. Gastric craniosacral pathway.

Preganglionic neurones. Cells in the dorsal motor nucleus of the vagus, fibers by way of the vagus nerve to end in the intrinsic ganglia of the stomach.

Postganglionic neurones. Cells in the intrinsic gastric ganglia, fibers to end on the gastric musculature.

Function—excites peristalsis.

b. Gastric thoracolumbar pathway.

Preganglionic neurones. Cells in the intermediolateral column of the spinal cord, fibers by way of the white rami from the 5th or 6th to the 12th thoracic nerves, through the sympathetic trunk without interruption, and along the splanchnic nerves to the coeliac ganglion where they end.

Postganglionic neurones. Cells in the coeliac ganglion, fibers by way of the coeliac plexus and its offshoots to the stomach to end on the musculature of the stomach.

Function—inhibits peristalsis.

It will be noted that the organs receive a double autonomic innervation and that the impulses transmitted along the craniosacral pathways are usually antagonistic to those transmitted along the thoracolumbar paths.

The afferent innervation of the viscera. General visceral afferent fibers are found in the IX and X cranial nerves and in the spinal nerves. Their cells of origin are located in the cerebrospinal ganglia. The fibers run through the sympathetic

nervous system, passing through the ganglia and plexuses without interruption, to end in the viscera. There is no satisfactory evidence that any afferent neurones have their cell bodies located in the sympathetic ganglia. The function of these afferent fibers is to convey to the central nervous system impulses giving rise to vague sensations, and other impulses, which never rising into consciousness, give rise to visceral reflexes.

Visceral reflex arcs. In the gastrointestinal tract there may be a mechanism for purely local reflexes, i.e., there are probably reflex arcs complete within the gut wall. With this exception the evidence strongly indicates that all visceral reflex arcs pass through the cerebrospinal axis and involve a series of three neurones: 1) visceral afferent; 2) preganglionic autonomic, and 3) postganglionic autonomic. The purely local reflexes which seem to occur within the gut wall after section of all the nerves leading to the intestine are known as the myenteric reflexes and must depend upon a mechanism different from that of other visceral reflexes. We do not know what this mechanism is, but it must be located in the enteric plexuses. The term enteric nervous system should be restricted to the elements responsible for the myenteric reflex.

In the papers which follow there will be presented some of the evidence that has led me to take the general position in regard to the sympathetic nervous system outlined in the preceding pages. For much of the evidence, however, it will be necessary for the reader to refer to the papers of Langley. To this evidence Dr. Johnson has made an important contribution in showing that there are no commissural neurones in the ganglia of the sympathetic trunk of the frog. The papers of Dr. Billingsley and myself are primarily concerned with details of structure, a knowledge of which will be necessary for any future attempt to map the functional pathways of the sympathetic nervous system.

THE SUPERIOR CERVICAL GANGLION AND THE CERVICAL PORTION OF THE SYMPATHETIC TRUNK

S. W. RANSON AND P. R. BILLINGSLEY

From the Anatomical Laboratory of Northwestern University Medical School¹

FIFTEEN FIGURES

In this paper we shall report observations on the superior cervical ganglion and the nerves immediately associated with it. But in dealing with the literature it has been necessary to treat the subject in a somewhat broader way and to set forth what is known concerning the sympathetic ganglia in general.

The general plan of the cephalic end of the sympathetic trunk, according to the evidence obtained by the nicotine and degeneration methods, is as follows: The trunk below the superior cervical ganglion consists of fibers ascending to end in that ganglion (fig. 1). These are preganglionic fibers, the axons of cells located in the intermediolateral cell column of the spinal cord, which have entered the trunk through the upper thoracic white rami and are ascending to the ganglion. Having reached the superior cervical ganglion, these fibers end in synapses with the postganglionic neurones, whose cell bodies are located there, and to which belong the postganglionic fibers that leave this ganglion through its various branches of distribution. Those branches which run to the internal carotid artery, known collectively as the internal carotid nerve and forming the internal carotid plexus, carry postganglionic fibers which are distributed to the eyeball, lacrimal gland, mucous membrane of the nose, mouth, and pharynx and many of the blood-vessels of the head. The fibers to the salivary glands run by way of the branch to the external carotid artery

¹ Contribution No. 54, February 15, 1918.

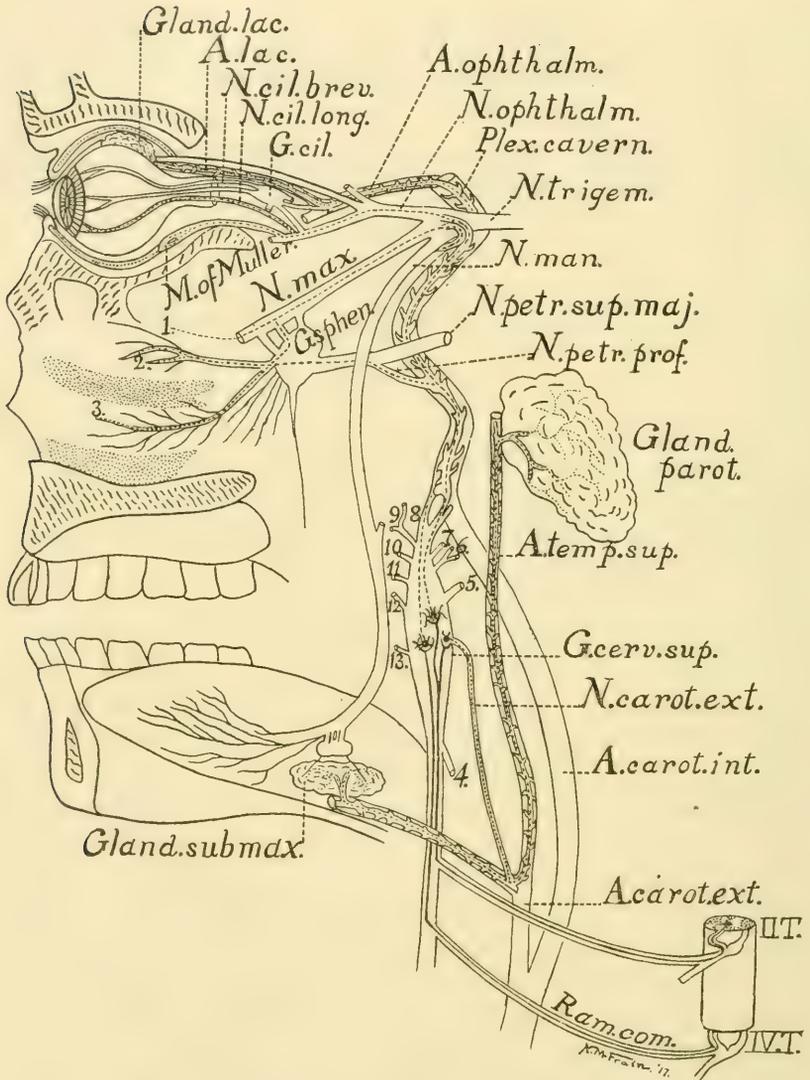


Fig. 1 Diagram representing the arrangement of the more important thoracicolumbar autonomic pathways to the head in man. The preganglionic fibers are indicated by dotted lines. The cells of the postganglionic neurones are located in the superior cervical ganglion and their fibers are indicated by solid lines. 1, Postganglionic fibers to sweat glands of the face; 2 and 3, to the mucous membrane of the nose; 4, N. cardiacus superior; 5, Rr. laryngopharyngei; 6, branch to the N. hypoglossus; 7, branch to the N. vagus; 8, n. caroticus internus; 9, branch to the N. glossopharyngeus; 10, 11, 12, 13, Rami communicantes (gray) to Nn. cervicales I, II, III, and IV.

and follow along its branches to the glands. Through the superior cardiac nerve postganglionic fibers run to the heart in man. Other postganglionic fibers join the upper four spinal nerves and the ninth, tenth, and twelfth cranial nerves to be distributed to the blood-vessels and glands in the regions supplied by these nerves, and still others run by the laryngopharyngeal branches of the superior cervical ganglion to the larynx and pharynx.

This will serve as a general survey of the field to be studied. In the pages which follow we will take up in detail the structure of the superior cervical ganglion, sympathetic trunk and internal carotid nerve and pay particular attention to the synapses which occur in the ganglion.

MATERIAL AND METHODS

The superior cervical ganglion of man, the dog, and cat were prepared by the pyridine silver method and cut into sections 12 to 20 micra thick. Osmic acid preparations were also made from the dog and cat. Many of the preparations were cut into serial sections at right angles to the long axis of the ganglion, beginning at the internal carotid nerve and extending through the ganglion and some distance along the sympathetic trunk. Other ganglia were also examined, such as the stellate ganglion of the cat and the superior cervical ganglion in the rabbit.

In addition to the study of these parts in normal animals, experiments were carried out to determine the effect of partial and of complete degeneration of the preganglionic fibers. It had been noticed in a study of degenerating and regenerating nerves, made several years previously that certain fibers in the early stages of degeneration showed an increased affinity for silver. It was hoped that this might furnish a clue which would lead to the development of a differential stain for degenerating axons. A number of ganglia were prepared by the pyridine silver method sixteen or seventeen hours after section of the sympathetic trunk in the neck to see if by this method the preganglionic fibers might be made to stain more intensely through an increased affinity for the silver. So far we are not convinced

that any advantage was obtained by this procedure. It is true that the majority of our best preparations of the preganglionic fibers were obtained in this way, but since we occasionally obtained just as good stains in normal animals we are in doubt as to the value of the preliminary division of the fibers. We shall consider these as preparations of the normal ganglia since if there is any change it is only in the direction of an increased affinity of these fibers for the silver.

In order to obtain complete degeneration of the preganglionic fibers the sympathetic trunk was divided in the neck. The operation was performed aseptically on cats and dogs, the nerve being cut about 2 inches below the ganglion. After periods of from eight to fifty days some of the animals were killed. It was found that after the longer periods some regeneration had occurred and the shorter periods were scarcely adequate for full degeneration. In order to avoid these difficulties, a second operation was performed on some of the animals twenty to fifty days after the first, the nerve being cut cephalad to the neuroma. Eight days after the second operation the animals were killed.

In dealing with small nerves and ganglia we have found that the pyridine silver stain often fails to give good results apparently because the volume of the tissue is too small. In order to overcome this difficulty we find it desirable to imbed the small nerve or ganglion in the spinal cord. For this purpose we have tied a fine silk thread to the sympathetic trunk and with a long fine needle have drawn the trunk with the attached superior cervical ganglion and internal carotid nerve into a lateral half of the spinal cord along the line of the ventral gray column. After fixation for two hours in ammoniated alcohol the block of spinal cord can be pared down with a razor until it forms a bar the cross-section of which is not more than 4 mm. square. Within this block of cord the nerve is held extended and straight and is protected from the two direct action of the reagents. The cord is dissected away from the nerve just before it is dehydrated and cleared in preparation for imbedding.

STRUCTURE OF THE CEPHALIC END OF THE SYMPATHETIC TRUNK

As has been said, the cervical portion of the sympathetic trunk serves to convey preganglionic fibers from the upper white rami to the superior cervical ganglion. Whether it also contains other than preganglionic fibers is a question which we will consider in this paper. In the cat this nerve, a short distance below the superior cervical ganglion, has the structure shown in figure 2. In cross-section it is uniform throughout except for one or two small well-defined bundles at the periphery. These bundles are not constant and, as we shall see, represent fine branches of distribution from the ganglion which have been incorporated for a short distance in the trunk.

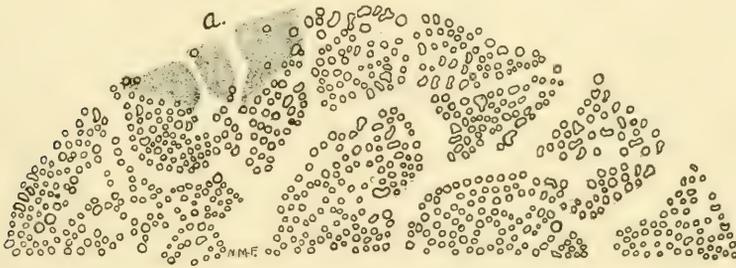


Fig. 2 From a section of the truncus sympathicus a short distance below the ganglion cervicale superius in the cat. *a*, area occupied by a bundle of unmyelinated fibers. Osmic acid. $\times 425$.

Exclusive of these peripheral bundles which really do not belong to it, the sympathetic trunk below the superior cervical ganglion in the cat consists almost exclusively of myelinated fibers as shown in figure 2. These are uniformly distributed and closely packed. It is as well myelinated a nerve as there is anywhere in the body. The fibers are all rather fine. The majority vary in diameter from 1.5μ to 3.5μ . Between these two extremes there are fibers of all sizes and about as many of one size as another. Fibers larger than 4.5μ are few in number but there may be two or three as large as 6.5 or 7μ . Pyridine silver preparations show rather small axons, each surrounded by an unstained halo representing a myelin sheath; these are uniformly distributed, each well separated from its neighbor. There are

no bundles of closely packed unmyelinated axons and no individual ones can be made out with certainty. From a study of the normal truncus sympathicus we may conclude that it is composed almost exclusively of small myelinated fibers.

The fine peripheral bundles, which represent branches of distribution from the superior cervical ganglion, can usually be followed in serial sections to the point where they are given off as fine branches from the trunk. They do not degenerate after section of the nerve more caudally. The structure of these peripheral bundles is entirely different from that of the rest of the nerve and corresponds to that of the other branches of distribution given off from the superior cervical ganglion. They contain a few small myelinated fibers, 1.5μ to 6μ in diameter, scattered among the unmyelinated fibers. Such a bundle is seen at *a* in figure 2 where the area occupied by the unmyelinated fibers is indicated by stippling. In osmic acid preparations bundles of unmyelinated fibers are recognized by their being somewhat more darkly stained than the rest of the background. A fascicle of axons, even though lightly stained, is easily differentiated from connective tissue. Additional information may be obtained by the study of the degenerated nerve. In an osmic acid preparation taken from a cat eight days after neurotomy of the sympathetic trunk in the neck most of the medullated fibers are degenerated, although a few cannot be distinguished from normal fibers. But eighteen days after the operation all the medullated fibers were degenerated except for a small number in a single peripheral fascicle, such as has been described and which is not to be regarded as belonging to the nerve. There were 16 myelinated fibers in this bundle varying in size from 1.8μ to 3.6μ . All the other myelinated fibers in the nerve were degenerated. From this we may conclude that all the myelinated fibers in the cephalic end of the sympathetic trunk (exclusive of branches of the superior cervical ganglion which may be incorporated with it for a short distance) are ascending fibers. There are no medullated fibers arising in the superior cervical ganglion and running to the ganglia placed more caudally in the truncus sympathicus.

Waller and Budge showed long ago that the sympathetic trunk after section in the neck degenerated toward the superior cervical ganglion. Their results have been confirmed by Langley ('96, '00). This author used the rather unsatisfactory method of examining the degenerated nerve in teased preparations stained with osmic acid. He found, however, just as we, in sections stained with osmic acid, that some fine branches of the superior cervical ganglion may accompany the nerve for a certain distance. He also found that occasionally a branch from the vagus might run to the superior cervical ganglion and accompany the nerve for a way. This may have been the depressor nerve (p. 374).

After the sympathetic trunk below the stellate ganglion and the rami communicantes to the first and second thoracic nerves were cut and time allowed for degeneration, he found no sound myelinated fibers in the cervical portion of the nerve, aside from the bundles just mentioned which may happen to be included in the same sheath with it. He concluded that no myelinated fibers run from ganglion to ganglion through this nerve and none join it from the cervical rami communicantes.

We have pyridine silver preparations of the degenerated nerve in both cat and dog. In each case the structure is the same. Take, for example, Cat XII which was killed fifteen days after the division of the sympathetic trunk in the neck. In that part of the nerve just below the superior cervical ganglion the sections stained with silver showed two fascicles of fine undegenerated axons mostly unmyelinated at the periphery of the trunk. Following the sections caudally through the series, one of these fascicles can be seen to leave the trunk, but the other remains with it as far as our series goes, although it would no doubt separate off a little farther down.

Aside from these two peripheral fascicles, which, properly speaking, do not belong to the nerve, almost all of the axons have degenerated. Here and there throughout the section there seems to be an isolated unmyelinated axon of normal appearance. These normal unmyelinated fibers are not numerous. In fact, since we have never seen such isolated unmyelinated axons

elsewhere except in regenerating nerves, we are somewhat skeptical of this observation. The presence of these few axons descending from the superior cervical ganglion, however, raised the questions, are there commissural fibers joining the superior cervical with the stellate or other ganglia?

Here we can take up only the question of the existence of fibers connecting cells in different ganglia, and will leave out of account for the moment that of the interconnection of the cells within a single ganglion. According to Langley, there is no evidence which would justify us in assuming the existence of commissural fibers between the cells of different ganglia, and in certain parts of the sympathetic nervous system he has given strong evidence that no such connections exist. The mass of evidence which he has presented is very convincing, but is too extensive to be summarized here. The reader is referred to the account in Schäffer's *Physiology*, vol. 2, p. 683, and other articles by Langley in the *Journal of Physiology*, vol. 25, p. 468, and vol. 31, p. 244. We can refer here only to that part of the evidence which concerns the cervical portion of the sympathetic trunk. After this nerve was cut below the ganglion stellatum, and the rami communicantes to the first and second thoracic nerves divided and time allowed for degeneration, stimulation of the trunk in the neck produced no effect on the pupil, nictitating membrane, eyelids, hairs, or blood-vessels. Hence the cells of the ganglion stellatum or the middle cervical ganglion do not send nerve fibers to the superior cervical ganglion or to the head by way of this nerve. Even in the normal cat stimulation of this nerve produces no vasomotor, pilomotor, or secretory effect in the territory supplied with such fibers by the ganglion stellatum. It is clear, then, that the superior cervical ganglion does not send commissural fibers to the vasomotor, pilomotor, or secretory nerve cells of the ganglion stellatum which include the great majority of the cells in the ganglion. It is easy to show that stimulation of the sympathetic trunk in the neck is without appreciable effect on the heart of the cat. Hence no fibers descend from the superior cervical ganglion to the cardio-accelerator neurones of the middle cervical and stellate ganglia.

Langley has shown that stimulation of the sympathetic trunk in the neck causes no general body reflexes of any kind. It must, therefore, be devoid of sensory fibers, at least of those carrying painful afferent impulses. We have been able to confirm this physiological observation and our histological results are also in agreement with it. On page 432 we will show that the characteristic sensory fibers of the sympathetic trunk are the large myelinated and the unmyelinated. Except for two or three large myelinated fibers, there are no fibers which would be interpreted as sensory ascending in the cervical portion of the sympathetic trunk.

STRUCTURE OF THE NERVUS CAROTICUS INTERNUS

The chief set of branches given off by the superior cervical ganglion ascends from its upper pole to the internal carotid artery. Of these one or two are of large size in the cat. These large ones are easily and positively recognized in serial sections of the ganglion and its branches. The entire group of from three to five branches forms the nervus caroticus internus. It consists of both myelinated and unmyelinated fibers the latter of course predominating. Figure 3 shows the relative size, number, and arrangement of the myelinated fibers in this nerve in the cat. These fibers are rather widely separated by great numbers of unmyelinated axons and are of about the same size as those of the sympathetic trunk. They vary in diameter from 1.5μ to 4.5μ with an occasional larger fiber up to 7μ . Their distribution is quite uniform throughout the nerve. The thickness of their myelin sheath seems to be somewhat less than that of those in the sympathetic trunk.

These myelinated fibers are so numerous that interest is at once aroused as to their source, and the possibility suggests itself that they are preganglionic or perhaps afferent fibers from the trunk which have run through the ganglion without interruption. This possibility is easily excluded, however, by section of the trunk below the ganglion. After all the myelinated fibers in that trunk have degenerated the structure of the internal

carotid nerve remains unchanged and contains as many myelinated fibers as the nerve of the opposite side. Measurements show that fibers of all sizes from 1.5 to 7μ are present, showing that there has not occurred a dropping out of the fibers of a particular size. In fact, figure 3 represents an internal carotid nerve after the complete degeneration of the sympathetic trunk below the superior cervical ganglion of the same side, but illustrates perfectly well the normal structure of the nerve.

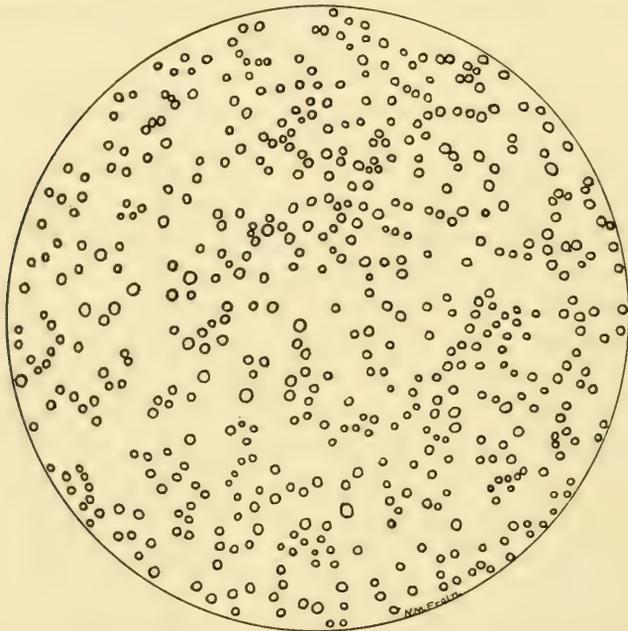


Fig. 3 From a section of the nervus caroticus internus in the cat. Osmic acid. $\times 425$.

One must also consider the possibility of these myelinated fibers being contributed through the rami connecting the superior cervical ganglion with the upper cervical and certain of the cranial nerves. Against this assumption are the observations that can be made on serial sections through the superior cervical ganglion and the internal carotid nerve after degeneration of the trunk.

The myelinated fibers in such a ganglion are extremely few at the caudal pole, but increase gradually toward the cephalic end of the ganglion. They are scattered uniformly through the cross-section of the ganglion, until they begin to assemble at the upper pole to enter the internal carotid nerve. The few myelinated fibers that can be seen in the various side branches of the ganglion (to the cervical and cranial nerves) are at once lost in the ganglion. There are no bundles of medullated fibers running through the ganglion from one branch to the other. We believe that all or at least most of the myelinated fibers in the branches of the superior cervical ganglion arise from cells located in that ganglion. This will receive additional support from more detailed study of the structure of the superior cervical ganglion to follow.

Langley ('96) has shown that after section of the branches peripherally of the superior cervical ganglion nearly all of the myelinated fibers which remain connected with the ganglion are normal, while nearly all of those separated from the ganglion have degenerated, showing that the cells of origin of the great majority of these fibers are located in that ganglion. These observations were made on the cat. In the dog he has traced two small bundles of fibers from the tympanic plexus by way of the internal carotid artery to the superior cervical ganglion.

It is therefore evident that a considerable number of the axons arising in the superior cervical ganglion acquire a myelin sheath. This is in keeping with the results of v. Kölliker ('94), Dogiel ('95), Langley ('96), Michailow ('11), and others. It is interesting to note, however, that Cajal ('11) is of the opinion that the axons of the cells of the sympathetic ganglia never acquire myelin sheaths. It is easy to understand how he may never have been able to trace such an axon into a myelinated fiber, but as we have seen this is not the only line of evidence that can be brought to bear on the problem. All things taken into consideration, the evidence is conclusive that postganglionic axons not uncommonly acquire myelin sheaths.

STRUCTURE OF THE SUPERIOR CERVICAL GANGLION

While we have examined a number of ganglia, including the stellate and coeliac, the observations which we have to report are restricted to the superior cervical ganglion. In the account which follows we will consider the results obtained by others, topic by topic, as we present our own. Unless otherwise stated, citations from the literature are applicable to the collateral ganglia and to all the ganglia of the sympathetic trunk. They should not be carried over without qualification to the terminal ganglia. These present special problems and require separate consideration.

Ganglion cells. It is well known that almost all of the neurones in the sympathetic ganglia are multipolar, although there are also a restricted number of unipolar and bipolar cells located near the poles of a ganglion or within its longitudinal fiber bundles, Huber ('99). Like other nerve cells these neurones have but a single nucleus, except in rodents. In the rabbit we have seen many cells with two nuclei. These have been figured and described with a summary of the related literature by Huber ('99). The neurofibrils of the cells of the sympathetic ganglia have been described by a number of authors, including Michailow ('08) and Cajal ('11). The Nissl granules have been described and figured by Carpenter and Conel ('14).

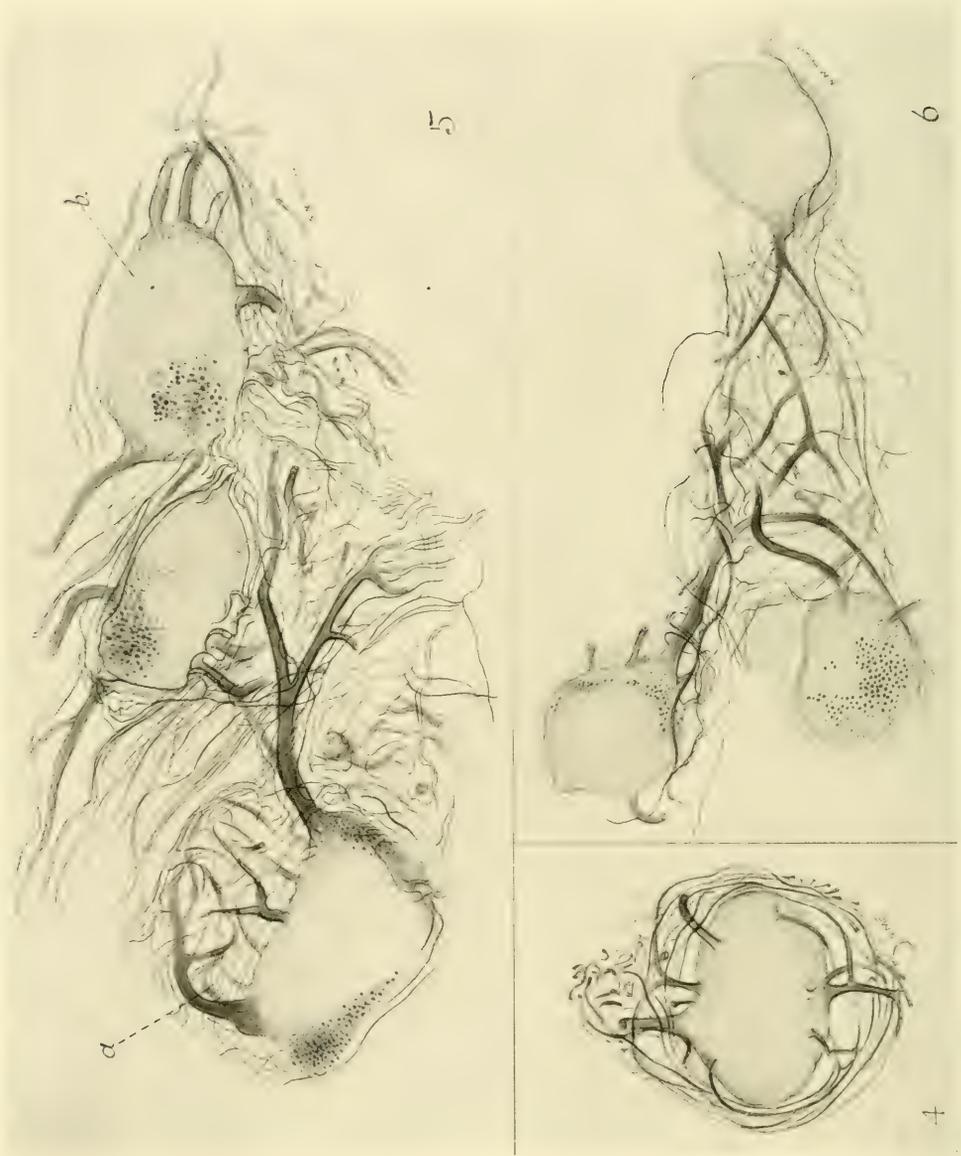
Dendrites. The dendrites of the cells of the sympathetic ganglion may be divided into two chief categories—intracapsular and extracapsular. The former, although presenting great variety in length and form, are all situated beneath the cell capsule. Although these intracapsular dendrites are common in the sympathetic ganglia of man, they are rarely met with in the other mammals. Michailow ('11), in his careful study of the collateral and trunk ganglia in horses, dogs, cats, rabbits and guinea-pigs, described and figures only one form of subcapsular dendrite. These are present on his cells of types II and V. They are short and club-shaped (fig. 8, *a*). There are usually from five to seven of them and they begin as relatively thick fibers soon going over into bulbous endings. A fiber may divide and end in two such clubs. The expanded ends of these

dendrites usually contain pigment in large quantities and are sometimes vacuolated. Cajal ('11) does not describe any subcapsular dendrites in the sympathetic ganglia of animals, although they are very prominent in his descriptions and figures of these ganglia in man. But these dendrites were demonstrated in the human ganglia by means of his silver stain which was not used in his earlier studies on animals.

It might be supposed that the use of the newer silver stains would demonstrate their general occurrence in the mammalian sympathetic ganglia, but in pyridine silver preparations of the superior cervical ganglia of cats and dogs we have seen no cells with subcapsular dendrites. This shows that they must be relatively rare here and establishes a very striking contrast between the superior cervical ganglion of man and that of the carnivora.

The intracapsular dendrites reach their highest development in man. Here they give rise to complicated subcapsular formations which were first described by Cajal ('11), whose observations have been confirmed by Marinesco ('06). Both investigators worked with the superior cervical ganglion stained by the Cajal method. Their observations are confirmed by our own observations on the human superior cervical ganglion stained by the pyridine silver method. The account which follows is based on our own preparations, but is in accord with the results of the two investigators who preceded us. The subcapsular dendrites are arranged in a great variety of ways underneath the capsule of the cell from which they take origin. In general they may be said to give rise to two types of complicated intracapsular networks which Cajal has called dendritic crowns and glomeruli.

Figure 4 furnishes a good example of a dendritic crown. Numerous dendrites of varying caliber come off from the cell and run toward the inner surface of the capsule where, with or without branching, they turn to run in the subcapsular space. Here they cross and recross, but do not anastomose, and form an open network more or less uniformly distributed around the cell. In some cases these dendrites can be seen to end in small bulbs



or rings. The long thick process which is seen piercing the capsule in the illustration is probably the axon, although it might be an extracapsular dendrite. In that case one would have to assume that the axon came off from that surface of the cell which has been cut away at the plane of section.

According to Cajal, these dendrites frequently apply themselves against the capsule to terminate on its internal surface or among the satellite cells by pear-shaped thickenings. Sometimes they are more delicate and bend in beneath the capsule to terminate by fine pale extremities. Sometimes they run beneath the capsule in great circles about the cell. The dendritic nest which envelops the cell is easy to distinguish from the ramifications of axons by the greater caliber of its fibers and the rarity of its divisions. Cajal's figures show that the spaces among the subcapsular dendrites contain small cells which he calls satellite cells.

The dendrites which enter into the formation of the glomeruli are also subcapsular, but are usually coarser than those just described. Instead of coming off from all parts of the surface of the cell, they usually arise from a restricted region. Branching repeatedly and interlacing they form a mass of considerable size over which the capsule of the cell is continued. Cajal has shown that the spaces between the dendritic branches are occupied by satellite cells. Following his classification, we may enumerate simple, bicellular, tricellular, and multicellular glomeruli according to the number of neurones the dendrites of which enter into their formation.

The simple glomeruli are formed from the dendrites of one cell. They are short and thick, come off from one side of the cell, and raise the capsule to form a pocket within which these dendrites

Fig. 4 Nerve cell surrounded by dendritic crown from the ganglion cervicale superius of man. Pyridine silver. $\times 800$.

Fig. 5 From the ganglion cervicale superius of man. *a*, unicellular dendritic glomerulus; *b*, cell provided only with extracapsular dendrites. Pyridine silver. $\times 800$.

Fig. 6 Tricellular glomerulus from the ganglion cervicale superius of man. Pyridine silver. $\times 700$.

branch and intertwine (fig. 5, *a*). All transition stages are found between the simple glomeruli and the dendritic crowns. When the glomerulus is located on the side from which the axon arises it may be prolonged out for a short distance along the axon, giving rise to a comet-shaped formation.

The glomeruli formed from the dendrites of more than one cell may be called composite glomeruli and are somewhat more complicated than the simple glomeruli just described. The large subcapsular dendrites of two or more cells converge toward each other to form a circumscribed mass of branching and interlacing dendrites. Figure 6 gives a good idea of a tricellular glomerulus, which, along with the three cells, seems to be enclosed in a single capsule. The capsules and subcapsular satellite cells are not well differentiated in pyridine silver preparations, but, according to Cajal, the glomeruli are surrounded by a capsule that separates them from the fiber bundles. The capsule is better defined in the bi- and tricellular than in the multicellular forms.

The fine black fibers seen interlacing with the dendrites in figures 5 and 6 are the branches of axons and will be discussed in another place.

The extracapsular dendrites pierce the capsule and run for longer or shorter distances among the cells, helping to form an intercellular plexus of dendritic and axonic ramifications. The cells of the superior cervical ganglion of the dog and cat are provided almost exclusively with this type of dendrite. Such dendrites are also numerous in this ganglion in man. Here they may come from cells devoid of subcapsular processes (fig. 5, *b*) or from cells provided with dendritic crowns or glomeruli (fig. 5, *a*). They are usually coarse fibers and may branch near the cell or may remain unbranched until they leave the section. Often it is possible to trace them much longer distances than is indicated in the figure, but in no case could they be followed to what seemed to be their true termination (fig. 7). Cajal differentiates three types of cells in the human superior cervical ganglion: 1) cells provided exclusively or almost exclusively with subcapsular dendrites; 2) cells provided only with long dendrites, and 3)

cells provided with both kinds of dendrites. While such a classification facilitates description it must not be supposed that these types are separated by sharp lines of cleavage or that there is any reason to assign them different functions.

In pyridine silver preparations of the superior cervical ganglion of dogs and cats the dendrites have not been very well stained. We could find only extracapsular dendrites, but could trace none of them to their termination. Figure 12 gives an idea of how they look when freed from intercellular axonic ramifications. In order to make an intelligent analysis of the functional con-

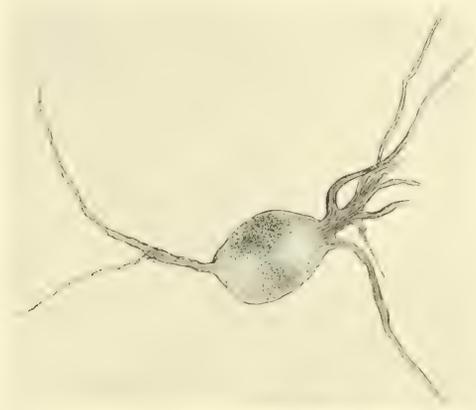


Fig. 7 Cell with long extracapsular dendrites from the human superior cervical ganglion. Pyridine silver. $\times 400$.

nections in the ganglia it is necessary to have a clear idea of the course and termination of these extracapsular dendrites.

Concerning the true endings of these dendrites our preparations, which could not be made very thick, give us no information because all the long dendrites seem to be cut off at the surface of the section. According to Cajal ('11), there are three ways in which these long intracapsular dendrites in the human superior cervical ganglion end: 1) They may run into a fascicle of dendritic fibers where they run parallel to the other fibers of the fascicle and within which they may end with long interstitial appendages. At other times they end in olive-shaped extremities, or in fusiform swellings which give rise to fine varicose branches.

2) They may end in glomeruli where they encounter the branches of other dendrites of the same kind. As indicated in his figures, such glomeruli are located at a distance from the cells of origin of the dendrites concerned. 3) They may end in pericellular baskets. These dendritic baskets have been found in animals by Cajal ('11), Van Gehuchten ('90), Sala ('92), and Michailow ('11), and will be discussed more in detail in connection with the account given by the latter author.

Michailow ('11) has enumerated nine types of cells in the sympathetic ganglia of mammals. This grouping like that of other authors is chiefly of value as an aid to description, since there is no evidence that any one type is responsible for a particular function. From among the various forms, which, according to him, the dendrites of the cells in the sympathetic ganglia may assume, we have selected five as the most typical and significant. Such dendrites may be found in the ganglia of the sympathetic trunk as well as in the collateral and terminal ganglia. They are represented in figure 8.

1. Dendrites ending in a brush formation (fig. 8, *a*). These are given off in small numbers (1 to 4) from Michailow's Type II cells. They run between the cells of the ganglion where some of them end; others enter bundles of fibers that leave the ganglion. He has followed such a dendrite from a ganglion of the solar plexus of the horse and seen it run as a typical unmyelinated fiber into another ganglion of the same plexus. These dendrites end in special formations in the shape of little brooms, consisting of numerous end branches beset with enlargements. These thickenings are of various shapes and sizes. Usually they are flattened and have the appearance of end plates or of large varicosities.

2. Dendrites terminating in end plates (fig. 8, *b*). These are given off from Michailow's Type III cells. They begin as rather thick processes which in unipolar and bipolar cells may be so thick that it is hard to tell where the cell body ends and the dendrite begins. Sometimes these dendrites end in the same ganglion, sometimes they join bundles of nerve fibers and either end in them or run with them to end in other ganglia. Some remain thick and coarse to their end, others branch and become

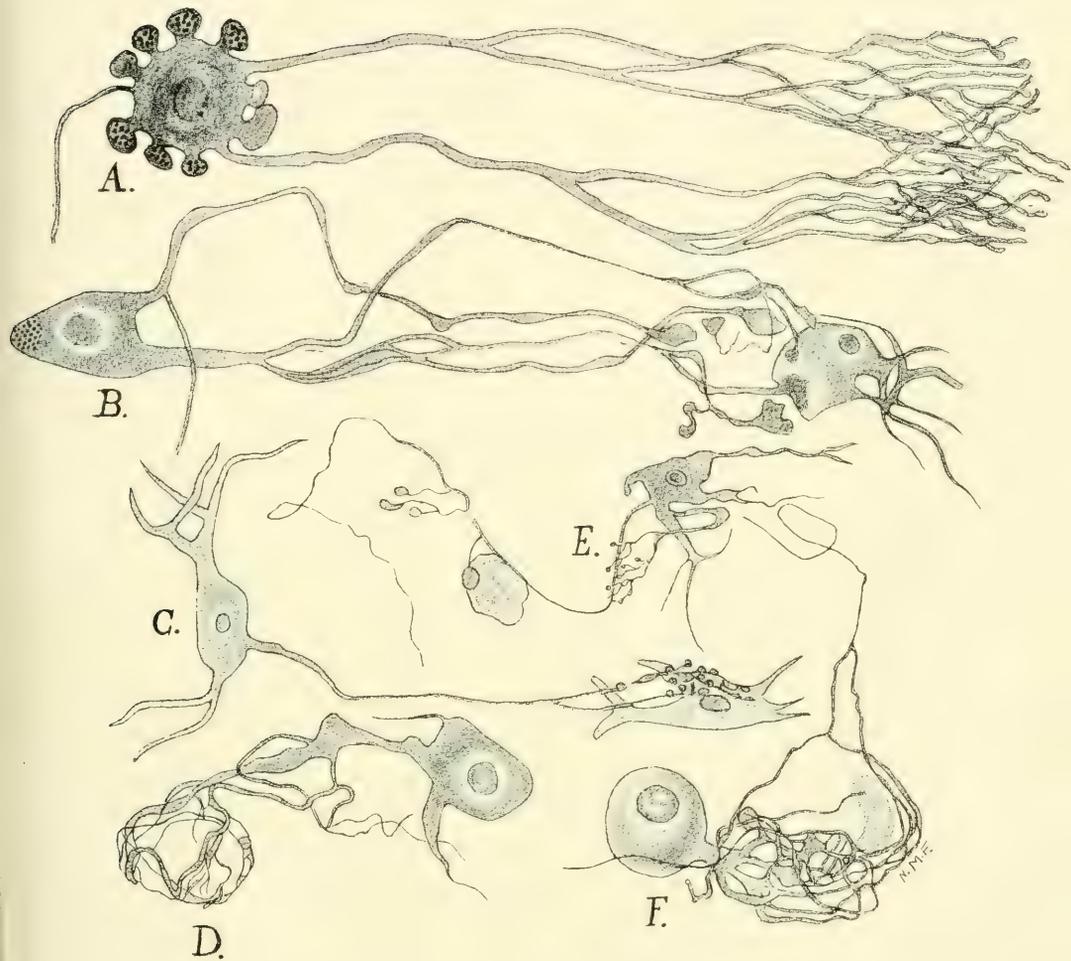


Fig. 8 Sympathetic ganglion cells showing various types of dendrites. Re-drawn from Michailow ('11). All were stained with methylene blue; *a*, cell of Michailow's Type II from the ganglion mesentericus superius of the horse; *b*, cell of Type III from the ganglion coeliacum of the horse; *c*, cell of Type IV from the ganglion stellatum of the horse; *d*, cell of Type VI from the ganglion cervicale superius of the dog; *e*, cell of Type IX from the ganglion coeliacum of the horse; *f*, cell of Type VIII from the ganglion cervicale superius of the dog.

thin, take on the character of unmyelinated fibers and run out of the ganglion. The endings are in the form of plates of various sizes and shapes. These may lie free in the connective tissue or may be pressed against the outside of the capsules of other cells so close as to produce an impression on the cells. Other end plates of this type are found in the fiber bundles outside the ganglia. He found great numbers of such end plates in the fiber bundles of the solar plexus.

3. Dendrites ending in a number of fine branches with end bulbs closely grouped together as illustrated in figure 8, *c*. Such dendrites arise from Michailow's cells of Type IV. They branch freely and occupy much space, greatly increasing the territory of these neurones. They may end in the same or in other ganglia. Near their termination they begin to divide di- and tricotomously. The branches are provided with terminal enlargements which may be rounded or pear-shaped. All the branches of a dendrite form together an end-apparatus, which may vary in size and appearance, but is always applied to the outer surface of the capsule of a cell of Type IV. That is to say, these fibers arise from cells of Type IV and end upon the surface of the capsules of other cells of Type IV.

4. Dendrites forming pericellular nests (fig. 8, *d*). These arise from the cells of Michailow's Type VI, are usually short, and divide repeatedly. The branches approach another cell, and anastomosing with each other form a network that encloses the cell. Sometimes such a basket-like network surrounds the cell from which the dendrite arose. Similar formations have been described by Dogiel, according to whom they are always extracapsular. As already mentioned, Cajal, Van Gehuchten, and Sala have seen such dendritic nests. The significance of these structures can best be discussed in a later paragraph.

5. Dendrites the branches of which anastomose to form a true net out of which a fine fiber, probably the axon, arises (fig. 8, *f*). One or more dendrites break up into a great number of fine branches which anastomose with each other, giving rise to a network. Out of the net fine filaments arise, which join together to form a smooth fiber that remains unaltered as far as it

can be followed. Michailow thinks it probable that these smooth fibers are axons. It will be seen that these neurones resemble some described by Dogiel in the spinal ganglion.

Are there special sensory dendrites in the sympathetic ganglia? This problem has been in the foreground ever since 1896 when Dogiel published his paper on "Zwei Arten sympathischer Nervenzellen." The one type of dendrite which he thought belonged to motor cells branched repeatedly in the neighborhood of the cell and ended within the ganglion; the other, which he thought belonged to sensory cells, resembled unmyelinated nerve fibers and could be traced long distances. Many of them could be followed out of the ganglion and were thought to end as sensory fibers in the viscera. Cajal ('11) finds no evidence in favor of the sensory function of these long dendrites and was not able to find any of them leaving the ganglia and associated nerve trunks to end in the viscera.

Carpenter and Conel ('14), working with Cajal's method on the superior cervical ganglion of the cat, could find cells answering to the description of Dogiel's two types, but were not convinced that such cells represent two distinct categories, since all gradations between the two extremes were found. In Nissl preparations all the cells of the sympathetic ganglia appeared to Carpenter and Conel to be of one type. In the cerebrospinal system it is easy to recognize sensory and motor cells by the arrangement of their chromatophile substance, but all the sympathetic ganglion cells seemed to have a structure intermediate in character between that of the cerebrospinal sensory and motor types. Since these results would indicate that there is but one functional type of cell in these ganglia and since we know that the majority of the cells are motor, the probability against the presence of sensory cells is increased.

So far as we have been able to find no one has confirmed Dogiel's account of the sensory type of cell except Kuntz ('13), who found certain structures which could be interpreted in this way. Nor has the correlated observation of Dogiel, that fibers, arising from sensory cells in the sympathetic ganglia, run to end in pericellular baskets about spinal ganglion cells, been much better

supported. In regard to this point Huber ('13) has recently said

the evidence presented by Cajal, Dogiel, Retzius, Huber, and others cannot be regarded as entirely conclusive, since it has not been determined that the fine medullated fibers or the unmedullated fibers which appear to enter the spinal ganglia from without and end in pericellular plexuses, are, in fact, the neuraxes of sympathetic neurones.

Very strong evidence has been presented by Langley ('03) to show that no medullated sensory fibers run from the sympathetic to the spinal ganglia.

As regards the white rami, which contain most of the afferent visceral fibers, there is conclusive evidence that the very great majority of them have their trophic center in the posterior root ganglia. It consists in the fact that after intraspinal section of a nerve just peripherally of the posterior root ganglia, either all, or all but a few, of the medullated fibers in the white rami degenerate; and that after section of the sympathetic or of the splanchnic or of the inferior splanchnics no degenerated fibers are present in the white rami.

Similarly in the sacral autonomic system, the pelvic nerves contain about 1,000 afferent nerve fibers, and about twice this number of efferent nerve fibers; on cutting the roots of the sacral nerve, as shown by Anderson and myself, about half a dozen fibers only remain undegenerated in the pelvic nerve, and these are probably post-ganglionic medullated fibers.

Axons of the cells of the sympathetic ganglia. In pyridine silver preparations of the superior cervical ganglia of the cat, dog, and man, it is very difficult to follow an axon for any considerable distance. In fact, it is usually no easy matter to tell which of the several processes of a cell is to be regarded as an axon. In a preceding section of this paper it has been shown that some of these axons acquire a myelin sheath. According to Kölliker ('96) and Langley ('00), these axons always end at the periphery, and never terminate in the sympathetic ganglia.

According to Cajal ('11), who worked with the Golgi and methylene blue stains on the sympathetic ganglia of animals and with his silver stain on the superior cervical ganglion of man, the axons of the cells of the sympathetic ganglia are rather thick, smooth, and devoid of branches. He says that his anatomical studies are in accord with the physiological experiments of Lang-

ley and indicate that the axons of these cells dispose themselves in one of the three following ways: 1) Usually they run transversely to the long axis of the ganglion to enter a gray ramus. In the initial part of their course these fibers do not give rise to branches. 2) The axons may run through a connecting nerve trunk into another ganglion. He is not able to say whether these axons only run through the second ganglion or whether they make connections with its cells. In the chick embryo he at one time described collaterals coming from those longitudinal fibers of the ganglia which take origin in neighboring ganglia. He is now inclined to doubt this observation and thinks it likely that these collaterals all come from fibers that have entered the sympathetic trunk through white rami at other levels. 3) In some cases they leave the ganglion and run toward the neighboring arteries in the visceral nerves.

Sala ('93) described two kinds of fibers in the sympathetic ganglia. Those of one variety are unbranched, varicose, and unite to form smaller or larger fascicles which run through the ganglion in every direction. These are the axons of the cells of the sympathetic ganglia. The fibers of the other kind are a little larger, non-varicose, and give off collaterals which are finer and in their turn ramify abundantly. These are less numerous than the first and are found almost exclusively in the branches from the cerebrospinal system. It is not improbable, he says, that these are of cerebrospinal origin.

In his elaborate description of nine types of cells in sympathetic ganglia Michailow has given very few details regarding the axons. However, it is to be noted that in none of these nine types does he describe the axon as terminating in a sympathetic ganglion and in only one does he describe it as giving off collaterals (fig. 8, *e*).

v. Lenhossék ('94), using Golgi preparations of the chick, traced axons of sympathetic ganglion cells into the neighboring ganglia, but did not say what became of them there. In one case he saw fibers entering a ganglion from a visceral nerve break up into branches. He considered these the axons of cells lying somewhere in the visceral ganglia. From what we know now they might just as well be interpreted as the endings of long dendrites.

The axons of Dogiel's Type II cell are figured by that author as passing through several ganglia giving off collaterals and finally ending by branching in another ganglion. In the text, however, he does not claim to have followed such an axon to its termination. But, as we have said before, no one has been able to confirm Dogiel's findings in regard to these cells.

Both Dogiel ('95) and Huber ('99) are of the opinion that the fine fibers which enter the ganglion through its various branches and take part in the formation of the intercellular plexuses are the axons of cells in other sympathetic ganglia. Satisfactory evidence of this is not presented, however, and in the next section of this paper we will present what seems to be conclusive evidence that these fine fibers are of cerebrospinal origin.

While it has not been shown that the axons of sympathetic ganglion cells ever end in connection with the cells of the same or adjacent ganglia, it seems to be well established that these axons may give off collaterals within these ganglia. The axons have been seen to give off collaterals either in the same or adjacent ganglia by v. Lenhossék ('94), Dogiel ('95), and Michailow ('11). These do not seem to be present on the majority of the axons. Michailow is the only one who has seen the mode of termination of these collaterals. According to him (fig. 8), they end in little plates, either in the connective tissue of the ganglion between the nerve cells or pressed against the capsule of a cell. From their mode of termination it is not evident how these collaterals could serve to transmit impulses from one neurone to another. They rather resemble certain collaterals on the axons of spinal ganglion cells, seen by Huber, Dogiel, and Ranson, which since many of them end on the cell from which the axon arose cannot serve for the spreading out of nerve impulses.

Huber ('13), in summing up the evidence concerning the interconnections of the cells of the sympathetic ganglia, concludes that "there is at hand morphologic evidence that the neuraxes of sympathetic neurones, the cell bodies of which are in one ganglion, terminate either on the cells of the same ganglion or of other ganglia." To us the evidence seems far from convincing. Such fragmentary and unsatisfactory histological evidence as

may exist is more than offset by the strong physiological evidence against such connections. Some of this physiological evidence will be briefly presented in a succeeding paragraph.

The intercellular plexus. Throughout the ganglion there is a rich plexus of dendritic branches and fine axons. This has been described and figured by Dogiel ('95), Huber ('99), and Michailow



Fig. 9 Intercellular plexus formed by dendrites and myelinated and unmyelinated fibers from the semilunar ganglion of the cat. Redrawn from Huber ('99).

('11). The part which the dendrites take in this formation has been discussed in a preceding section. We are interested here chiefly in the axonic ramifications which help to constitute it. According to Huber, one of whose drawings is reproduced in figure 9, there are in addition to the medullated fibers entering the ganglion from the white rami, "small medullated fibers, which may be traced from this or that nerve root of a ganglion" into

the ganglion where "they are found branching and rebranching, and forming, with the dendritic processes of the ganglion cells, what Dogiel has described as the intercellular plexus." Huber quotes with approval the conclusion of Dogiel ('95): "Die feinen Fasern, welche in den Ganglien mit intercellularem Geflechte endigen, zu den sympathischen, augenscheinlich vorzugsweise markhaltigen Fasern gehören." It is interesting to note that Huber was able to trace some of the fine unmyelinated fibers of this plexus to definite endings on neighboring dendrites.

According to Dogiel ('95), whose observations were made on the terminal ganglia, the finer myelinated and unmyelinated fibers enter the ganglion, branch and intertwine, and break up into fine branches which cross in various directions and finally break up into finer fibers of uncountable number. These form a thick plexus among the cells and at the periphery of the ganglion. The fibers of the plexus are in contact with the dendrites, but separated from the cell bodies by their capsules. All the fibers of the plexus are beset with varicosities.

Michailow's ('11) conception of the intercellular plexus differs from that of the two preceding authors in that, according to him, the constituent fibers of the plexus anastomose with each other forming a closed network. By means of this network all or at least many of these fibers are united together, one neurone being in this way united with many others. As will be seen later, there are good reasons for discarding this part of Michailow's description of the intercellular plexus.

In preparations of the superior cervical ganglion of the cat or dog by the pyridine silver method one can readily see a plexus of fine unmyelinated fibers running among the cells in every direction through the ganglion (fig. 10). The dendrites are not well stained in these preparations and only their coarser branches are visible. The finer dendritic ramifications, which, according to those who have worked with the methylene blue stain, help to form the intercellular plexuses, are not to be seen. In these preparations the network of fibers under discussion corresponds only to the axonic constituents of the intercellular plexuses of Dogiel and Huber.

The constituent fibers of this plexus stain rather heavily with silver and range in color from light brown to black. They also vary greatly in size, the smallest being perhaps not more than one-eighth the thickness of the largest. The larger axons can often be seen to branch, but the smaller ones seem to run for

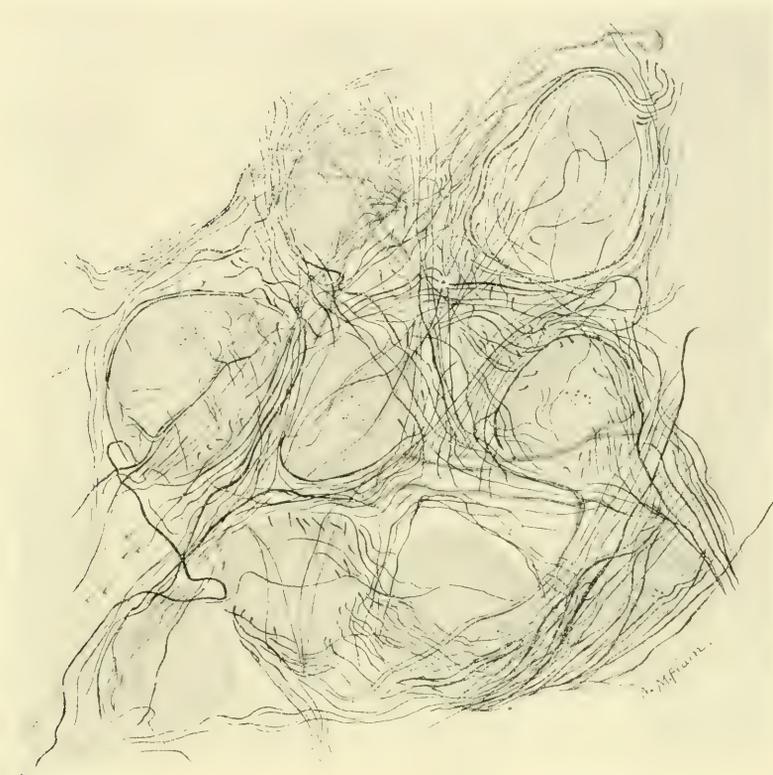


Fig. 10 Intercellular plexus in the ganglion cervicale superius of the dog. Section 20μ . Pyridine silver. $\times 800$.

considerable distances without branching. The majority of the fibers are very fine. They run in and out among the cells, twisting and turning, crossing and recrossing and forming together a dense interlacement. That practically all of these fibers are unmyelinated can be seen at once by comparing such a prepara-

tion with one stained by osmic acid. In the latter, in place of the dense interlacement of fine fibers just described, one sees only here and there an isolated myelinated fiber. In many parts of the ganglion these are less numerous than the nerve cells.

So far as we can determine the intercellular plexus is entirely extracapsular. Although some of the fibers wrap themselves about the cells and form what might seem to be pericellular plexuses (fig. 11), these are found not to be in any way separated from the general plexus which fills in the intervening spaces. We believe that these apparently pericellular baskets are really pericapsular and represent merely portions of the general plexus which are in contact with the cell capsules. It is not clear

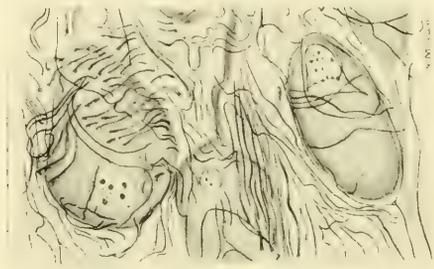


Fig. 11 Three cells from the ganglion cervicale superius of the dog showing fibers of the intercellular plexus wrapped about them. These fibers seem to be extracapsular. Pyridine silver. $\times 800$.

whether these formations correspond to the pericapsular nets of Michailow or not. It is evident, however, that they do not correspond to Huber's pericellular plexus which is endocapsular and forms a closed network. That all of the fibers of the intercellular plexus are extracapsular is shown by the examination of sections in which the ganglion cells have shrunk, leaving a cleft between them and their capsule. In such cases the fibers in question always remain in or upon the capsule and never lie on the shrunken cell. An additional point of distinction is found in the fact that the pericellular plexus is a closed network while as we shall see anastomoses do not seem to occur among the fibers under discussion. Furthermore, we have twice seen a fragment

of a closed network on the surface of a cell which we were inclined to regard as a true pericellular plexus. From all these facts we conclude that the pericellular network is ordinarily not stained in the pyridine silver preparations, but that the axonic constituents of the intercellular plexuses come out with great clearness.

It will be remembered that Michailow regarded the plexus under discussion as forming a true net by means of which all or at least many of the fibers are united together, one neurone being thus united to another. This would mean diffuse conduction in the ganglion, which must then act as a whole. This is directly at variance with what is known of the physiology of the sympathetic ganglia. There is no evidence that diffuse conduction occurs in any of them, and in at least two, the superior cervical and the coccygeal ganglia, Langley ('00 a, '04) has been able to show that diffusion does not occur. We will take this up in connection with a discussion of the synapses in the sympathetic ganglia.

Neither Dogiel nor Huber gives the impression that the intercellular plexus is a closed net and we have carefully examined pyridine silver preparations for evidence in this regard. While branching fibers are common, it can usually be seen that a larger fiber is dividing into two smaller ones. The junction of three fibers of the same size as at the nodal point of a net does not seem to occur. Often two fibers could be seen crossing, one immediately over the other, but each retained its individuality and sharp contour. If the plexus were a true network, one should be able to find closed meshes surrounded on all sides by anastomosing fibers—an arrangement which does not seem to occur.

In the pyridine silver preparations of the human superior cervical ganglion the fibers of the intercellular plexus stand out prominently, as is seen in figure 5. The fibers of this plexus mingle with the branches of the long or extracapsular dendrites. Except that the plexus is not as uniformly distributed throughout the ganglion and is perhaps not quite so dense, it resembles that in the dog. There is, however, one important feature in which the human ganglion differs. Fine axons, apparently continuous

with those of the intercellular plexus, penetrate into the dendritic glomeruli and the dendritic crowns forming subcapsular plexuses in close relation to the subcapsular dendrites. This is well illustrated in figure 5, *a*. Cajal has considered these fine darkly staining axons as preganglionic fibers of spinal origin. From what has been said and from the accompanying illustrations it will readily be seen that these fibers are the same as those which form the intercellular plexuses in the superior cervical ganglion of the dog and cat. In a paragraph which follows evidence will be presented to show that these are fibers of spinal origin.

Here and there in this plexus in the superior cervical ganglion of the dog or cat one can see faintly stained yellow axons about the size of the larger dark fibers forming the plexus. In many places these lightly stained axons are united into bundles of parallel fibers which run as straight a course as is possible through the ganglion. These light yellow axons and the bundles into which they unite do not seem to belong to the plexus, although necessarily they run through it. The color contrast between the two kinds of fibers is quite sharp in good preparations, but since all gradations are found the color alone is not sufficient to distinguish them. The light axons are among the largest in the ganglion, are of uniform contour and apparently unbranched. They show a marked tendency to group themselves into bundles of parallel fibers in contrast with the more irregular course of the dark fibers.

Distribution of nerve fibers in the ganglion. In regard to the termination of axons in the sympathetic ganglia, Cajal ('11) states that in his first work in this field he described two kinds of terminal arborizations, one set representing the branches of the longitudinal sympathetic fibers arising in neighboring ganglia, the other representing branches given off by fibers from the white rami. That distinction does not seem probable to him any longer because of the results of Langley's experiments and because of the presence of many medullated fibers in the commissural cords which are known to come from the spinal cord (Langley, '03, and Müller, '09). Cajal now believes that the two kinds of terminations belong to spinal motor fibers, distinguished

only by their course in the sympathetic trunk. One innervates the ganglion to which the ramus brings it. The other runs through two or more ganglia before it terminates.

A study of serial sections through the superior cervical ganglion of the cat stained with osmic acid is instructive. At the lower pole a large bundle of myelinated fibers can be traced into the ganglion from the sympathetic trunk. This comes to lie near the center of the ganglion and breaks up into smaller bundles. Many of the fibers seem to lose their myelin sheaths while still within the smaller bundles. At least this seems to be the best explanation of the fact that the number of myelinated fibers scattered among the ganglion cells is so small.

When the sympathetic trunk is cut and time allowed for degeneration all these bundles of fibers have degenerated. There are, however, still present even in the caudal pole of the ganglion a very few scattered myelinated fibers which have their cells of origin in the ganglion. The number of such fibers increases toward the cephalic pole. Here the myelinated and the more numerous unmyelinated postganglionic fibers accumulate in bundles located especially near the periphery of the ganglion. From the pole large branches representing the internal carotid nerve are given off. Other smaller branches are given off in various places from the ganglion.

The small number of myelinated fibers which are scattered among the ganglion cells in comparison to the number entering and leaving the ganglion would indicate that they run considerable distances in the ganglia as unmyelinated fibers.

In following through a series of sections stained by the pyridine silver technique, one sees that the fine axons entering the ganglion from the sympathetic trunk are all stained a dark brown. Each fiber is surrounded by a thin unstained ring of myelin. This central bundle of the ganglion can be seen to break up into smaller and smaller bundles of dark fibers and the constituent fibers of these smaller bundles can be seen to run into and become a part of the intercellular plexus described in the preceding section.

Following the series toward the cephalic end of the ganglion, one sees bundles of axons collecting especially near the periph-

ery of the ganglion and these can be followed into its various branches of distribution. These fibers are stained yellow or light brown in contrast to the darker fibers entering by way of the trunk. The staining reaction of these axons is exactly like that of the bundles of 'sympathetic fibers' described in the vagus and its branches by Chase and Ranson ('14) "where they are differentiated from the vagus fibers by their lighter stain." We have repeatedly noticed this characteristic light staining of postganglionic autonomic fibers in the various spinal and cerebral nerves. Here the contrast with the darker unmyelinated fibers of cerebrospinal origin could not easily be overlooked.

It is true that these lightly stained axons run among the cells and therefore through the intercellular plexus, but the great bulk of that plexus is composed of fibers whose staining reaction resembles that of the fibers entering by way of the sympathetic trunk. And the impression is gained by a study of such serial sections that this intercellular plexus is formed by the fibers derived from the trunk, and that the other fibers run through the plexus as directly as possible to their point of exit from the ganglion. Were it not for the difference in the color of the two kinds of axons, however, the impression would undoubtedly be given that the plexus is formed by fibers that stream into the ganglion through all its branches. This is the impression that Dogiel, Huber, and Michailow have gained from the study of methylene blue preparations.

The proof that the intercellular plexus is formed by the ramifications of the preganglionic fibers is furnished by the experiment of cutting the sympathetic trunk in the neck and allowing time for degeneration to take place. Pyridine silver preparations of the superior cervical ganglion in which the preganglionic fibers have degenerated show no trace of an intercellular plexus (fig. 12). Our technique does not stain the finer branches of the dendrites and these do not appear in either the normal or altered ganglia, but the fine axonic ramifications that form the normal network are gone. One can readily recognize small bundles of the lightly staining postganglionic fibers and many such fibers running an isolated course. But these fibers do not coil and

turn about the cells, and wherever several are grouped together they run parallel to each other in small compact bundles. They do not give in any way the appearance of the intercellular network.

By way of summary we may say that the fine myelinated fibers entering the ganglion through the sympathetic trunk are pre-ganglionic elements and form by their ramifications a complicated intercellular plexus of fine unmyelinated fibers. The other branches of the ganglion consists of many unmyelinated and a few myelinated fibers. These all represent the axons of



Fig. 12 Three cells from the ganglion cervicale superius of a dog in which the sympathetic trunk had been cut 58 days before the dog was killed. The fine fibers of the intercellular plexus are absent. Pyridine silver. $\times 800$.

the cells in the ganglion and take no part in the formation of the intercellular plexus. They are the postganglionic fibers of Langley.

SYNAPSES IN THE SUPERIOR CERVICAL GANGLION

Where are the synapses on the paths through the superior cervical ganglion located? Langley ('00), using his method of paralyzing the endings of preganglionic fibers by nicotine, has shown that the fibers of the sympathetic trunk, destined for the superior cervical ganglion, come from the upper thoracic white rami and run without interruption through the upper thoracic ganglia.

By the same method he has shown that all these fibers end in the superior cervical ganglion. After painting that ganglion with a solution of nicotine no response can be obtained on stimulation of the upper thoracic nerves, showing that all the pathways through the ganglion are blocked. It is generally admitted that this blocking occurs at the synapse. The same effect can be obtained by the intravenous injection of nicotine. Since, however, large doses of nicotine given intravenously will not eliminate the effects of stimulating the internal carotid nerve or other branches of distribution from the ganglion, it is argued that there are no other synapses interposed between this ganglion and the tissues innervated. This conclusion is shown to be correct by the results of the method of degeneration.

That the degeneration, after section of the internal carotid branches, spreads to the periphery, is shown by stimulating the sclerotic before and after degenerative section. In the former case, there is a double effect—local contraction of the radial muscle leading to local enlargement of the pupil, and local contraction of the circular muscle of the iris; in the latter case, the radial contraction is lacking, the circular takes place as before.

The results obtained from section of the sympathetic trunk in the neck and of the internal carotid nerve are all in accord with the conclusions to be deduced from the nicotine experiments.

Our own observations are in full agreement with the conceptions just presented. The trunk consists almost exclusively of medullated fibers, which would not be the case if it contained postganglionic fibers ascending from the thoracic ganglia. All, with the exception of a small bundle of unmyelinated fibers, degenerate in an ascending direction and the degeneration stops in the superior cervical ganglion. The internal carotid nerves are not affected either as to their myelinated or unmyelinated constituents. The conclusion that the only synapses on the functional pathways through the superior cervical ganglion are located in that ganglion is well established. We may now ask what is the nature of the synapses which are to be found there.

Is there a mechanism within the ganglion for the general diffusion of impulses such as occurs in the central nervous system? As a result of the diffusion of impulses in the brain and spinal cord the

stimulation of a small sensory nerve may bring about reflex activity of the skeletal and involuntary musculature over the entire body. Are impulses disseminated in a similar way in the sympathetic ganglia? Langley ('00) maintains that a preganglionic fiber branches and becomes associated with several postganglionic neurones and that these taken together form a functionally isolated unit. That is to say, there is no general diffusion of impulses through the ganglion. This is beautifully illustrated by his experiments on the pupilodilator pathway.

As pointed out by Hoffmann ('04), the stimulation of a long ciliary nerve causes local dilation of the pupil, while stimulation of the white ramus of either the first or second thoracic nerve causes a general and symmetrical dilation. This might appear to be due to a spreading of the impulses within the superior cervical ganglion to all postganglionic pupilodilator neurones. This is not the case, however, as Langley ('04) has shown: 1) Because stimulation of a small number of postganglionic fibers as they leave the ganglion in any one of the four bundles that form the internal carotid nerve will also cause a symmetrical general dilation. Fibers from such a bundle undergoing rearrangement in the internal carotid plexus are distributed to all parts of the iris. It is therefore unnecessary to assume any spreading out of nerve impulses through diffusion in the ganglion. 2) Local dilation of the pupil can, on the other hand, be obtained by stimulating a few preganglionic fibers in one of the rootlets of the upper thoracic nerves. It is difficult to see how, on any theory of the cells being connected together to form a coördinating center, stimulation of a small number of preganglionic fibers could cause rather marked local dilation of the pupil. The spreading out of the impulses which does occur is due to the intermingling of the postganglionic fibers in the preterminal plexuses.

An even more striking case has been made out against the general diffusion of nerve impulses within sympathetic ganglia in the case of the coccygeal ganglion.

In all compound ganglia it is obvious that stimulation of certain of the preganglionic fibers running to the ganglia excites some only of the nerve cells, and no increase in the strength of the stimulus can cause

irradiation of nervous impulses to other cells of the ganglion. And the nerve cells which cannot then be brought into action may be nerve cells of the same class as the cells which are in a state of excitation. Of this we may give an example. In the cat, at times, when the arrangement of nerves is posterior, the fourth lumbar nerve causes erection of hairs on the tip of the tail; the nervous impulses pass through nerve cells in the coccygeal ganglion; other nerve cells in the coccygeal ganglia will, on stimulation cause erection of hairs in the greater part of the rest of the tail; but no stimulation of the fourth lumbar nerve will affect this region. Hence, pilomotor nerve cells, set in action by the fourth lumbar nerve, send no commissural fibers to the other pilomotor nerve cells of the coccygeal ganglion. (Langley, '00.)

It thus appears that there is no physiological evidence indicating that diffusion of nerve impulses occurs in the sympathetic ganglia and in certain cases, like those cited, there is positive evidence that diffusion does not occur. We shall now see that there is no histological evidence of any mechanism which could serve to bring about such diffusion.

We may picture such a diffusion mechanism in three ways. The first that suggests itself is a diffuse network formed by anastomosing branches of the preganglionic fibers. Such a network has been assumed by Michailow ('11), but without adequate evidence. In this respect his description of the intercellular plexus does not coincide with that given by Dogiel and Huber. Very clear pictures of the intercellular plexus are obtained in pyridine silver preparations, and these give no indication of anastomosing fibers or of a closed network. The histological evidence is therefore distinctly against the existence of this sort of mechanism for diffusion of nerve impulses.

In the second place, the purpose of diffusion might be served by purely intraganglionic neurones whose axons would branch repeatedly and end within the ganglion. So far as we have been able to find, no one has ever described an axon of a sympathetic ganglion cell as ending within the ganglion where it began. Wherever axons have been traced they have always been seen to leave the ganglion through one or other of its branches. The intercellular plexus of fine fibers, which Dogiel and Huber thought represented the ramifications of such axons, and which, if interrupted in this way, might serve as a mechanism for diffusing

nerve impulses through the ganglion, we have shown to be formed by the branching of the preganglionic fibers. In a paper which follows, Johnson presents conclusive evidence that commissural neurones do not exist in the ganglia of the sympathetic trunk of the frog.

Finally, diffusion of nerve impulses might occur through collaterals given off by the postganglionic axons before they left the ganglion.

That such collaterals exist has been shown by Dogiel, but we must conclude from his descriptions and figures that they do not occur on the majority of the axons. Michailow does not find them except on the axons of his cells of Type IX. He shows that they end in plates located in the connective tissue of the ganglia between the nerve cells or against the outside of the capsule of a nerve cell. This mode of termination does not speak for them as serving the function of transferring impulses from one neurone to another. In fact, they rather resemble certain collaterals from the axons of spinal ganglion cells which in all probability serve no such function.

The complete absence of fine branching axons in the superior cervical ganglion after degeneration of the preganglionic fibers is strong evidence against the existence of connections between the various cells of the ganglia. In such a ganglion the postganglionic axons can be seen to accumulate in bundles of parallel fibers and run as directly as possible toward the emerging nerves.

From all that has been said we may conclude that there is no physiological or histological evidence for the existence in the superior cervical ganglion of a mechanism for the general diffusion of nerve impulses. And the same conclusion would probably be equally valid for all the ganglia of the sympathetic trunk. We have already discussed the question of commissural fibers joining cells located in adjacent ganglia.

Are there any synapses between sensory and motor neurones within the superior cervical ganglion such as would be required by the conception of the ganglion as a center for visceral reflexes? So far as we have been able to learn, no one has ever described any reflex through this ganglion. According to Langley ('00 a),

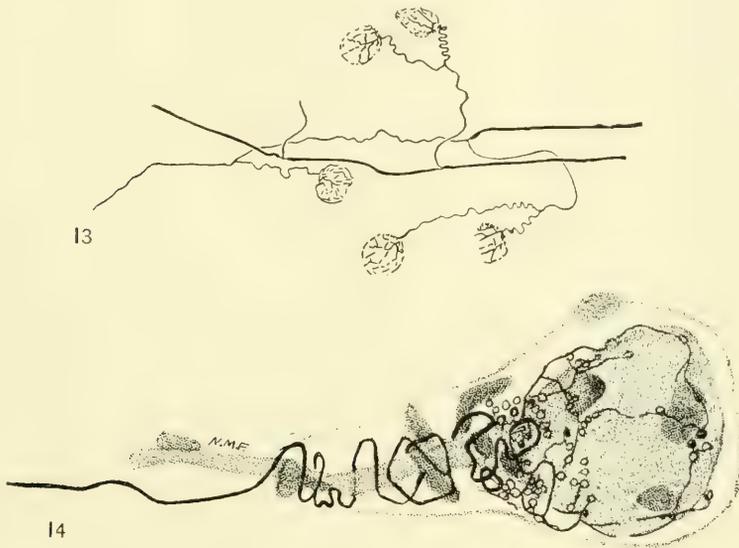
there are no sensory fibers in the cervical sympathetic trunk, since stimulation of this trunk produces no reflex effect through the spinal cord. Since no one has ever claimed that this ganglion contained sensory elements, it is not necessary to discuss this question in detail here. The question of the presence of sensory neurones in the sympathetic ganglia was discussed at some length in the section of this paper dealing with the dendrites. The negative evidence (the absence of fine branching axons in the ganglion after degeneration of the preganglionic fibers) which indicated the absence of connections between the sympathetic ganglion cells would also speak against the existence of sensory-motor synapses.

Synapses between pre- and postganglionic neurones are the only ones of which physiological experiments have given evidence. These are also the only ones that have been demonstrated histologically. The clearest demonstration has been given by Huber ('99) on the frog (fig. 13 and 14). In preparations stained with methylene blue he was able to trace the fibers of the white rami into the trunk ganglia and see them divide repeatedly. Some of these branches he was able to follow to their termination as subcapsular pericellular baskets. In a well stained ganglion it could be seen that the cell body of each neurone was enclosed in such a pericellular plexus. As a rule, the fibrillae of the plexus form a closed network, but now and then fibrillae were found ending free. Similar pericellular plexuses were observed by him in the trunk ganglia of mammals and here again the evidence pointed to their being the endings of fibers from the white rami. These pericellular plexuses have been seen by others, including Ehrlich ('96), Retzius ('89), Arnstein ('87), Aronson ('86), Sala ('93), Van Gehuchten ('92), v. Lenhossék ('94), Dogiel ('95), and Kölliker ('96).

Dogiel ('95) and Huber ('13) could not determine whether all or only a part of the cells of a sympathetic ganglion were surrounded by pericellular plexuses. I take these statements to refer to the mammalian ganglia since Huber ('99) has himself shown that all these cells are so surrounded in the frog. For a full account of this form of synapse the reader is referred to

Huber's three papers. It seems that the pyridine silver method usually does not stain these pericellular networks; only occasionally have we seen fragmentary impregnations of them. This is in keeping with the fact that the method does not readily yield pictures of nerve endings.

In addition to the pericellular endings thus described there are, we believe, synapses between preganglionic fibers and the dendrites of the cells in the superior cervical ganglion. This is true



Figs. 13 and 14 Preganglionic fibers and pericellular plexuses of the frog. Redrawn from Huber ('99). The preparations were stained with methylene blue. 13, preganglionic fibers, the branches of which form pericellular plexuses; 14, a sympathetic ganglion cell, unipolar, in connection with which a preganglionic fiber is terminating.

of the subcapsular dendrites in man as well as of the long extracapsular dendrites of man and the dog and cat. As was first shown by Cajal in the superior cervical ganglion of man, the subcapsular dendrites forming glomeruli and dendritic crowns are in close relation to fine, darkly staining fibers, which run among them in every direction. This is illustrated in figure 5 and 6. These fibers have the same appearance, caliber, and

staining reaction as the fine fibers of the intercellular plexus in the cat and dog, and they bear the same relation to these subcapsular dendrites that that plexus bears to the extracapsular dendrites. There is every reason to believe that these fibers, like those of the intercellular plexus, are the branches of preganglionic axons. There seems to be no essential difference between the intercellular plexus in man and that which surrounds the subcapsular dendrites except that of location. So far as we are able to judge from our preparations, the intercellular plexus is not so well developed nor so uniformly distributed in man as in the dog. In the cat and dog there are almost no subcapsular dendrites, and so far as we have been able to see the intercellular plexus does not extend beneath the capsule.

We have already given a somewhat extended account of this intercellular plexus and shown that it consists of the ramifications of preganglionic axons. Just what is the relation of the ramifications to the dendritic branches? In pyridine silver preparations the fibers do not seem to end on the dendrites, but rather to form an interlacing feltwork with them. It is probable, however, that here the actual terminations of the axonic ramifications are not stained. In methylene blue preparations Huber ('99) was able to trace some of the fine fibers of the pericellular plexus to their termination on neighboring dendrites.

It seems to be well established that one preganglionic fiber may activate several postganglionic neurones (Langley, '00 b). Histological evidence points to three ways in which this can be brought about: 1. The branching of preganglionic fibers, each branch ending in a pericellular basket about a different neurone. The best evidence of this has been given by Huber ('99). Figure 13 is a reproduction of one of his drawings of fibers from a white ramus entering a sympathetic ganglion of the frog. One of these fibers is associated with three pericellular plexuses. This mechanism for bringing several postganglionic neurones under the control of one preganglionic fiber is illustrated diagrammatically in figure 15, *b*.

2. The ending of dendrites of one cell in the neighborhood of another cell so as to come under the influence of the axonic ramifications in connection with that cell. This relationship is

illustrated diagrammatically in figure 15, *c*. The ending of dendrites of one cell in the immediate neighborhood of another cell has been observed by a considerable number of investigators. Such endings occur in a variety of different forms which can scarcely be accidental. A dendrite may end by forming a pericellular basket about another cell as seen in figure 8, *d*. Such formations have been seen by Cajal ('11), Dogiel ('95),

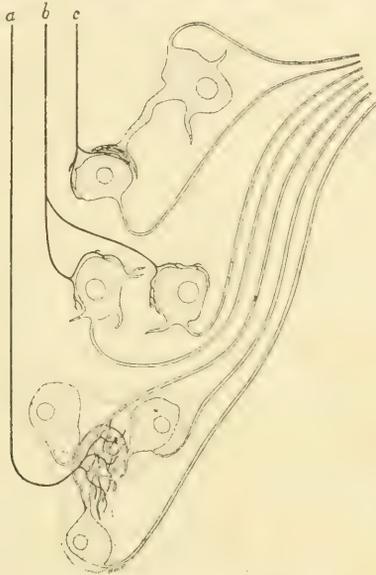


Fig. 15 Diagram illustrating three ways by which one preganglionic fiber may come into relation with two or more postganglionic neurones. *a*, preganglionic fibers ending in a tricellular glomerulus in connection with the dendrites of three neurones; *b*, a preganglionic fiber branching to form two pericellular plexuses; *c*, a preganglionic fiber ending in connection with the cell body of one neurone and the dendrite of another which is applied to the outer surface of the capsule of the first neurone.

Michailow ('11), and others. According to Dogiel, such dendritic baskets are always extracapsular. It is obvious that such formations cannot serve to transmit impulses from one sympathetic ganglion cell to another unless we are prepared to admit exceptions to the law of the dynamic polarity of neurones. But even then the capsule would be interposed between the nerve cell and the surrounding dendritic nest. So characteristic an

arrangement cannot be entirely accidental; and the most obvious functional significance of the dendritic nest would be that the two neurones are thereby in position to be activated by the same preganglionic fiber. This is now Cajal's interpretation of the pericellular dendritic baskets. Such baskets must not be confused with the basket-like appearances produced by dendrites winding their way between the cells without encircling them as has been done by Van Gehuchten and Sala. Functionally similar structures are the plate-like endings of dendrites outside the capsule of another cell as in Michailow's cells of Type III (fig. 8, *b*) and the smaller egg-shaped endings of the terminal branches of the dendrites of Michailow's Type IV cells which are also applied to the outer surface of the capsule of another cell (fig. 8, *c*). We believe that all of these formations are designed to place two neurones under the influence of the same preganglionic fiber as illustrated in figure 15, *c*.

3. Another arrangement of dendrites which seems designed to favor the simultaneous activation of two or more neurones by one preganglionic fiber is found in the bi-, tri-, and multicellular glomeruli in the human superior cervical ganglion. This is illustrated diagrammatically in figure 15, *a*. Such glomerulae, formed by the dendrites of two or more cells, are numerous in the human ganglion, and one is illustrated in figure 6. A single axon ramifying within such a glomerulus would be in position to activate each neurone contributing dendrites to the glomerulus.

SUMMARY AND CONCLUSIONS

Although attention is directed in this paper particularly to the cephalic end of the sympathetic trunk and the superior cervical ganglion, the comments drawn from the literature are for the most part applicable to the entire trunk.

A study of the literature based on the evidence obtained by the nicotine and degeneration methods shows that the cephalic end of the sympathetic trunk consists of preganglionic fibers arising in the upper segments of the spinal cord and terminating in the superior cervical ganglion, and that the cells located in this ganglion give rise to fibers which run to terminate in the glands and smooth muscle of the head.

In fact, the cephalic end of the sympathetic trunk consists almost exclusively of fine medullated fibers, most of which vary in size from 1.5μ to 3.5μ . These fibers degenerate in an ascending direction after section of the nerve. In pyridine silver preparations no unmyelinated fibers can be distinguished in the normal sympathetic trunk at this level except for some fine branches of distribution from the superior cervical ganglion which happen to be included for a short distance in the same sheath with that nerve. Our observations along with those of Langley show that the superior cervical and stellate ganglia are not connected by myelinated commissural fibers and that unmyelinated commissural fibers if present are very few in number. Physiological experiments conducted by Langley failed to show any evidence of commissural fibers joining these two ganglia. Physiological and histological evidence is also against the presence of afferent fibers in the cervical portion of the trunk.

The nervus caroticus internus in the cat contains, in addition to great numbers of unmyelinated fibers, a very considerable number of fine myelinated fibers, mostly from 1.5μ to 5.5μ in diameter. The fibers in this nerve do not degenerate after section of the sympathetic trunk in the neck; all or nearly all of them are postganglionic fibers with their cells located in the superior cervical ganglion.

The dendrites of the cells in the superior cervical ganglion are of two kinds, intracapsular and extracapsular. The intracapsular dendrites are rare in the sympathetic ganglia of mammals but abundant in the human superior ganglion. Here they give rise to the complicated subcapsular formations that have been designated as dendritic crowns and glomeruli. A glomerulus may be formed from the dendrites of a single cell or from those of two or more cells and is designated accordingly as an unicellular, bicellular, tricellular, or multicellular glomerulus.

The extracapsular dendrites are long branched processes which run in every direction among the ganglion cells. In pyridine silver preparations it is not possible to follow them to their true terminations. We have summarized Michailow's account of the termination of these dendrites in preparations stained with methylene blue and illustrated them in figure 8. The dendrites

of one cell may form baskets or other special endings about neighboring cells, but these dendritic endings seem to be always outside the capsule of the second cell and therefore could not transmit impulses to it.

Sensory neurones with long dendrites have been described in sympathetic ganglia by Dogiel, but a review of the literature on this point shows that his interpretation of these structures has received little support from the observations of others. It is also doubtful if the axons of cells in the sympathetic ganglia run to spinal ganglia to form baskets about the cells located there.

The axons of sympathetic ganglion cells may acquire myelin sheaths, but usually do not. A study of the literature would indicate that they usually run, without giving off collaterals, into one of the branches of distribution arising from the ganglion. Some run through a connecting nerve to another ganglion, but there is no evidence to show that they ever end there. It would seem more likely that these fibers merely run through this second ganglion to join the nerve to which they are distributed. Some postganglionic fibers give off collaterals either in the original ganglion or in a second ganglion through which they pass, but these collaterals have been shown by Michailow to have endings not well adapted for the transference of nerve impulses.

Between the cells is a rich plexus of fine axonic ramifications which is formed by the branching of the preganglionic fibers. This disappears when the preganglionic fibers degenerate. It is probable that many of the fibers of the intercellular plexus form synapses with the dendrites of the sympathetic ganglion cells.

In pyridine silver preparations of the superior cervical ganglion of the cat it is possible to trace the darkly stained preganglionic fibers from the sympathetic trunk and to see that they undergo repeated branching and take a large part in the formation of the intercellular plexus. The postganglionic fibers, which are more lightly stained, and for the most part devoid of branches, take only a minor part in the formation of this plexus, but become grouped into bundles of parallel fibers which run toward the branches of distribution of the ganglion.

There is no evidence for the existence of synapses, either commissural or sensory-motor, between the neurones located in the

ganglion and there appears to be no mechanism for a diffusion of incoming nerve impulses to all of the cells nor to all of the cells of a given function within the ganglion.

Evidence furnished by nicotine and degeneration experiments shows that all the synapses between the pre- and post-ganglionic neurones on the pathways through the superior cervical ganglion are located in that ganglion. There are no ascending postganglionic fibers in the cervical portion of the sympathetic trunk and no preganglionic fibers are continued through the superior cervical ganglion into the branches of distribution. The pre-postganglionic synapses seem to be of two kinds: 1) pericellular networks and 2) relations established between the dendrites and axons in the intercellular plexus. One preganglionic fiber activates several post-ganglionic neurones. The dendrites of the post-ganglionic neurones serve to increase the complexity of these relationships and may aid in bringing two or more neurones under the influence of a single axon as indicated in figure 15.

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ON THE NUMBER OF NERVE CELLS IN THE GANGLION CERVICALE SUPERIUS AND OF NERVE FIBERS IN THE CEPHALIC END OF THE TRUNCUS SYMPATHI- CUS IN THE CAT AND ON THE NUMERICAL RELA- TIONS OF PREGANGLIONIC AND POSTGANGLIONIC NEURONES

P. R. BILLINGSLEY AND S. W. RANSON

From the Anatomical Laboratory of the Northwestern University Medical School¹

It is well known that the preganglionic fibers of the white rami divide and terminate in connection with a number of sympathetic ganglion cells. But no attempt has as yet been made to secure data with regard to the number of nerve cells which may be activated by one preganglionic nerve fiber.

The drawing made by Huber ('99) of the preganglionic fibers in the frog shows one fiber with seven branches, four of which end in pericellular baskets. This would indicate that in the frog one preganglionic fiber might be associated with at least seven postganglionic neurones.

Langley ('03) has given us data regarding the number of ganglia which may receive nerve fibers from a given white ramus and the number which may receive branches from a given preganglionic fiber.

It must be noted that in the sympathetic system the preganglionic fibres of any given spinal-nerve have a more extensive connection with the peripheral ganglia than any single fibre in it has. As an example I may quote the probable arrangement of the pilomotor fibres of the first lumbar nerve. The nerve sends fibres to five ganglia, the separate fibres usually send branches to three ganglia only.

Gaskell ('86) has called attention in a forceful manner to the great increase in the number of fibers leaving the sympathetic ganglia by way of the gray rami and other branches of distribu-

¹ Contribution No. 55, February 15, 1918.

tion over those which enter the ganglia by way of the white rami and truncus sympathicus.

It is generally acknowledged, since the publication of Bidder and Volkmann's paper, that an increase of nerve fibres takes place at the various ganglia. The nature of such increase is easily seen by the mere inspection of the nerves which are in connection with such ganglia as the superior cervical; the number of non-medullated fibres which pass out of it to proceed peripherally along the internal and external carotid nerves and along the peripheral grey rami communicantes of the upper cervical and lower cranial nerves is immensely greater than all the fibres both medullated and non-medullated which pass to it from the central nervous system along the cervical splanchnic (cervical sympathetic) nerve. So too the masses of non-medullated fibres which leave the semi-lunar ganglia to be distributed to the stomach, liver, intestines, etc., are very much greater than all the fibres contained in the rami afferentes of these ganglia. It is only necessary to picture to one self the number of fine medullated nerves contained in the various nerve roots, in comparison with the number of non-medullated fibres which pass out of the various ganglia of the body, to see what a great increase of nerve fibres must have taken place in the course of the nerves between the central nervous system and the periphery. Doubtless such increase is partly to be accounted for by the direct division of non-medullated nerve fibres. Such division however takes place chiefly in connection with the passage of the nerve through a ganglion.

It is obvious from all this that the impulses carried by one preganglionic fiber must be passed on to several postganglionic neurones. But no observations are furnished which would enable us to estimate the number. It would add precision to our conception of the interrelation of these neurones if a fairly definite numerical ratio could be assigned.

The superior cervical ganglion offers a favorable field for the investigation of this question. As we have seen in the preceding paper, there is no reason to suppose that fibers enter it except those which ascend in the cervical trunk. Aside from a small peripheral bundle consisting chiefly of unmyelinated fibers, the truncus just caudal to the ganglion consists of ascending myelinated fibers. These vary in size from 1.5μ to 4.5μ , i.e., are typical preganglionic fibers. In some specimens there are also a few fibers as large as 6μ or 7μ which might be interpreted as being sensory. But in the nerve counted, the largest fiber measured 5μ and only eight other fibers approached this in size. In this

specimen the peripheral bundle of unmyelinated fibers formed a separate fascicle entirely outside of the perineurium of the trunk. The few myelinated fibers which this fascicle contained were descending from the ganglion and were not enumerated. In the absence of large myelinated fibers which might possibly be interpreted as being sensory, we believe that all of the fibers in the cephalic end of the trunk proper are ascending preganglionic fibers (p. 317). So far as we can determine these fibers are not mixed with any unmyelinated axons.

From these considerations it is evident that an enumeration of the myelinated fibers in the sympathetic trunk just below the superior cervical ganglion should give the number of preganglionic fibers entering the ganglion. We have also ascertained the number of cells in that ganglion and the ratio between these cells and the preganglionic fibers.

TECHNIQUE

The cervical portion of the sympathetic trunk was exposed for its entire length and fixed in osmic acid. During fixation it was held taut by stretching it over a glass cover-slip with fine silk threads tied at either end, the upper enclosing the branches of the internal carotid nerve well above the superior cervical ganglion. All the other branches of the ganglion were cut off close to their origin. The tissue was blocked in paraffine and serial sections prepared, 10μ in thickness, from the superior to the inferior pole of the ganglion, and sections 7μ in thickness were made through the trunk.

The number of fibers in the trunk was determined as follows. A ruled ocular, No. 10, was used, the ruling enclosing an area of 1 sq. cm. subdivided into one hundred forty-four smaller squares. The lines of the ocular were made parallel to the anteroposterior and lateral lines of movement of a mechanical stage, the latter being at right angles to each other. A 7a objective was used. Beginning at the left side of a section, the fibers within the area of the ruled square were counted. Then, using only the anteroposterior movement of the stage, the section was moved the full

width of the ruled square, using some well-isolated fiber as a landmark. This was continued until a column of fibers was counted extending anteroposteriorly clear through the section. Then by means of the lateral movement of the stage, the section was moved the full width of the ruled square and a second column of fibers counted, and so on until the field was covered.

The number of cells in the ganglion was determined by counting the nucleoli in every fourth section and multiplying the result by four. The method of using the square ruled ocular and mechanical stage was the same as in counting the fibers. Here especial care had to be taken to avoid overlooking small nucleoli which fell behind the ruled lines as well as those which might be out of focus.

There are several possible sources of error in counting the cells by this method. Since only every fourth section was counted and the result multiplied by four to find the total number of cells, an inaccuracy is introduced, which, however, is made negligible by the large number of sections counted. A second source of error may be found in the fact that some few cells contain two nucleoli and the knife may pass between them and they will then lie in adjacent sections and may each be counted as representing a cell. This possibility would represent an error so small as to be negligible. A third and real source of error is found in the fact that a certain percentage of all nucleoli are cut and the parts come to lie in adjacent sections. Parts of nucleoli would then be counted as whole ones.

Measurements showed that the diameter of the average nucleolus is 2.25μ , and since the sections of the ganglion were 10μ in thickness we must assume that $22\frac{1}{2}$ per cent of all nucleoli were cut at some point in their diameters. If the knife passes through the nucleolus at any point in the middle one-half of its diameter, each of the resulting parts will probably be thick enough to permit of its being seen and counted as if it were an entire nucleolus. If the cut passes through either of the outer one-fourths the major part will be counted but the minor part will be so thin as to be overlooked. We may therefore assume that one-half of the $22\frac{1}{2}$ per cent of cut nucleoli will be so cut as to be seen in two sections

and one-half will be so cut as to be recognizable in one section only. For example, if there actually were four hundred nucleoli in a ganglion, $77\frac{1}{2}$ per cent of these, or 310, would lie wholly in the sections and be correctly counted. Of the remaining 90 nucleoli which are cut, 45 will be counted twice, and 45 will be counted once, so that the total number of nucleoli will seem to be 445. This source of error, amounting to approximately 10 per cent of the number obtained by enumeration, was not taken into account in the enumerations made by Ranson ('06) and others on the cells of the spinal ganglia. It seems probable to us that the results of earlier enumerations are therefore somewhat too high.

RESULTS

The total number of fibers in the sympathetic trunk just below the ganglion was 3851. In the 138 sections of the ganglion which were searched for nucleoli 34,334 of them were found. Since this was done in every fourth section the total for all the sections would be approximately 137,336. As already stated, we believe that some nucleoli were cut in such a way as to be recognizable in two succeeding sections, and for this error a correction of 10 per cent must be made. This would give us 123,603 as the number of cells actually present in the ganglion.

In this particular specimen, then, there were 3851 myelinated preganglionic fibers entering the superior cervical ganglion which contained approximately 123,603 cells. The ratio of fibers to cells was approximately 1 to 32.

DISCUSSION

Does this ratio of 1 to 32 represent the proportion of preganglionic to postganglionic neurones? This question raises two others: Are all the neurones in the ganglion postganglionic, i.e., cells with axons which run from the ganglion to the tissue innervated, and to what extent have the preganglionic fibers given off collaterals to postganglionic neurones in ganglia located farther caudalward in the truncus sympathicus? The first question has been discussed in detail on pages 345-354 of this issue.

The evidence is against the existence of any purely intraganglionic or commissural neurones; and there is no evidence of the existence of any sensory neurones in this ganglion. No doubt the high ratio of fibers to cells will appear to some as an evidence of intraganglionic commissural neurones. But a careful reading of the paragraph from Gaskell quoted on page 360 should do away with any feeling that the ratio of preganglionic to postganglionic neurones here given is unreasonably high.

To one who is familiar with the intricate feltwork produced by the fine branches of the preganglionic fibers which we have described under the name of intercellular plexus (p. 337) it does not seem unreasonable that one preganglionic fiber should form direct synaptic connections with thirty-two postganglionic neurones. However, we do not wish to urge this point and must admit that, although no satisfactory evidence of their existence has ever been presented and although we have very strong evidence against their presence in certain ganglia, it is nevertheless possible that there may be some intraganglionic commissural neurones in sympathetic ganglia. If there were any in the superior cervical ganglion the ratio here stated would be by that much reduced. With regard to the second question we cannot say with certainty to what extent the fibers ascending in the cervical sympathetic trunk may have given off collaterals in the middle cervical and stellate ganglia. We possess, however, information which makes it possible to form an intelligent opinion on the question.

The middle cervical ganglion is small and inconstant. The stellate ganglion, on the other hand, is large and contains many cells. All the preganglionic fibers running to the superior cervical ganglion must pass by or through it. To what extent do they give off collaterals to its cells? Some information on this subject may be gained by a study of the results obtained by Langley (192) from stimulating the upper thoracic nerves of the cat within the spinal canal. So far as the fibers running to the superior cervical ganglion are concerned, he has shown that those for the dilation of the pupil arise from the first three thoracic nerves, those for the nictitating membrane, submaxillary sali-

vary gland, and blood-vessels of the head from the first five, those for the hairs of the face and neck from the first seven. The fibers to the middle cervical and stellate ganglia for the acceleration of the heart arise from the second to the fifth thoracic nerves, inclusive. The origin of the fibers terminating in the stellate ganglion has been determined as follows: pilomotor fibers from the fourth to the ninth thoracic nerve, secretory and vasomotor fibers as determined by reactions of the fore-foot from the fourth to the ninth thoracic nerves.

Since there is no cardiac branch from the superior cervical ganglion in the cat it is unlikely that the cardiac accelerator fibers from the second to the fifth thoracic nerves send any branches beyond the middle cervical ganglion. With the exception of the accelerator fibers, those from the first three cervical nerves appear to run exclusively to the superior cervical ganglion. So far as we can tell, then, there are no fibers running from the first three cervical nerves which give off collaterals in the stellate or the middle cervical ganglion and pass on to end in the superior cervical ganglion.

But the fourth and fifth thoracic nerves send many fibers to both the superior cervical and stellate ganglia while the sixth and seventh send a few to the superior cervical ganglion. To what extent single fibers from these nerves may be connected with cells in both of these ganglia is uncertain. But there are certain points worth considering in this connection. Most of the functions controlled through the superior cervical ganglion are highly specialized, such as dilation of the pupil, movement of the nictitating membrane, salivation and lacrimation; and it is not probable that preganglionic fibers controlling these functions give off collaterals in a ganglion of quite different functions like the stellate. On the other hand, it is quite possible that vasomotor preganglionic fibers from the fourth and fifth, and pilomotor fibers from the fourth to the ninth thoracic nerve send branches to both the stellate and superior cervical ganglia.

The inference to be drawn from this discussion is that while a majority of the fibers ascending to the superior cervical ganglion in the truncus sympathicus pass by the other ganglia in their

path without giving off collaterals, a certain unknown percentage of them may possibly give off such collaterals. Since in our enumeration the fibers were counted just below the superior cervical ganglion the possibility that collaterals had been given off from some of these fibers at a lower level makes it not unlikely that the ratio of postganglionic to preganglionic neurones as determined in this paper is somewhat too low.

SUMMARY

Careful enumerations show that the superior cervical ganglion in the cat contains some 123,603 nerve cells and that the truncus sympathicus near the ganglion contains 3851 ascending preganglionic myelinated fibers. The ratio between these fibers and the cells in the ganglion is 1 to 32. We believe that this ratio may be taken as expressing the approximate numerical relations between preganglionic and postganglionic elements for this ganglion.

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BRANCHES OF THE GANGLION CERVICALE SUPERIUS

P. R. BILLINGSLEY AND S. W. RANSON

From the Anatomical Laboratory of the Northwestern University Medical School¹

ONE FIGURE

The superior cervical ganglion, which forms the cephalic end of the sympathetic trunk, has a greater variety of connections than any other ganglion in the body. Its branches run to three cranial nerves, three spinal nerves, several arteries, the carotid glomus, the thyroid, salivary, and lacrimal glands, smooth muscle of specialized function like that of the eye, the glands and blood-vessels of the mucous membrane of the head, the glands and blood-vessels of the skin, and the smooth muscle of the hair follicles. More information concerning the branches running to these structures is needed for a proper understanding of the ganglion. It is possible that fibers ascending through the sympathetic trunk might leave the ganglion in one of these branches. The connections with the cervical and cranial nerves bring it within the bounds of possibility that fibers from one of these nerves might be running to the ganglion. Neither of these propositions has much probability in its favor, yet they should be more carefully ruled out than has as yet been done. Our chief interest, however, concerns the myelination of the postganglionic fibers arising from the ganglion.

Throughout the sympathetic nervous system a varying number of postganglionic fibers acquire myelin sheaths. One might with reason assume that there is some functional difference between those which are myelinated and those which are not. On that assumption some uniformity in the distribution of the two kinds would be expected. The numerous and functionally

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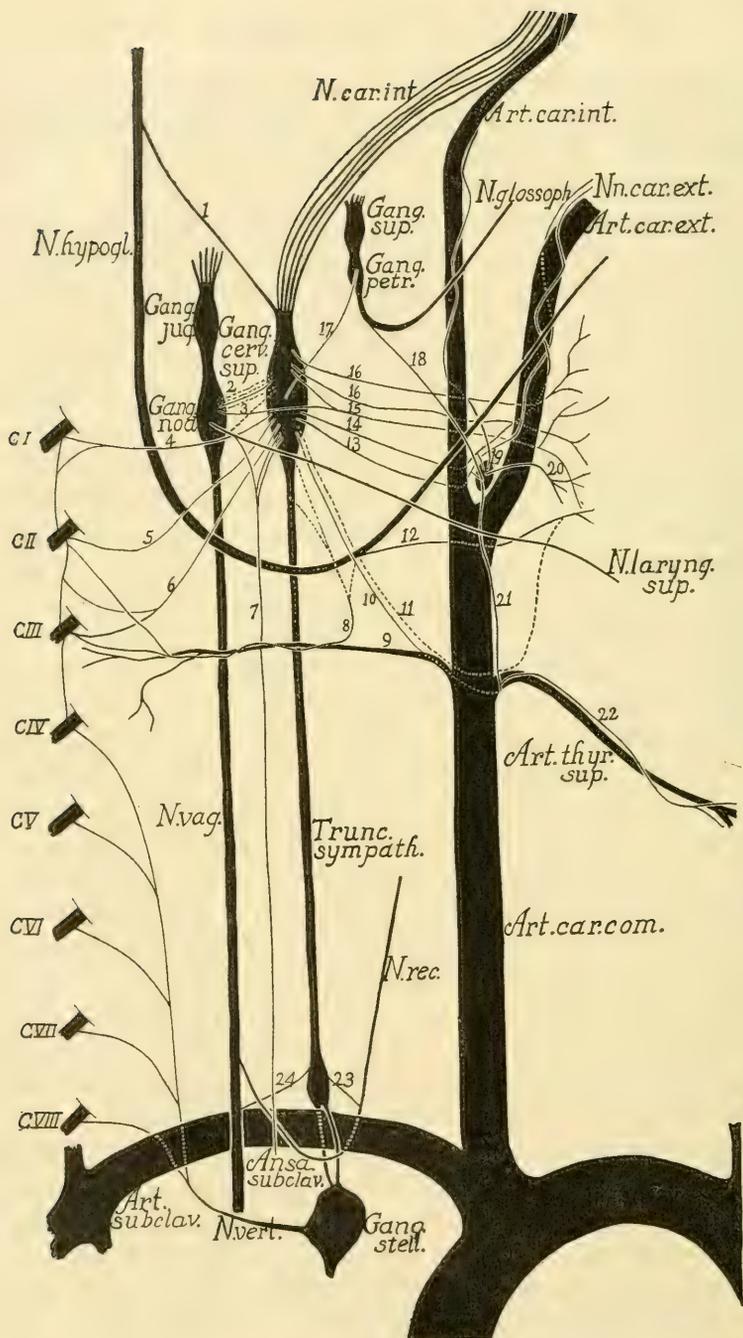
diverse branches of the superior cervical ganglion offer an unusual opportunity for determining whether or not myelination is characteristic of any particular functional group of these fibers. A study of these nerves in several cats also furnishes data as to how constant the degree of myelination is in any particular nerve.

Since the cat is largely used for experimental work on this part of the nervous system, it seems desirable to have more accurate data than has as yet been published concerning the gross anatomy and topography of these branches in that animal.

In a considerable number of cats the nerves in question were dissected out, their topographical relations noted, and a stretch of each fixed in osmic acid. The cats were anesthetized and bled by cutting the abdominal aorta, to render the field of dissection free of blood. The dissection was done with the aid of binocular lenses of $\times 2$ magnification. Without such magnification many of the smallest branches would undoubtedly have been overlooked. Dissection was further aided by fine threads tied to the vagus, sympathetic, and other nerve trunks, and to the carotid arteries. By attaching the threads to iron standards these structures could be pulled apart at any desired angle and the exposure of the minute branches of the ganglion rendered more easy. The field was kept moistened with normal salt solution throughout. Sections of each nerve were studied and an enumeration made of its myelinated fibers. It was also determined what proportion of the fibers fell into each of three dimensional groups. In the case of the branches to the superior thyroid artery and the cervical nerves the fibers were grouped into the three following sizes: 1.5 to 3.3μ , 3.3 to 6.6μ , $6.6\mu +$. In the other nerves another grouping was used, namely, 1.5 to 3.3μ , 3.3 to 4.5μ , $4.5\mu +$. Where the number of fibers was not large the fibers falling into each group were counted separately with the aid of an ocular micrometer. Where the number was large, as in the internal carotid nerve, all the myelinated fibers were counted together with the aid of an ocular ruled in squares. Then the micrometer eye-piece was placed in the microscope and the fibers which lay under the micrometer lines were counted separately according to size. The field was then shifted and the

process repeated until a total of one hundred fibers was counted. From these data the proportion of fibers of the three sizes was determined. An oil-immersion objective was used throughout in measuring the fibers.

In order to determine the relative richness in myelinated fibers, i.e., the proportion of the myelinated to the unmyelinated, the area of the section was determined in each case by projecting its outline with the aid of the camera lucida onto millimeter paper and determining the number of square millimeters which it covered. Knowing the magnification, it was easy to determine the actual area of the nerve in cross-section. This is expressed in square millimeters in the first column of each table. The second column gives the total number of myelinated fibers in the nerve, and the third shows the number of myelinated fibers per square millimeter. Since none of the nerves had an area as large as 1 sq. mm., the figures in the third column are greater than those in column 2. Since the greater part of the area is filled with unmyelinated fibers, this ratio (myelinated fibers into area) gives a rough method of comparing the number of myelinated and unmyelinated fibers in the different nerves. Considerable error is necessarily introduced into the determination of the area of the cross-section of a nerve by two factors, unequal shrinkage during fixation and unequal spreading of the sections on the slide. But these factors can account for only a small part of the actual variation of a given nerve in different cats as shown in the tables. Where a nerve was presented by two or more separate fascicles their areas were added together and the sum taken as the area of the nerve. It is probable that in some cases fascicles belonging to a nerve were lost during dissection, and if so, this would help to account for a part of the variation in size of the nerves in different cats. It may be also that there is some individual variation in the course taken by the postganglionic fibers or in their number. This variation in size is of interest and may be of significance, but except in so far as it is due to shrinkage or spreading, does not affect the question with which we are here primarily concerned, namely, the number of myelinated fibers per square millimeter of the cross-section of the nerve.



BRANCHES TO THE CERVICAL NERVES

In accordance with the observations of Langley ('93), the superior cervical ganglion was found to send branches to the first three cervical nerves only. There was no constant arrangement in the manner of their distribution. A maximum number of branches is three. They are seen to arise from the lower pole of the ganglion at the lateral side, and are indicated in figure 1 by numerals 4, 5, and 6. Their distribution is effected in several ways, directly with the main trunk of the cervical nerve; to the communicating loops between the latter, or, especially when there are less than three branches, they may divide, and connect with several main trunks, with both communicating loops, or with a main trunk and a loop. They are directed ventrally across the nodose ganglion of the vagus to their terminations.

A fairly constant branch (8) comes from the medial side of the lower pole, or from the branch to the superior thyroid artery, or from the main sympathetic trunk just below the ganglion. It is continued downward a short distance along the common carotid artery to the level of the origin of the superior thyroid artery (which arises from the common carotid in the cat) and a small unnamed artery which turns laterally to the muscles on the side of the neck. It runs along this latter artery and communicates with either or both of the second and third cervical nerves.

Fig. 1 A diagram of the cervical portion of the sympathetic trunk and of the branches of the superior cervical ganglion of the cat. The middle cervical ganglion (23) has been called the inferior by physiologists; but since it is located at the upper end of the subclavian ansa, it is more like the middle ganglion in man. The inferior cervical ganglion is fused with the stellate. 1, branch to the hypoglossal nerve. 2, 3, branches to the vagus nerve. 4, 5, 6, 8, gray rami. 9, small branch of the common carotid artery. 10, 22, branches to the superior thyroid artery. 11, 12, anastomosis with a branch of the hypoglossal nerve. 13, 14, branches to the external carotid artery. 15, 16, 20, branches to the pharynx. 17, branch to the glossopharyngeal nerve. 18, branch from the glossopharyngeal nerve to the carotid glomus. 19, carotid glomus. 20, branch from carotid glomus to the pharynx. 21, perithyroid ansa. 22, branch to the superior thyroid artery. 23, middle cervical ganglion and branch to the recurrent nerve. 24, branch from the middle cervical ganglion to the vagus nerve.

When arising from the ganglion or from the sympathetic trunk, it follows very closely the course of the branch to the superior thyroid artery as far as the origin of that artery, and then turns laterally to end as stated above. It is undoubtedly identical with the branch which Langley says constantly arises as one of the two terminal divisions of a nerve from the lower pole which runs downward along the truncus sympathicus and common carotid artery, the other terminal division being directed along the superior thyroid artery (see branch to superior thyroid artery).

As table 1 shows, the branches from the superior cervical ganglion running to the cervical nerves contain relatively few myelinated fibers. Some of these contained none, and for such branches the area was not computed. In no case did a branch going entirely or in part to the third cervical nerve contain any myelinated fibers, but in view of the wide variations in the number of such fibers contained in the other branches it is doubtful if this is of any significance. The largest number, 44, was found in the branch to the first cervical nerve in Cat IV. The number per square millimeter in this branch varied from 7447 to 251 in the several cats. A study of the table makes it apparent that there is no regularity in the distribution of the myelinated fibers nor in the relative proportion of myelinated and unmyelinated fibers. If any particular functional group were myelinated one would expect more regularity both in the relative and absolute number of these fibers than is apparent in the table. The great majority of these fibers did not exceed 3.3μ in diameter. In some of the branches larger fibers were present, and in one case 50 per cent had a diameter of 6.6μ or greater. Are these larger fibers of the same character as the smaller ones, or are we dealing here with an occasional admixture of fibers of another category? These larger fibers, for example, might be sensory and be directed toward the superior cervical ganglion. Are the small myelinated fibers preganglionic and coming from the cervical nerves, or postganglionic and taking their origin in the superior cervical ganglion? These questions can best be discussed after the other branches from the ganglion have been studied. The table is instructive, however, in showing

TABLE 1

Branches to the cervical nerves

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS		
				1.5 to 3.3 μ	3.3 to 6.6 μ	6.6 μ plus
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
To nerve 1:						
I	0.0079	2	253.57	50		50
II	0.0041	7	1678.25	43	57	
III	0.0046	11	2888.75	45	55	
IV	0.0053	40	7447.17	97.5		2.5
V	0.0021	9	4214.00	100		
VI	0.0039	1	251.49	100		
VII	0.0061	5	757.56	100		
To nerve 2:						
II	0.0076	3	431.81	67	33	
IV		0				
VI	0.0029	1	339.32	100		
VII	0.0043	14	3246.25	100		
To nerve 3						
II	0					
To nerves 2 and 3:						
VIII	0					
X	0					
To loop between nerves 1 and 2:						
VI	0.0049	15	3111.5	81	12.5	6.5
VIII	0.0035	9	2572.5	100		
X						
To loop between nerves 2 and 3:						
VIII		0				

the complete lack of regularity in the distribution of the myelinated fibers in the branches to the first three cervical nerves.

BRANCHES TO THE VAGUS

A constant communication is found with the nodose ganglion of the vagus (2) or with the superior laryngeal branch of the vagus (3) just after it has left the ganglion. The most frequent arrangement is found in a very small and short twig which passes laterally from the middle part or from the superior pole of the superior cervical ganglion to the nodose ganglion. In

TABLE 2
Branch to the vagus nerve

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS		
				1.5 to 3.3 μ	3.3 to 4.5 μ	4.5 to 6.6 μ
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
I	0.0029	18	5939.25	67	28	5
II	0.00027	11	39604.25	100		
III	0.0019	1	510.45	100		
IV	0.0018	0				
V	0.0021	97	45547.75	100		
VI	0.0018	0				
IX	00068	0				

one instance as many as four of these twigs were found. In all other cases there was only one.

In two cases there was no branch to the nodose ganglion, but instead a short branch was given off to the superior laryngeal branch of the vagus just after it had left the ganglion, and seemed in these cases to replace the usual branch.

In table 2 we see that the area of the cross-section of the branch or branches of communication between the superior cervical ganglion and the vagus nerve was very much less in Cats II and IX than in the others. In these cases it is probable that an additional communicating branch was overlooked when the dissection was made. Irrespective of this variation in size, there was a great variation in the number of myelinated fibers; one nerve contained ninety-seven of them and another nerve of about the same size contained none. There was an equally great variation in the number per square millimeter. In most cases all of the fibers measured 1.5 to 3.3 μ , but in one nerve there were some fibers between 3.3 and 6.6 μ . A comparison of tables 1 and 2 shows no essential difference between the myelinated fiber content of the branches to the cervical nerves and that to the vagus.

The depressor nerve (7) is sometimes a branch of the superior laryngeal nerve. It follows the sympathetic trunk and vagus nerve through the neck into the thorax. Not uncommonly the fibers of this nerve run to the superior cervical ganglion and leave

TABLE 3
Branch to the hypoglossal nerve

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS			
				1.3 to 3.3 μ	3.3 to 4.5 μ	4.5 to 6.6 μ	6.6 to 7.5 μ
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
IV	0.0020	6	3123.75		100		
VII	0.0019	48	24696.0	86	7	7	
VII	0.0049	6	1108.85	50		50	
VIII	0.0029	6	1984.5	50	50		
IX	0.0025	22	8734.25	95	5		
X	0.0068	20	2964.5	40	25	15	15

it again as a branch from its lower pole. This nerve contains a large number of medullated fibers which are for the most part of medium size. When it comes from the superior laryngeal nerve it may receive a branch from the superior cervical ganglion consisting chiefly of unmyelinated fibers.

BRANCHES TO THE HYPOGLOSSAL

A constant branch (1) is found coming from the upper pole, and is the most lateral of the group of basal bundles, the remainder of which are continued along as the internal carotid plexus. It runs upward toward the base of the skull, and is found to communicate with the twelfth nerve within its bony canal.

In one instance (11) a small branch was found to come off from the medial part of the lower pole beside the usual branch to the superior thyroid artery. It was continued downward with that nerve to the thyroid artery, along which it coursed for a short distance, and then ran slightly upward to communicate with a branch of the twelfth nerve.

A glance at table 3 will show the variation in the myelinated fiber content which we have already noted in other nerves. The actual number found varies from six to forty-eight, and there is an even greater variation in the number per square millimeter. The great majority of the fibers did not exceed 4.5μ in diameter, but in certain specimens larger fibers were also found. In one instance 15 per cent measured more than 6.6μ , seven of these fibers having a diameter of 7.5μ .

TABLE 4
Branch to the glossopharyngeal nerve

CAT	AREA IN SQUARE MILLI- METERS	NUMBER OF FIBERS	FIBES PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS	
				1.5 to 3.3 μ	3.3 to 4.5 μ
				<i>per cent</i>	<i>per cent</i>
II	0.0033	28	8244.25	93	7
IV	0.0621	655	10547.25	98	2
VI	0.0086	85	9934.75	94	6
X	0.0043	26	6000.5	84.5	15.5

BRANCH TO THE GLOSSOPHARYNGEAL NERVE

Although it is probable that a branch to the glossopharyngeal nerve is constantly present, it was identified with certainty in only a few instances. It comes from about the middle of the anterior surface of the ganglion and runs directly upward with the branches to the internal carotid and hypoglossal nerve (17). It joins the petrous ganglion of the glossopharyngeal nerve. This ganglion is hard to locate in the gross specimen, but was identified by microscopic examination of that part of the nerve with which the branch communicated.

Table 4 shows that the relative proportion of myelinated fibers found in four specimens of this branch was somewhat more constant than in the case of the preceding nerves studied. These fibers varied from 6,000 to 10,547 per square millimeter, numbers which are well within the range of variation found in the other nerves. The great majority of these fibers did not exceed 3.3 μ , and none measured more than 4.5 μ .

PHARYNGEAL BRANCHES

These are so small as to be frequently lost in dissection. The commonest arrangement is to find minute branches coming from the medial side near the upper pole which run medially over the carotid artery to the pharynx (16). They are usually paralleled by the pharyngeal branch of the vagus, and a fusion between the two may be noted (15). In addition to this there have been found minute branches from the plexiform arrangement at the

TABLE 5
Pharyngeal branches

CAT	AREA IN SQUARE MILLI- METERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETERS	DIAMETERS OF MYELINATED FIBERS	
				1.5 to 3.3 μ	3.3 to 4.5 μ
				<i>per cent</i>	<i>per cent</i>
IV	0.0044	80	18230.25	100	
V	0.002	25	12446.0	96	4
VIII	0.0031	4	1274.0	100	

bifurcation of the carotid artery (20), where the external carotid plexus has its origin.

These branches contain about the same proportion of myelinated fibers as the other branches of the superior cervical ganglion already studied. These varied from four to eighty in actual number and from 1,274 to 18,230 per square millimeter. Practically all of the fibers had a diameter which did not exceed 3.3 μ . and in one case 80 per cent of them measured less than 2 μ .

BRANCH TO SUPERIOR THYROID ARTERY

A constant branch is to be found coming off from the lower one-third of the ganglion on the medial side (10 and 22). It is continued downward along the sympathetic trunk and common carotid artery to the level of the superior thyroid artery, springing from the common carotid. Here it may give off a lateral branch (8) which courses along a small unnamed arterial twig to the second and third cervical nerve. This is the arrangement noted by Langley ('93) and considered under the description of the branches to the cervical nerves.

The main part of the nerve can be traced along the superior thyroid artery to the upper pole of the thyroid gland. It was thought that in a few instances a twig (21) could be followed upward along the common carotid artery after curving around the superior thyroid. If this is true, it would suggest that this is the perithyroid ansa described by Garnier and Villemin ('10, p. 405). They do not describe their ansa in the cat, but it is present in the rabbit and the dog. It is said to give off branches along the superior thyroid artery and the superficial or ascending

TABLE 6
Branch to the superior thyroid artery

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS		
				1.5 to 3.3 μ	3.3 to 6.6 μ	6.6 μ plus
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
VI	0.0044	28	6238.25	78.5	21.5	
VII	0.0128	45	3503.5	84.5	15.5	
VIII	0.004	67	16709.0	100.0		
IX	0.0069	42	6076.0	95.0	2.5	2.5
X	0.0059	14	2303.0	28.5	50.0	21.5

branch terminates in the plexuses about the lingual and facial arteries.

On the whole, the myelinated fibers in the branch to the superior thyroid artery do not differ materially from those in the other nerves studied. The number per square millimeter shows great variation and the majority of the fibers do not exceed 3.3μ in diameter. But larger fibers are also found, and in one case 21 per cent measured more than 6.6μ .

BRANCHES TO THE EXTERNAL CAROTID ARTERY (NN. CAROTICI EXTERNI)

In all but two cases the external carotid plexus was seen to be formed by two large branches from about the middle of the medial side of the ganglion (13 and 14), which ran upward and slightly medialward to the bifurcation of the common carotid artery. These branches commonly pass medial to the internal carotid artery, but in one case they passed to either side of the artery and then joined. At the bifurcation of the common carotid they communicate by small twigs with the carotid body and then at once form a rich plexus of fibers which is spread out, upon the external carotid artery. At the point of communication with the carotid body several minute twigs can be traced to the region of the pharynx.

In two cats, Nos. VIII and X, only one branch was found, in the others the two branches were treated as one in making up table 7. The area given in that table is the sum of their areas,

TABLE 7
Branches to the external carotid artery

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS		
				1.5 to 3.3 μ	3.3 to 4.5 μ	4.5 μ plus
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
III	0.0297	168	5656	83	13.5	3.5
V	0.0442	56	1273	91	6.5	2.5
VII	0.0296	87	2949	85.5	14.5	
VIII	0.015	21	1433	100		
IX	0.0224	111	4937	88.5	11.5	
X	0.0153	298	19428	87	10	3

and the number of fibers is the sum of their fibers. The table shows that in relative number and size of their myelinated fiber content these branches do not differ from the others already studied. Here again we see the now familiar variation in the number of fibers per square millimeter. Very few fibers exceed 4.5 μ in diameter.

BRANCHES TO THE INTERNAL CAROTID ARTERY (N. CAROTICUS INTERNUS)

From the upper end of the ganglion spring some four or five large branches which are continued directly upward and enter the skull with the internal carotid artery. These taken together constitute what is known as the internal carotid nerve. There does not seem to be any constant number or arrangement of these bundles and we were unable to verify the scheme of construction outlined by Langley ('04). We have never found more than five branches.

In each cat the areas of all the bundles belonging to this nerve were added together and the sum given in table 8. In the same way the number of myelinated fibers given there is the sum of that found in the individual bundles. The table shows that the number of myelinated fibers is both absolutely and relatively higher in this than in the other nerves studied. The lowest ratio found was 9,934 per square millimeter and the highest 17,774. While high ratios were found in individual specimens of other

TABLE 8
Branches to the internal carotid artery

CAT	AREA IN SQUARE MILLIMETERS	NUMBER OF FIBERS	FIBERS PER SQUARE MILLIMETER	DIAMETERS OF MYELINATED FIBERS		
				1.5 to 3.3 μ	3.3 to 4.5 μ	4.5 μ plus
				<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
III	0.1173	1346	11466	68	32	
VI	0.1038	1845	17774	86	14	
VIII	0.1642	2311	14075	68	32	
IX	0.3149	3933	12482	68	32	
X	0.1751	1741	9934	54	45.5	0.5

nerves, none of these showed the consistently high ratio of the internal carotid nerve. All of the fibers were under 4.5 μ , except in one specimen, not included in the table, in which 32 per cent of the fibers ranged from 4.5 to 9 μ in diameter.

DISCUSSION

A comparison of the tables which have been given in this paper will make it plain that the myelinated fiber content of the various branches of the superior cervical ganglion is in no way characteristic of the individual nerves. All of these branches are characterized by great variation in the absolute and relative number of myelinated fibers found in different specimens. It is true that the branches to the cervical nerves show consistently a relatively low ratio of fibers to area, and the internal carotid nerve shows consistently a rather high ratio, but we are not sure that even this represents a significant difference. It would seem, however, that the relatively small number of myelinated fibers in the branches going to the cervical nerves might be characteristic of these branches.

How are we to interpret the myelinated fibers found in the branches of the superior cervical ganglion? Are they preganglionic or postganglionic efferent fibers or are some afferent? Evidence that postganglionic fibers may acquire a myelin sheath has been presented in other papers of this series (pp. 321-323 of this issue). The myelinated fiber content of the gray rami of the other spinal nerves is similar to that of the rami of the

first three cervical nerves. On page 419 we will consider the structure of the gray rami and the character of the myelinated fibers they contain. A majority of them are postganglionic. Sometimes, but not commonly, a few preganglionic fibers, passing to the sympathetic trunk by white rami, leave it again by gray rami to end among small groups of cells lying in these rami. There are also a few afferent medullated fibers in the gray rami. Most of these enter the trunk through white rami and run out again through the gray. But it may be that a few, especially the larger ones, run to the sympathetic trunk by the gray rami. These statements are based on Langley's ('96) experiments in which by a variety of experimental lesions he caused the degeneration of different groups of fibers and in this way determined the origin of the myelinated fibers in these rami.

There is no reason for supposing that the myelinated fibers in the other branches of the superior cervical ganglion differ from those in the gray rami. The majority are certainly postganglionic fibers. After section of the sympathetic trunk in the neck and complete degeneration of all the preganglionic fibers ascending to the superior cervical ganglion there is no degeneration of the myelinated fibers in the internal carotid nerve. Hence no preganglionic fibers go through the ganglion into this nerve (p. 321). The great variation in the proportion of myelinated fibers in different specimens of the same branch of the ganglion can only be understood on the assumption that the postganglionic fibers occasionally acquire myelin sheaths, but that there is no regularity in this. No special functional group of these fibers acquires such a sheath regularly or exclusively. The way in which the myelin sheaths are distributed seems to be entirely accidental.

Kölliker ('94) was of the opinion that some functional groups of postganglionic fibers were better myelinated than others; for example, the pilomotor fibers of the cat were supposed to be covered throughout by myelin sheaths, while the fibers to the intestine, liver, and spleen soon lost their sheaths. If the pilomotor fibers were myelinated, consistently, and in any considerable number, we should find a different picture in the gray rami through which these fibers are distributed. But, as we have seen,

these rami contained, if anything, fewer myelinated fibers than the other branches of the superior cervical ganglion.

It will also be clear that there could be no considerable number of preganglionic or afferent fibers regularly running toward the superior cervical ganglion in any of its branches without their presence being indicated in such tabulated data as has already been presented. The small number of myelinated fibers present in most of these branches as well as the great variation in the ratio of such fibers to the area of the nerve speaks against these fibers being anything other than postganglionic fibers which have acquired myelin sheaths, and this apparently without rule or regularity.

The internal carotid nerve is the one which most regularly contains a high absolute and relative content of myelinated fibers. But, as has already been said, degeneration experiments show that this nerve contains no preganglionic fibers continued into it through the ganglion from the sympathetic trunk. On the other hand, Langley ('96) has shown that section of this nerve close to the ganglion causes degeneration of its myelinated fibers, which shows that these fibers are running from and not toward the ganglion. His statements appear to apply to all the branches of the superior cervical ganglion, but we are not sure that he means to include more than the large anterior branches going to the carotid artery. He says:

On section of the branches peripherally of the ganglion, nearly all the fibers which remain connected with the ganglion are unaffected, whilst nearly all the fibers separated from the ganglion degenerate. Hence, then, nearly all the medullated fibers contained in the nerve strands given off by the superior cervical ganglion arise from nerve cells in that ganglion. As to the remaining fibers I have shown (*J. Physiol.*, 14, p. II) that in the dog there are usually two small bundles which pass from the tympanic plexus to the internal carotid artery, and run thence to the superior cervical ganglion by the side of the anterior branches of the ganglion. Probably in the cat there are some homologous nerve fibers.

In a few specimens of certain of the branches a limited number of larger myelinated fibers were found. See tables 1, 3, and 4. In one specimen of the internal carotid nerve not recorded in

table 8 we also found a considerable number of these larger sizes. Are we to regard these fibers measuring about 6.6μ as very large postganglionic elements or as fibers of another character, for example, sensory, which, as a variation, have been included in these particular specimens?

CONCLUSIONS

All of the branches of the superior cervical ganglion, exclusive of the sympathetic trunk, contain, in addition to great numbers of unmyelinated fibers, also a limited number of myelinated fibers. Nearly all of these have a diameter of less than 4.5μ , though in a few specimens we have found some fibers measuring more than 6.6μ . The internal carotid nerve seems to contain regularly a rather large number of myelinated fibers and the gray rami to the first three cervical nerves a smaller number. The same relation holds for the proportion of myelinated fibers per square millimeter in these nerves. Otherwise there is nothing characteristic about the myelinated fiber content of any of these branches.

The great majority if not all of these fibers are postganglionic. This has been ascertained for the internal carotid nerve by degeneration experiments. If regularly myelinated preganglionic or afferent fibers were present in any of the branches we should expect to find evidences of them in the tabulated data given in this paper. The best explanation of the great variation in the number of myelinated fibers in different specimens of the same nerve is that myelination takes place in a limited number of postganglionic fibers and that this occurs without law or order. If any functional group of postganglionic fibers was more likely to become myelinated than another we should expect to find certain of the functionally diverse branches of the superior cervical ganglion better myelinated than others, but this is not the case, except for a slightly better myelination of the internal carotid nerve and a somewhat poorer myelination of the gray rami. The indications are that myelination is not related in any very direct way to the function of the fibers.

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ON THE QUESTION OF COMMISSURAL NEURONES IN THE SYMPATHETIC GANGLIA

SYDNEY E. JOHNSON

From the Anatomical Laboratory of Northwestern University Medical School¹

FIFTEEN FIGURES

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INTRODUCTION

The physiological and histological work of J. N. Langley has lent new interest to the question concerning the occurrence of commissural or intrinsic sensory neurones in the sympathetic ganglia. Langley's contention against the presence of such neurones is supported by evidence of a convincing nature. A number of anatomists, on the other hand, have produced evidence of a strictly morphological character which stands in opposition to the results obtained by the author just named. Dogiel's ('96) description of two types (sensory and motor) of sympathetic nerve cells is well known. Cajal, von Lenhossék, and Huber (*Jour. Morph.*, vol. 16, fig. 25, c., and *Jour. Comp. Neur.*, vol. 7, fig. 7, b) have reported finding nerve endings in the sympathetic ganglia which they have regarded as sensory or commissural in nature.

¹ Contribution No. 57, February 15, 1918.

Michailow has described no fewer than nine varieties of autonomic cells, although he does not specifically state that any one variety is sensory in character.

The morphological evidence in support of the commissural neurone hypothesis appears, however, to be gradually breaking down. Autonomic cells of all intermediate stages between the supposedly sensory and motor types of Dogiel have been reported by Carpenter and Conel ('14), and these authors have also failed to differentiate two types of autonomic cells by the Nissl method.

For discussion of Langley's nicotine and degeneration experiments the reader is referred to Huber ('99, '13) and Ranson ('18), as well as to Langley's original papers.

The observations referred to have been made largely on mammals whose sympathetic ganglia are complicated in structure by the presence of an intercellular plexus of nerve fibers and by the dendrites of the multipolar autonomic cells. In the frog the sympathetic ganglia are relatively simple in structure and if, as Huber and Langley have stated, the structural relations are fundamentally the same in the autonomic ganglia of all the vertebrates, this form would appear to be particularly suitable for disclosing these relations.

The autonomic ganglia of amphibia have been the subject of many contributions. Ehrlich ('86) and Retzius ('89) were among the first to demonstrate clearly the relations of the spiral fibers to the neuraxes (straight processes) and to the pericellular baskets. They believed that the spiral fibers were of cerebrospinal origin. Smirnow, Feist, Arnstein, and others held different views as to the origin and termination of these fibers. (For a review of the literature from 1863 to 1896 see Huber, *Jour. Morph.*, vol. 16.)

Although the belief is now generally held that the spiral fibers and pericellular baskets are of cerebrospinal origin, this has not been definitely proved on a morphological basis, and it also remains an open question whether or not nerve endings of any other type occur in the sympathetic ganglia of amphibia. The purpose of the experiments reported below was to determine whether or not all of the spiral fibers and pericellular baskets are

of cerebrospinal origin and whether or not endings of any other type are present.

My thanks are due to Prof. S. Walter Ranson for many courtesies extended during the course of the experiments.

II. MATERIAL AND METHOD

Material for the observations reported below consisted of three separate lots of frogs (*Rana pipiens*), as follows: 1) six dozen winter frogs received March 20; 2) six dozen frogs received June 7; and 3) six dozen summer frogs, received September 21, 1917. The first two lots were operated only for destruction of the spinal cord by reaming the spinal canal with a hot, flat needle (Huber, *Jour. Morph.*, vol. 16, p. 50), approximately as far cephalad as the second vertebra. In the frogs of the third lot the spinal cords were destroyed as just noted and in addition, in order to eliminate preganglionic fibers which might enter and run caudally in the sympathetic trunks, from the anterior undamaged part of the spinal cord, both sympathetic trunks were severed between the sixth and the seventh, or the seventh and the eighth, sympathetic ganglia. This operation was accomplished through a small lateral incision just to the side of the transverse process of the sacral vertebra. Through this opening both trunks were caught with the aid of a hooked needle and snipped with a pair of fine scissors. The incision was then sutured, the frog tagged, and a record made of the date of the operation. On dissection after injection it was found that in two instances only one trunk had been severed and in one instance both trunks were still intact. These specimens gave interesting results, as will be noted later. Aseptic precautions were found to be unnecessary.

Two staining methods were employed, the *intra vitam* methylene blue process practically as described by Huber (*Jour. Morph.*, vol. 16), and the pyridine silver method. In the former it was found advantageous to use 3 or 4 per cent methylene blue in Ringer-Locke solution. This was injected into the ventral vein instead of the lateral vein as described by Huber. For pyridine



Fig. 1 Longitudinal section of sympathetic ganglion of a normal frog. The darkly stained white ramus fibers enter the central part of the ganglion and from this region course outwards along neuraxes of postganglionic neurones. Several can be traced to their termination in spirals and pericellular networks. Methylene blue. $\times 453$.

silver preparations sections of the sympathetic trunk were imbedded in brain or spinal cord before being immersed in the fixing fluid.

Every operated specimen was dissected at the end of the degeneration period in order to determine the condition of the spinal cord and the sympathetic trunks. Unless otherwise noted, the spinal cord was completely destroyed as far cephalad as the second or third vertebra. Both sympathetic trunks were severed in every specimen except the three referred to above.

III. OBSERVATIONS

A. On ganglia of normal frogs

The conditions found in the sympathetic ganglia of normal frogs are illustrated in figures 1 to 5. The first three figures represent methylene blue preparations, and figures 4 and 5 show preparations stained by the pyridine silver method. Both methods gave corresponding and uniform results, although the methylene blue technique was found to be much more convenient and to show, also, a larger number of spirals and pericellular networks (especially the latter), for a given area, than could be seen in pyridine silver preparations. The latter method was used chiefly as a check against the former.

Figure 1 shows a small section of ganglion at the site of entrance of a white ramus communicans. The darkly stained fibers of the white ramus stand out in marked contrast to all other nervous elements of the ganglion. A few fibers are seen to divide and a great many can be traced to their terminations in spirals and pericellular networks on the neuraxes and bodies of the autonomic cells. In many methylene blue preparations such terminations appeared to be present on practically every autonomic cell.

The characteristic relation of fibers to cells is shown in figure 2. This represents a longitudinal section of a sympathetic ganglion, and it will be noted that the cells are located near the periphery of the ganglion while the nerve fibers form the central part.

The neuraxes of the ganglion cells are only faintly stained, nevertheless many can be traced to the central fiber bundle and their course followed for a considerable distance cephalad or caudad in the sympathetic trunk. Preganglionic fibers, in many cases, are seen to accompany neuraxes for a long distance before terminating in spirals and pericellular networks.

Details of structure of the pericellular networks have been presented by several authors (Huber, '97, '99), and as this part of the subject is relatively a side issue I need only say that my observations on this point, to the extent carried out, are in accord with those of the author referred to above. Closed networks and free endings have been described, but it has been

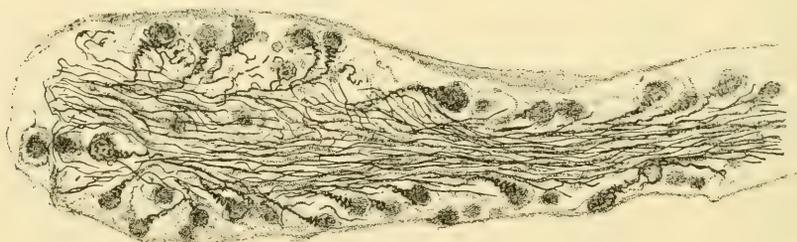


Fig. 2 Longitudinal section of a ganglion stained with methylene blue. Note the peripheral position of the cell-bodies and the central location of the nerve fibers. $\times 140$.

pointed out that one cannot be sure whether the free endings represent a normal condition or are due to imperfect staining or to the level of the section. Both free endings and a closed network are shown in figures 4 and 5. It should be noted that the neuraxes are more prominently stained in the latter than in methylene blue preparations. That the pericellular networks are intracapsular can be readily seen in preparations stained by either method.

The spirals and pericellular baskets described above constitute the only type of nerve ending that I have been able to find in the sympathetic ganglia of the frog, either in the normal condition or after degeneration of the preganglionic fibers.

B. On ganglia of operated frogs

1. *Winter frogs with spinal cords destroyed.* A first lot of six dozen frogs was received on March 20, 1917, and, as the season was backward, I have regarded these as winter frogs. Forty-two of the frogs were operated by destruction of the spinal cord to the second or third vertebra as described above. Thirty-four survived the operation and were later injected with methylene blue or their sympathetic ganglia removed and stained by the pyridine

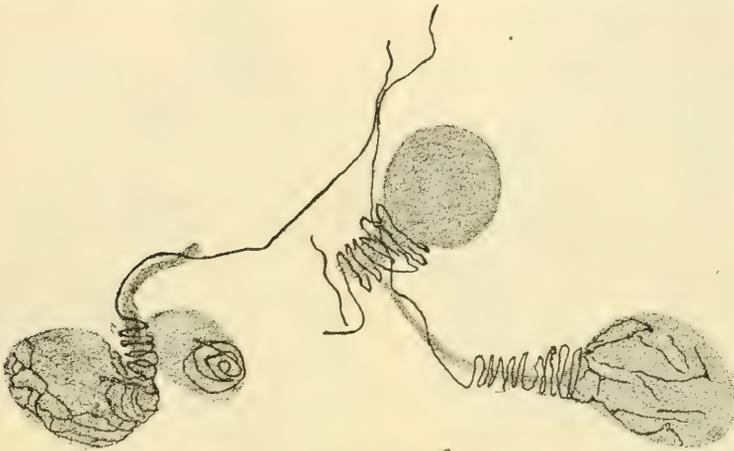


Fig. 3 Four autonomic cells and their related spirals and pericellular networks. In well stained ganglia the pericellular fibrils appear to form closed networks. Methylene blue. $\times 546$.

silver process. The anterior ganglia were always kept separate from the posterior ganglia and the results obtained on each compared. Degeneration was allowed to continue from nine to fifty-four days.

After nine days' degeneration methylene blue preparations gave normal histological pictures. No sign of degeneration could be seen, either in anterior or posterior ganglia. In pyridine silver preparations, however, evident signs of degeneration were present in the posterior ganglia. Spirals were less numerous and many were only faintly stained. Throughout my observa-

tions the pyridine silver stain appeared to be more sensitive to degenerative processes than methylene blue.

Twenty-eight days were allowed to elapse before the next specimens were injected with methylene blue. These showed a marked dropping out of pericellular baskets and spirals, especially in the posterior ganglia.

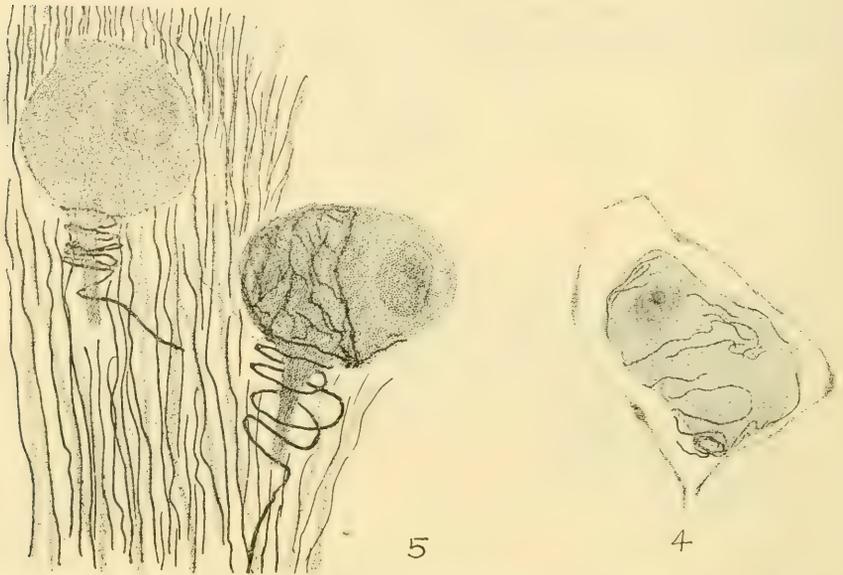


Fig. 4 Autonomic cell of normal frog, stained by pyridine silver method. $\times 1114$.

Fig. 5 Small section of a normal sympathetic ganglion stained by pyridine silver method. The preganglionic fibers are darkly stained and stand out in marked contrast to the neuraxes of the autonomic cells. $\times 1114$.

After thirty-three days the ganglia of four specimens were stained by the pyridine silver process, and all of these showed marked degeneration in the posterior ganglia. In these many spirals could be found in the anterior ganglia (fig. 8), and it is significant to note that the spirals present appeared to be as well stained as those of normal ganglia. This would appear to indicate that the cells of origin of these particular spiral fibers had not been destroyed by the operation. Thus these spirals could be

derived from cerebrospinal fibers entering the sympathetic trunks at a higher level than that to which the spinal cord was destroyed, or else endings of commissural neurones with cell bodies located outside of the spinal cord. In the posterior ganglia of the same specimens (pyridine silver preparation) no complete spirals have been observed, although an occasional darkly stained preganglionic fiber could be found. These fibers stand out in sharp contrast to the lightly stained postganglionic fibers. A typical histological picture for the posterior ganglia is shown in figure 9.

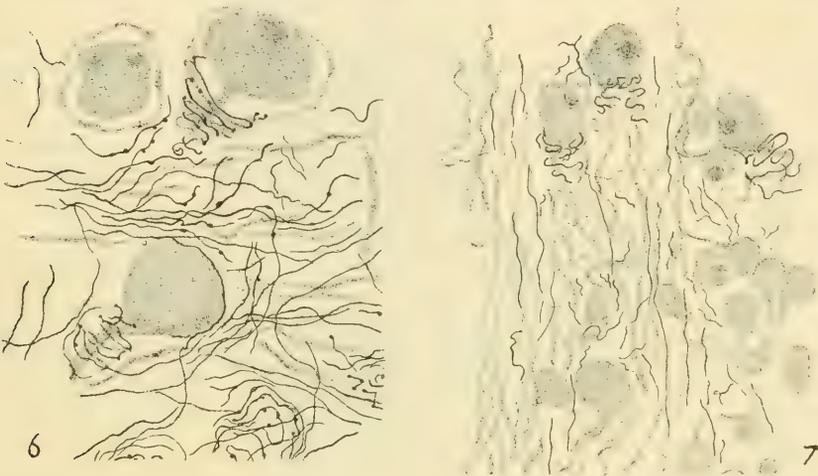


Fig. 6 Section of an anterior ganglion of a specimen injected with methylene blue forty-six days after destruction of the spinal cord. Many spirals can be found in the anterior ganglia. $\times 358$.

Fig. 7 From a posterior ganglion of the same specimen (as fig. 6). The specimens show distinct evidence of degeneration of preganglionic fibers. Methylene blue. $\times 358$.

Pyridine silver preparations made after a degeneration period of fifty-six days gave histological pictures identical with those just described.

The remaining frogs were injected with methylene blue after periods of 46, 48, 54, and 56 days. All of these gave similar results. Degeneration continued beyond forty-six days did not appear to affect the results obtained. The anterior ganglia of all of these specimens show uniformly a large number of spirals and pericellular baskets. Figure 6 shows a typical section.

The posterior ganglia (i.e., the 8th, 9th, or 10th) of the same specimens showed evident signs of degeneration. In these there could be seen only an occasional spiral and pericellular basket and a relatively small number of preganglionic fibers. The neuraxes of the autonomic cells, although faintly stained, show more prominently as they are not obscured by the presence of the darkly stained preganglionic fibers (fig. 7).

As the experiments described above were carried out on winter frogs, I was not sure that the time allowed had been sufficient

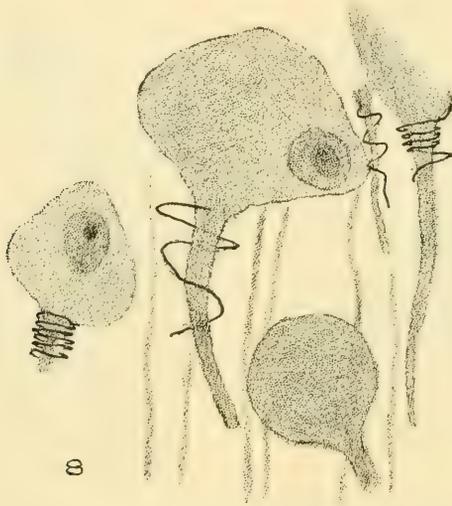


Fig. 8 Small section of an anterior ganglion stained by pyridine silver process thirty-three days after destruction of spinal cord. A few spirals could be found in all the ganglia of the anterior portion of the sympathetic trunk. $\times 1144$.

for complete degeneration of the preganglionic fibers. In order to remove all doubt on this point, a second lot of frogs was operated as indicated below.

Second lot of frogs—spinal cords destroyed. This lot of frogs was received on June 7, and fifty-four were operated in the same manner as described above. The operated frogs were put into a large tank and with them was included a small number of normal frogs for controls. Upon my return to the laboratory after an absence of three months, I found that all of the frogs had died

except one operated frog and one normal control specimen. Both were injected with methylene blue.

The ganglia of the control specimen were well stained and showed normal histological pictures on sectioning.

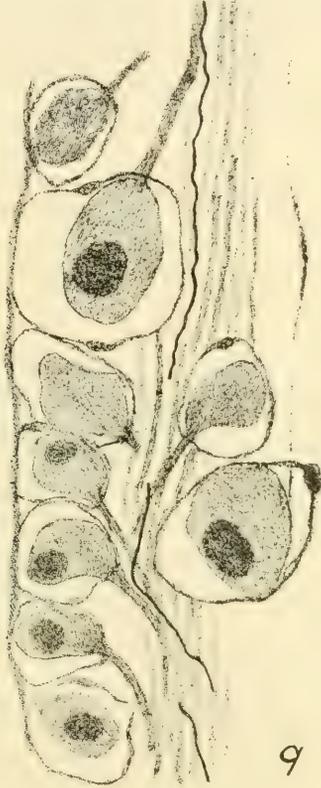


Fig. 9 Section of a posterior ganglion from the same specimen (as fig. 8). Note the absence of spirals. Occasional short sections of darkly stained, apparently preganglionic, fibers can be seen in these preparations. Pyridine silver. $\times 650$.

The ganglia of the operated frog were also successfully stained and showed results which were identical with the results obtained on frogs of the first lot in which degeneration had continued for forty-six days or longer. Figure 10 represents a small section from the fifth or the sixth ganglion of this specimen. In the more anterior ganglia spirals, baskets, and preganglionic fibers

are more in evidence. In the posterior ganglia (9 and 10) no spirals could be found and only a few broken sections of preganglionic fibers. The spinal cord of this specimen was found to have been destroyed as far forward as the third vertebra.

This experiment appeared to eliminate the possibility of incomplete degeneration, but it also left the origin of a large number of spiral fibers to be accounted for. Two possibilities presented themselves: 1) cerebrospinal fibers could still reach the sympa-

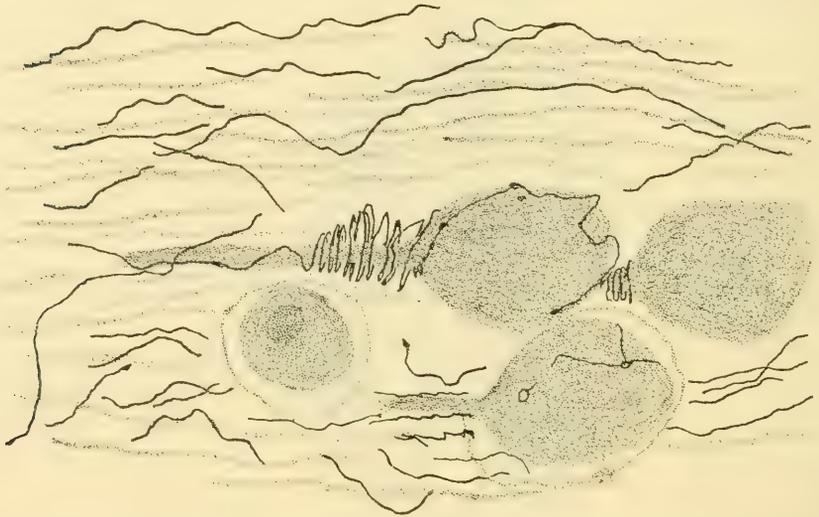


Fig. 10 Small section of 5th or 6th ganglion of a specimen injected with methylene blue three months after destruction of the spinal cord. Many spirals and pericellular networks were seen in the anterior ganglia of this specimen, but only a few in the posterior ganglia. $\times 1144$.

thetic trunks through two or three anterior white rami communicantes and could pass downward in the trunks, giving off collaterals to several of the ganglia (Langley and Orbeli, '11), or 2) they might be the neuraxes or dendrites of commissural neurones with cell bodies located without the spinal cord.

To exclude the possibility of cerebrospinal fibers reaching certain of the sympathetic ganglia a double operation was resorted to with the results reported below.

3. A *third lot of frogs* was received on September 21, and fifty-two were doubly operated, having their spinal cords destroyed and their sympathetic trunks divided between the seventh and eighth autonomic ganglia. Thirty-seven survived the operation and were later stained by one or the other of the two methods employed. In all but three of the specimens operated in this manner both sympathetic trunks were severed. The three specimens referred to (28, 29, 31) will be described separately.

Specimens 1 to 10 of this lot were allowed twenty-eight to twenty-nine days for degeneration and were then injected with methylene blue. Specimens 30 to 36 were operated at a later date, but were allowed about the same length of time (twenty-seven days) for degeneration. Specimens 11 to 13 were allowed thirty-six days, and specimens 14 to 29, thirty-one days for degeneration. Excepting specimens 28, 29, and 37, the posterior ganglia of all but the first gave uniform results.

In the posterior ganglia (all mounted on one slide) of the first specimen, two or three spirals were found, and a few darkly stained, evidently preganglionic fibers, but no pericellular baskets.

In the posterior ganglia of all the rest there was a striking and complete dropping out of all spirals and pericellular networks.

The anterior ganglia (i.e., the ganglia of the anterior sections of the sympathetic trunks) of the same specimens exhibited considerable variation in the number of spirals and pericellular networks. In some cases they gave practically normal histological pictures, in others, only a few spirals and networks could be found. This variation did not appear to be due to irregularity of staining and could probably be accounted for by the fact that the level to which the spinal cord was destroyed varied considerably in different specimens, probably enough to vary the number of normal white rami joining each sympathetic trunk by one or two.

Specimen 27 gave results the description and illustration of which will suffice for all the rest (except 28, 29, 37).

This specimen was operated on October 5, and after an elapse of thirty-one days was injected with methylene blue. It was found that the spinal cord had been destroyed to the fourth vertebra,

and the sympathetic trunks divided between the seventh and the eighth ganglia. Immediately after injection both anterior and posterior sections of the left sympathetic trunk were dissected out and treated by the pyridine silver process.

Figures 11 and 13 show typical sections of the anterior ganglia stained by the methylene blue (fig. 11) and the pyridine silver (fig. 13) method. It should be noted that figure 13 was drawn

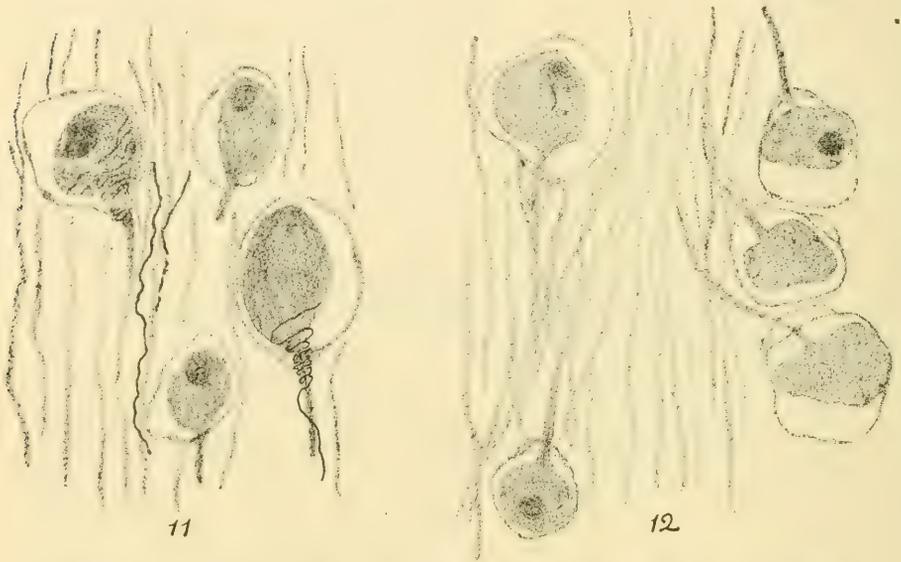


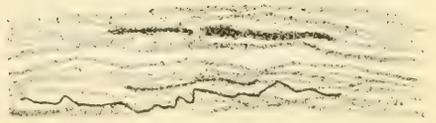
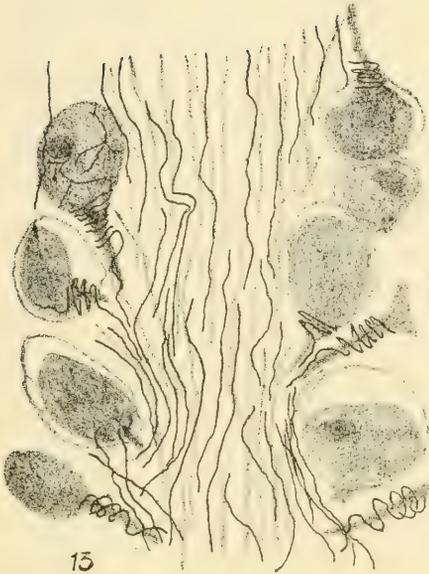
Fig. 11 Section from 5th or 6th ganglion of specimen No. 27. Spirals are readily found in these sections. This specimen was injected with methylene blue thirty-one days after section of both sympathetic trunks, between the 7th and the 8th ganglia of the trunks, and destruction of the spinal cord to the 4th vertebra. Both sections (i.e., anterior and posterior) of the left sympathetic trunk were removed and stained by the pyridine silver method (figs. 13 and 14). $\times 488$.

Fig. 12 Section of a ganglion of the same specimen (No. 27), from posterior section of the sympathetic trunk. Note total absence of spirals and pericellular baskets. Methylene blue. $\times 488$.

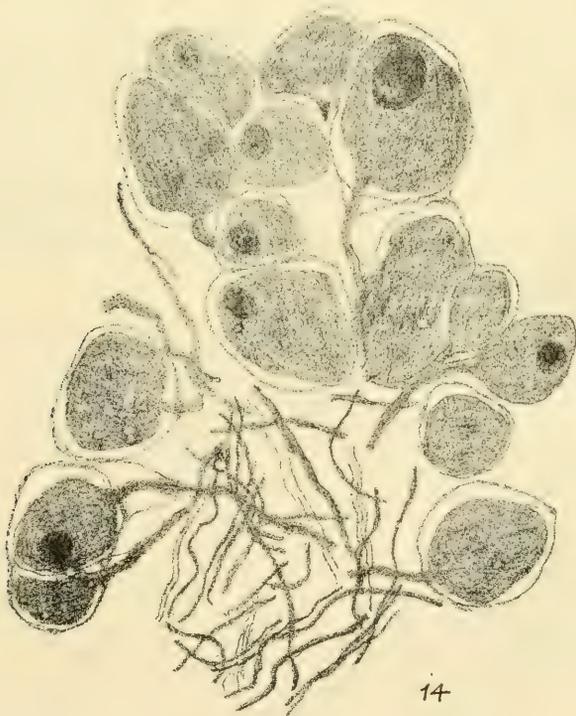
Fig. 13 From the second ganglion (anterior section) of the left sympathetic trunk, specimen No. 27. Note the large number of spirals and darkly stained preganglionic fibers. Pyridine silver. $\times 488$.

Fig. 14. Posterior ganglion of the left trunk of the same specimen (No. 27). No spirals or networks. Pyridine silver. $\times 488$.

Fig. 15 Interganglionic section of sympathetic trunk showing beaded, apparently degenerating, preganglionic fibers. Methylene blue. $\times 488$.



15



14

from the second ganglion of the sympathetic trunk, while figure 11 is from the fifth or sixth.

Figure 12 shows a methylene blue preparation of ganglion nine or ten (of the same specimen). The autonomic cells and their neuraxes are faintly stained as in normal ganglia, but there is a total absence of spirals and pericellular networks. No nerve endings of any type could be found.

A pyridine silver preparation made from a posterior ganglion of the left trunk of the same specimen (spec. 27) is shown in figure 14. It supports the results obtained with methylene blue.

Specimens 28, 29, and 37 require a word of explanation.

Dissection, after injection, disclosed the fact that the sympathetic trunks had been divided on one side only in specimens 28 and 29. Spirals and networks were easily demonstrated in the ganglia of the trunks which had not been divided, but could not be found in the posterior ganglia of the divided trunks.

Both sympathetic trunks were missed in specimen 37. The ganglia were stained, however, and they gave results identical with the results obtained on the first two lots of frogs in which the spinal cords only were destroyed, indicating that the devitalizing effect of the rather severe operation had no detrimental influence on the staining properties of the nerve terminations.

IV. SUMMARY AND CONCLUSIONS

The results obtained in the three sets of experiments may be summarized in tabular form as follows:

SPECIMEN NUMBER	DATE OF OPERATION	DAYS OF DEGENERATION	STAINING METHOD	SPIRALS AND NETWORKS IN ANTERIOR GANGLIA	SPIRALS AND NETWORKS IN POSTERIOR GANGLIA	REMARKS
<i>First lot, 72 frogs, received March 20, 1917—42 operated (spinal cords destroyed); 34 survived operation</i>						
1	Mar. 29, 1917	9	Meth.-bl.	Many	Many	Normal histological picture
2	Mar. 29, 1917	9	Pyri.-sil.	Many	Few	Evident signs of degeneration in the most posterior ganglia
3	Mar. 29, 1917	28	Meth.-bl.	Many	Several	Signs of degeneration in the posterior ganglia
4	Apr. 5, 1917	46	Meth.-bl.	Many	Few	Degeneration more evident in posterior ganglia
5	Apr. 5, 1917	56	Meth.-bl.	Many	Few	Marked degeneration in posterior ganglia
6	Apr. 5, 1917	56	Pyri.-sil.	Several	Very few	As above
7-10	Apr. 21, 1917	53	Pyri.-sil.	Several	Very few	As above
11-19	Apr. 21, 1917	48-54	Meth.-bl.	Several	Very few	As above
<i>Second lot, 72 frogs, received June 7, 1917—54 operated as described above, all dying but one during my summer absence of three months</i>						
1-54	June 7-14	97 or more	1 frog, Meth.-bl.	Several	Few	Marked dropping out of spirals in posterior ganglia
<i>Third lot, 72 frogs, received Sept. 21, 1917—52 operated (spinal cords destroyed and and both sympathetic trunks severed unless otherwise noted); 37 survived operation</i>						
1-10	Sept. 26, 1917	27-29	Meth.-bl.	Several	A few in specimen 1 only	Essentially a complete dropping out of spirals and networks in ganglia posterior to section of sympathetic trunks

SPECIMEN NUMBER	DATE OF OPERATION	DAYS OF DEGENERATION	STAINING METHOD	SPIRALS AND NETWORKS IN ANTERIOR GANGLIA	SPIRALS AND NETWORKS IN POSTERIOR GANGLIA	REMARKS
<i>Third lot—Continued</i>						
11-13	Sept. 26, 1917	36	Meth.-bl.	Several	None	
14-27	Oct. 5, 1917	31	Meth.-bl.	Several	None	Right trunk only of Spec. 27
28-29	Oct. 5, 1917	31	Meth.-bl.	Several	Several in right trunk, none in left	Dissection showed that right trunk had not been severed
30-36	Oct. 9, 1917	27	Meth.-bl.	Several	None	
27	Oct. 5, 1917	31	Pyri.-sil.	Several	None	Left trunk only
37	Oct. 5, 1917	21	Meth.-bl.	Like lots 1 and 2 above		Both trunks missed in operation

Destruction of the spinal cord alone (as far cephalad as the second or third vertebral segment) does not cause degeneration of all spiral and pericellular endings in the ganglia of the sympathetic trunks, but rather a progressive dropping out of these elements from the anterior to the posterior ganglia, a large number of networks appearing in the former and very few or none in the posterior ganglia.

When all possible routes of entrance of preganglionic fibers to the sympathetic trunks have been eliminated and sufficient time allowed for degeneration, there is complete dropping out of all spiral fibers and pericellular networks. A few spirals were found in specimen 1 (p. 397). These, I think, can be properly accounted for on the basis of incomplete degeneration, as there was only the one instance out of a large number of specimens.

Nerve endings of a different origin, if present, should be readily discovered in those preparations which are well stained and in which all preganglionic endings have been eliminated by degeneration. Such endings have not been found.

The observations presented above appear to me to show conclusively, 1) that all of the nerve fibers which end in spirals and

pericellular baskets in the sympathetic ganglia of the frog are of cerebrospinal origin (preganglionic fibers), 2) that many of the spirals and baskets in the posterior ganglia are the endings of preganglionic fibers which join the sympathetic trunks at a much higher (more anterior) level (this assumption is necessary to explain the progressive dropping out of the spirals and networks from the anterior to the posterior ganglia after degeneration caused by destruction of the spinal cord); 3) that commissural neurones or endings do not occur in the sympathetic ganglia of the frog.

To what extent the results of the observations reported above may be applicable to the sympathetic ganglia of higher vertebrates remains for future investigation to disclose. It has been asserted that the general scheme (of autonomic relations) is probably the same in all vertebrates. It is my belief, however, that this assertion should not be interpreted to exclude commissural connections from the sympathetic ganglia of all vertebrates solely on the basis of findings in the sympathetic ganglia of Amphibia. Considered, however, in connection with results obtained on higher vertebrates by Langley, Carpenter and Conel, Ranson, and others, the evidence here presented appears to me to afford additional weight to the argument against the ommissural neurone hypothesis.

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² For more extensive bibliographies see Huber ('99, '13) and Ranson (this number of this Journal).

THE THORACIC TRUNCUS SYMPATHICUS, RAMI COMMUNICANTES AND SPLANCHNIC NERVES IN THE CAT

S. W. RANSON AND P. R. BILLINGSLEY

From the Anatomical Laboratory of the Northwestern University Medical School¹

NINE FIGURES

In other papers of this series, which appear on the preceding pages, we have dealt with the cervical portion of the sympathetic trunk, the superior cervical ganglion, and the branches which it gives off. We come now to a consideration of the thoracic portion, its rami communicantes and the splanchnic nerves. Our preparations were obtained from cats because most of Langley's observations were made on these animals and we wished to compare our results with his.

The work was started with the hope of throwing some light on the origin of the various types of fibers in the splanchnic nerves. Since these fibers are known to belong for the most part to segments caudad to the fifth thoracic, we began by studying the rami from the sixth to the thirteenth thoracic nerves and the corresponding portions of the trunk. It was only after the study of this material had shown that many significant details concerning this nerve trunk had never been described that we began the study of it in the first five thoracic segments. Hence the material representing this part was taken from different cats than those in which the sixth to the thirteenth thoracic segments were studied. But in each case a sufficient number of specimens was secured to make sure that the peculiarities encountered at different levels were characteristic for those levels. In all nearly twenty cats were used, exclusive of those on which operations were performed to produce the degenerations to be reported in the following paper.

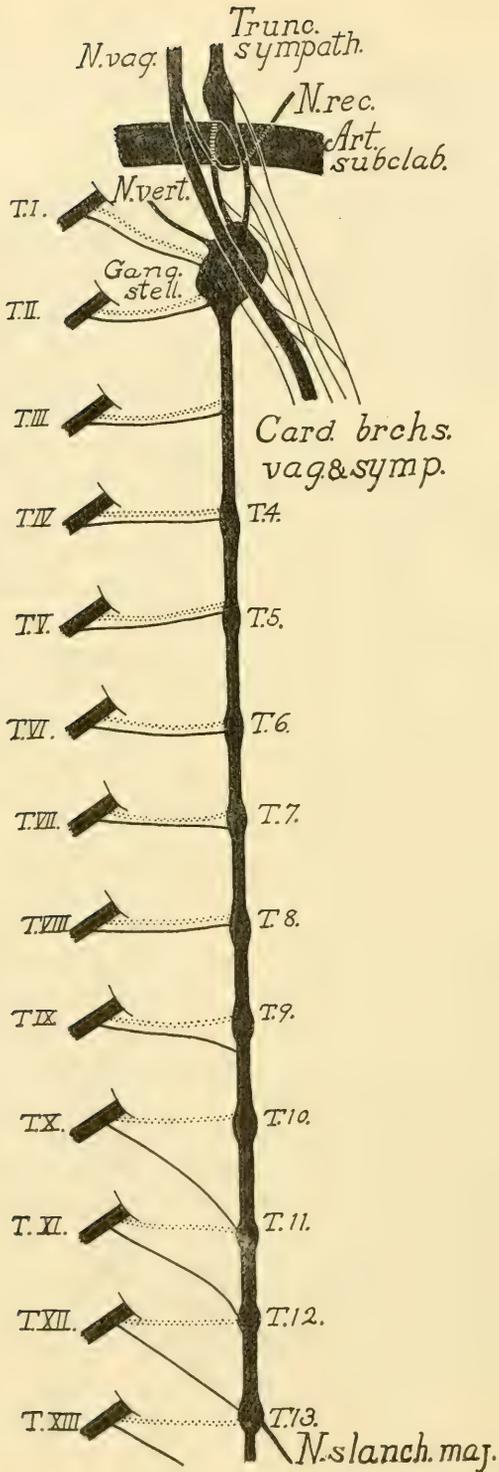
¹ Contribution No. 58, February 15, 1918.

About half of the material was fixed in osmic acid and the remainder in ammoniated absolute alcohol for the pyridine silver stain. The rami communicantes are so small and short that pyridine silver preparations were made in only a few instances, so that our observations on these are based chiefly on osmic acid preparations. For the rest of the work abundant material was available in which to compare the myelin sheath and axon content of the various parts of the sympathetic trunk and the splanchnic nerve.

When small nerves are subjected to the action of the silver and pyrogallic acid a diffuse precipitate forms throughout the specimen which renders it useless for microscopic study. In order to do away with this it is only necessary to subject large blocks of tissue to the action of the reagents. This can best be accomplished by imbedding the nerve in the spinal cord. The small nerve to be studied is dissected free and a fine silk thread is tied at either end of the stretch to be removed. With the aid of a long straight slender needle the thread attached to the end of the nerve is drawn through a piece of spinal cord and the nerve drawn in after it. The spinal cord should be prepared before the nerve is dissected out. The cervical portion of the cat's cord freed from dura and split in the median sagittal plane into two lateral halves makes satisfactory blocks. Each lateral half is then cut into segments a little longer than the pieces of nerve to be removed. During these manipulations the nerve and cord should be protected from drying by the use of normal salt solution. In drawing the nerve into the cord the needle is run longitudinally through the anterior gray column and the thread pulled through until the nerve lies imbedded in the cord. The segment of the cord is then laid with its lateral convex surface upon a glass cover-slip and the silk threads attached to either end of the nerve are tied over the cover-slip so as to put gentle traction on the nerve. After two hours in ammoniated alcohol the silk thread can be cut off near the cord, which is then removed from the cover-slip and pared down with a razor until it forms a bar, the cross-section of which is not more than 4 mm. square. This should consist chiefly of the anterior gray column in which the nerve lies imbedded.

ANATOMY

Truncus sympathicus. In the cat the thoracic portion of the sympathetic trunk presents an arrangement of its ganglia and branches somewhat different from that found in man. The chief differences are in the fusion of the upper thoracic ganglia to form the ganglion stellatum and in the mode of origin of the splanchnic nerves. The trunk lies along the sides of the bodies of the vertebrae ventral to the heads of the ribs, and consists of a series of ganglia, for the most part segmentally arranged, bound together by a continuous nerve cord. Each spinal nerve is connected with an adjacent ganglion by a gray ramus. A ganglion may send a gray ramus to two or more nerves, in which case it represents a combination of two or more segmental ganglia. Some compound ganglia are constant in their occurrence, as in the case of the stellate and the superior cervical ganglia; others may occur occasionally in any part of the trunk due to the fusion of two segmental ganglia. Thus the segmental character of the truncus is indicated by the gray rami, although in some cases adjacent segments may be fused. The white rami are much more irregular in their distribution. From all this it will be apparent that the best method of designating the ganglia is by giving them the number of the spinal nerve to which they are connected by their gray ramus. The facts concerning the connections of the fibers of the gray and white rami, which will be detailed later in this paper, also bear out this conclusion. Langley ('91 a) has made use of the same method of designating the ganglia. When we speak of the twelfth thoracic ganglion we shall have in mind the ganglion whose gray ramus runs to the twelfth thoracic nerve, although a glance at figure 1 will show that there are less than twelve separate ganglia in the thoracic region, and that this particular ganglion usually receives a white ramus from the eleventh thoracic nerve. The portion of the continuous nerve cord which joins two successive ganglia together we shall speak of as an internodal segment and shall number the successive segments to correspond to the numbers of the ganglia below which they lie.



The ganglion stellatum lies ventral to the first intercostal space and the angle of the second rib. It receives the gray and white rami from the first three thoracic nerves and sometimes from the fourth also. In addition it gives off a gray nerve, the ramus vertebralis, which follows the vertebral artery and gives off branches to the lower cervical nerves. According to Langley ('94), it can be traced in the cat as high as the third cervical nerve. The gray ramus to the eighth cervical nerve may run by itself. From its connection with the spinal nerves it is obvious that the stellate ganglion represents a fusion of elements which in man are found in the middle and inferior cervical and the first three (and sometimes four) thoracic ganglia. Beginning with the fourth or fifth thoracic segment, the ganglia are more regularly arranged. But sometimes a ganglion from which a gray ramus arises may be very small, and occasionally scattered ganglion cells or even fairly large ganglionic masses are found in the internodal segments.

Rami communicantes. While there is a gray ramus for each spinal nerve the white rami have a more limited distribution. Gaskell ('86) thought that in the dog they were associated with the second thoracic to the second lumbar nerves only. But Langley ('92 a) has shown that in the dog, cat, and rabbit, white rami run from the first thoracic to the fourth lumbar nerves inclusive. Miller ('09) has shown that in man, contrary to the usual statement, the third and fourth lumbar nerves possess white rami. The rami communicantes of the first two thoracic nerves in the cat run directly to the stellate ganglion, those of the third usually join the trunk a short distance below and ascend in a common sheath with the trunk to reach this ganglion. The gray and white rami of the upper two or three thoracic nerves are commonly fused together, forming one mixed ramus for each of these nerves. From the fourth to the eighth spinal nerve the

Fig. 1 Diagram of the thoracic portion of the sympathetic trunk in the cat. Any branches which may run to the pulmonary or aortic plexuses are usually so fine as to escape notice in a careful dissection carried out with the aid of binocular lenses of $\times 2$ magnification. In one case we found a branch from the sixth thoracic ganglion to the pulmonary plexus and one from the tenth to the aorta.

gray and white rami run close together and join the trunk at the level of the corresponding ganglion. From the level of the ninth or tenth thoracic nerve to the fourth lumbar the white rami are directed caudad and reach the truncus below the level of the ganglion to which the corresponding gray rami run, often at the level of the next ganglion below. In some cases a nerve may give off, in addition to this descending white ramus, a direct one which accompanies the gray ramus to the segmental ganglion.

A nerve may be connected with the corresponding ganglion by more than one gray ramus or a nerve may receive gray rami from two successive ganglia. This is particularly likely to be the case in the lower thoracic and lumbar regions where, in addition to the gray ramus from its own segmental ganglion, a nerve may receive a bundle of unmyelinated fibers from the next more caudal ganglion, which bundle accompanies the descending white ramus of the nerve. Langley ('94) has shown that "when the white ramus runs downward to a ganglion, as occurs from the ninth or tenth thoracic to the fourth or fifth lumbar nerves, the ganglion may supply pilomotor fibers to the two nerve areas, thus the fourth lumbar ganglion sends fibers to the fourth lumbar nerve by its gray ramus, and may also send fibers to the third lumbar nerve by the white ramus of this nerve."

Gaskell ('86) has shown that when a gray ramus is followed toward its corresponding spinal nerve it can usually be seen to give off branches which ramify in the connective tissue overlying the vertebrae. On these branches accessory ganglia may sometimes be found. In some cases the gray ramus could be seen to divide on reaching the spinal nerve, part of the fibers passing centrally, the rest peripherally.

The splanchnic nerves. In the cat the splanchnic fibers leave the sympathetic trunk in a series of six to ten small nerves. The first of this series is the largest and corresponds to the greater splanchnic nerve in man. The level of the trunk at which this nerve is given off varies. In a total of seventeen dissections it took origin from the thirteenth thoracic ganglion in six cases, from the thirteenth internodal segment in three, from the first lumbar ganglion in four, from the first lumbar internodal

segment in three and from the second lumbar ganglion in one. Since it is well known that fibers of the splanchnic nerve come from segments as high as the fifth and sixth thoracic, it is obvious that these fibers must have descended in the sympathetic trunk to the point of origin of the splanchnic nerve. In man these same fibers leave the trunk in small bundles from the level of the fifth or sixth thoracic ganglia downward to the ninth, and these bundles are then gathered together to form the greater splanchnic nerve. In the cat other splanchnic nerves are given off somewhat irregularly from the upper five lumbar ganglia and internodal segments.

The thoracic rami communicantes. It is not necessary to review the early literature dealing with the rami communicantes, since the work of Gaskell ('86) may be regarded as the starting point of modern investigations on this subject. He made a careful histological examination of the spinal nerves and rami communicantes. The gray rami were found to be composed chiefly of unmyelinated and the white rami chiefly of myelinated fibers. In the roots of the spinal nerves only myelinated fibers were found. He argued that, since he found only myelinated fibers in the roots of the spinal nerves as they left the spinal cord, the only connection between the spinal cord and sympathetic trunk must be by way of the myelinated white rami, and that through them occurred the only possible outflow of visceral efferent fibers from the spinal cord. The ventral roots of those spinal nerves which he found associated with white rami, the second thoracic to the second lumbar inclusive, were seen to contain large numbers of fine myelinated fibers like those in the white rami, while the ventral roots of the other spinal nerves contained very few such fibers. These he regarded as visceral efferent fibers. A gray ramus was found associated with each spinal nerve. On reaching the nerve such a ramus was seen to divide, one part passing centrally, the other peripherally. Most of the unmyelinated fibers which ran centrally were seen to pass into the sheath of the nerve and become lost in the dense layers of connective tissue within the intervertebral foramen. Since no unmyelinated fibers could be found in the ventral roots nor in the dorsal

roots proximal to the spinal ganglion, Gaskell asserted "that no non-medullated nerves leave the central nervous system either in the posterior or in the anterior roots, any such nerves being in reality peripheral nerves for the supply of the spinal membranes."

This was the status of the question when Langley began his work. In 1892 he said:

It may be regarded as shown that only medullated fibers run from the spinal cord to the sympathetic chain, and that the white rami contain very many medullated fibers whilst the gray rami contain very few. The asserted sharp distinction between white and gray rami stands, however, on a different footing. So far as concerns their histological characters the difference between them is rather one of degree than of kind, they both contain medullated fibers of various sizes, and non-medullated fibers.

On such evidence alone it could not be confidently asserted that no preganglionic fibers left the cerebrospinal nervous system by way of the gray rami. This question could best be attacked by physiological methods, i.e., by stimulating the spinal nerves within the spinal canal. Langley ('92 a) showed that, while stimulation of the nerves which were associated with white rami gave rise to responses in smooth muscles and glands, stimulation of those which possessed only gray rami produced no noticeable effect on these structures. He concluded that the myelinated fibers in the gray rami were either not preganglionic efferent fibers or were too few to produce any perceptible effect.

Most of Langley's histological observations were made on teased nerves, and it has seemed worth while in connection with the general review of the entire sympathetic nervous system which is being made in this laboratory to check up his histological observations by a careful examination of the rami communicantes of all the spinal nerves in sections stained with osmic acid. In this paper the rami of only the cervical and thoracic nerves are considered.

White rami communicantes. The course of the white rami within the sympathetic trunk will be taken up in connection with that nerve cord. Our present concern is with the character of the fibers. The white rami are not always pure, but are often accompanied by one or more fascicles of unmyelinated fibers

having all the characteristics of small gray rami. Such fascicles are, however, always sharply defined and do not form a part of the white ramus proper. These composite rami are especially frequent in the upper thoracic region where the gray and white rami are regularly fused. The first two or three thoracic nerves usually have each a single mixed ramus. Mixed rami are also not uncommon in the lower thoracic and upper lumbar regions where the white ramus runs downward.

Osmic acid preparations of the white rami of the cat show that these contain great numbers of small myelinated fibers with which are mingled some larger fibers varying in number in the different rami. In the dog Gaskell found that the small fibers measured 1.8 to 3.6 μ . He believed that all visceral efferent fibers were of this size. Langley ('96 a) states that:

In the cat, the medullated fibers of the sympathetic appear to be somewhat smaller than in the dog. In the dog, I found that most of the nerve fibers could be classed as belonging to one of three types, viz., large fibers about 8 μ in diameter, medium fibers about 5 μ in diameter, and small fibers about 3 μ in diameter, though all sizes from 2 to 12 μ were present. In the cat the corresponding fibers are about 7 μ , 4.5 μ and 2.5 μ ; fibers from 2 to 10 μ and occasionally of greater diameter than 10 μ being present.

Our measurements of the medullated fibers in the white rami of the cat show that the small fibers vary in diameter from 1.5 to 3.5 μ . Between these two extremes there are fibers of all sizes and in about equal proportion. There are also fibers of larger size, but in much smaller proportion. The second thoracic white ramus contains, however, a great many fibers measuring 4.5 μ or 5 μ , as will be seen in figure 2. The larger fibers, which vary in size from 5 to 13 μ are not evenly distributed in the white rami and will be considered more in detail when some of the individual rami are taken up.

There does not seem to be any reason for grouping the fibers into three classes as Langley has done. There would be more reason for making two groups: one less than 4.5 μ , the other larger. It is probable that nearly all of the preganglionic efferent fibers would fall in the first group, but this group would also contain, as we shall see, some of the smaller sensory fibers. The

second group would include the large and medium-sized sensory fibers.

Are there unmyelinated axons scattered among the myelinated fibers of the white rami? We must exclude from consideration

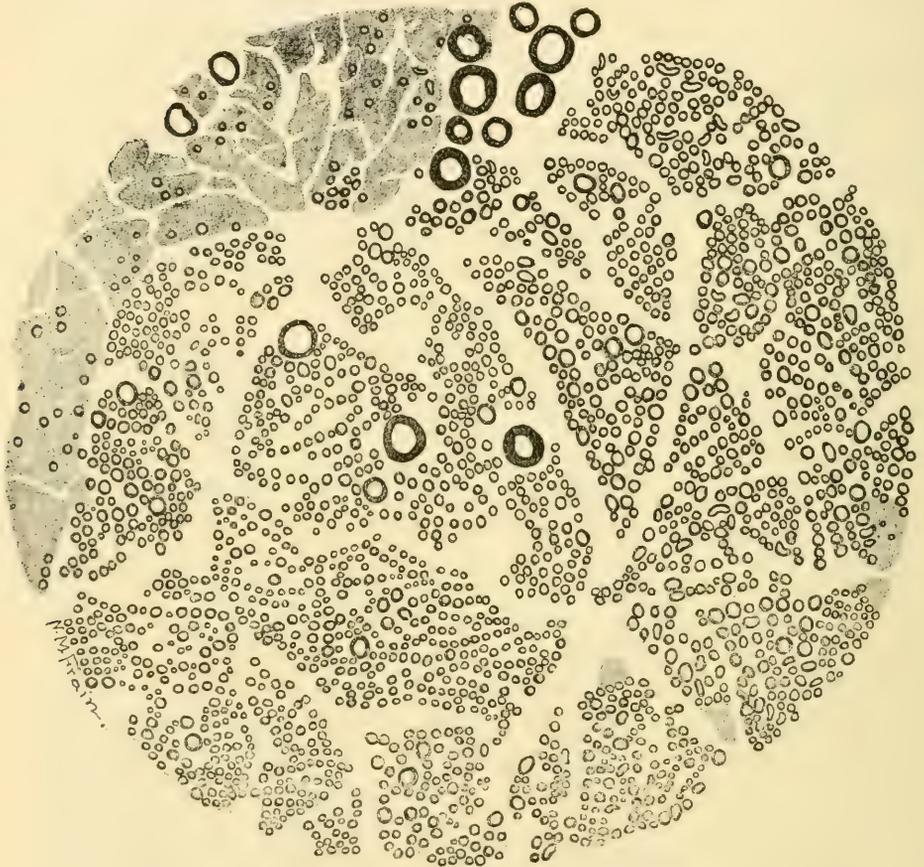


Fig. 2 Second thoracic ramus communicans in the cat consisting of two fascicles, the larger representing the white and the smaller the gray ramus. Osmic acid. $\times 425$.

here the bundles of unmyelinated fibers which run as definite fascicles and represent small gray rami included in the white. Gaskell ('86) found unmyelinated fibers in the white rami and said that "there is strong evidence that they arise from the

posterior root ganglia." It is clear from the context that he believed the spinal ganglia contained autonomic cells and that the unmyelinated fibers running from these ganglia by way of the white rami were of the same nature as the unmyelinated fibers arising from sympathetic ganglia.

We have pyridine silver preparations of the tenth, eleventh, and twelfth white rami from one cat. While these are not altogether satisfactory, it is possible to see that they contain a considerable number of unmyelinated fibers. In the paper which follows we shall present evidence to show that these fibers arise in the spinal ganglia, but we believe that they are to be interpreted as afferent, not as postganglionic efferent fibers. If they belonged to the latter category it would be hard to account for the negative results of stimulating the splanchnic nerves after injection of nicotine (p. 436).

There has been some difference of opinion concerning the rami of the first thoracic nerve. Gaskell ('86) found only a gray ramus connected with this nerve in the dog. Edgeworth ('92) found that this ramus in the dog contained unmyelinated, large myelinated, and a few fine myelinated fibers. From this account we would conclude that there was no clear separation of the fibers into fascicles representing gray and white rami. Langley ('92 a) studied the rami of the first thoracic nerve in the cat, dog, and rabbit, and in every case found the highest white ramus coming from the first thoracic nerve. In the cat we find the gray and white rami of the first thoracic nerve united in a mixed ramus in which they appear as separate fascicles. The white fascicle contains a rather large number of fibers over 6μ . It is particularly in the number of these large fibers that the white rami differ from one another. In individual white rami the content of large fibers was found as follows:

First thoracic white ramus, 40 fibers over 6μ in diameter, one of which was much larger than the others and measured 13μ .

Second thoracic white ramus, 17 fibers 6μ in diameter or larger. Of these 5 measured 13μ . There were also a rather large number of fibers from 4 to 6μ in diameter.

Third thoracic white ramus, 23 fibers 6μ in diameter or larger. There were no very large fibers like those in the two preceding rami.

Fourth thoracic white ramus, 10 fibers 6μ in diameter or greater. No very large fibers.

Fifth thoracic white ramus, 24 fibers 6μ in diameter or greater, of these 2 measured 13μ .

Sixth thoracic white ramus, 73 fibers 6μ in diameter or greater, the largest of which measured 10μ .

Seventh thoracic white ramus, 109 fibers 6μ in diameter or larger. There were no fibers of 10 to 13μ diameter.

Eighth thoracic white ramus, 101 fibers 6μ in diameter or greater. None of them very large fibers.

Ninth white ramus, contained 174 large fibers, but many of them were a little under 6μ in diameter.

Tenth white ramus. In this specimen we found a direct ramus to the tenth thoracic ganglion and a descending ramus to the eleventh. The direct white ramus contained 130 large fibers, one of which measured 10μ ; the descending white ramus in this case consisted very largely of fibers 6 to 8μ in diameter, 106 in number. The total number of large fibers coming from the tenth thoracic nerve was thus 236.

Eleventh thoracic white ramus. Here again we found a direct and a descending white ramus and in both together there were 59 large fibers.

Twelfth thoracic white ramus, 11 large myelinated fibers, of which the largest was 8μ .

Thirteenth thoracic white ramus, 56 large myelinated fibers.

While these white rami did not all come from a single animal—the first was from one cat, the second to the fifth from another, and the sixth to the thirteenth from a third cat—the results have been checked on a sufficient number of other cats to show that the larger differences between the rami of the several levels are significant. The greatest outflow of large fibers occurs through the seventh to the tenth or eleventh white rami, inclusive. Figure 3 shows the relatively large number of them in the tenth.

There seems also to be a rather large number in the first thoracic ramus. The upper two thoracic rami are also characterized by the presence of fibers as large as 13μ , which are usually absent from the others.

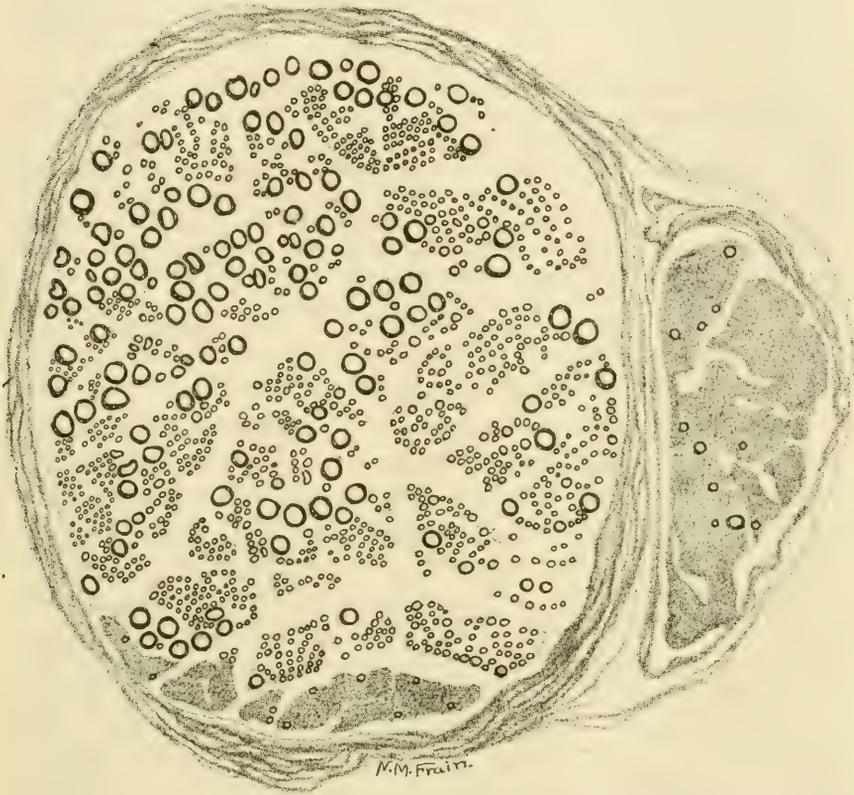


Fig. 3 Tenth thoracic white ramus of the cat with associated gray fascicles. There was a large separate gray ramus not shown in the figure. Osmic acid. $\times 425$.

Bidder and Volkman ('42) were the first to consider these larger fibers as sensory. Langley ('92 a) found difficulty in correlating the degree of sensitiveness of different parts of the sympathetic system, as evidenced by the ease with which their stimulation would produce general reflexes, with the number of

large myelinated fibers they contained. He suggested the possibility that many of the larger fibers mediate some special sense or subserve special visceral reflexes. Many of them can be traced to the Pacinian corpuscles (Langley, '00). Edgeworth ('92) devoted special attention to the "large-fibered sensory supply of the thoracic and abdominal viscera" in the dog. According to him,

It was found that the large medullated sympathetic fibers exist in the rami communicantes of the nerves from the first dorsal to the third lumbar inclusive; none were found in the rami aboral to this. The large sympathetic fibers are found scattered among the other fibers in the nerve bundles forming the ramus, and not grouped together or isolated by any septa from the other fibers. In the uppermost dorsal rami the large sympathetic fibers are fairly plentiful, in the upper and middorsal rami they are somewhat fewer in number, whilst in the lower dorsal rami a sudden large increase takes place, which continues as far as the second lumbar ramus where the outflow practically ceases. A few however are constantly to be found in the third lumbar ramus—whilst below this as stated above none are seen.

Edgeworth included among the large fibers those measuring 7.2 to 9 μ and ignored the even larger number of fibers measuring less than 7 μ but still distinctly larger than preganglionic fibers, so that his results are only in a general way comparable to ours. He states that the large fibers are as numerous in the gray as in the white rami. In the cat, as we shall see, they are usually not present in the gray rami of the cervical and thoracic regions. Langley ('92), working with the cat, found some large fibers, 7.2 μ or upwards, in the gray rami of the lower cervical nerves; in the white and in the gray ramus of the fourth lumbar nerve, and in the gray rami of the fifth, sixth, and seventh lumbar nerves. These were not numerous, but with them were a considerable number of fibers about 5 μ in diameter.

It has been assumed that all the large myelinated fibers are afferent, but are all the visceral afferent fibers large? Added precision could be given to this question of the myelinated visceral afferent fibers by the study of the white rami after degeneration of the preganglionic fibers resulting from section of the corresponding spinal nerve roots proximal to the spinal ganglia. We have examined the white rami of the ninth, tenth, and elev-

enth thoracic nerves after all the preganglionic fibers had been eliminated. As is shown in the figure on page 444 of the eleventh thoracic white ramus, the majority of the fine myelinated fibers have degenerated, but a considerable number of all sizes remain. In this particular case the small and medium-sized fibers are more numerous than the large ones. In some other degenerated white rami the large ones are relatively more numerous. On the whole, the sensory fibers of the white rami may be said to be of all sizes from 1.5 to 8 or 10 μ , no one size greatly predominating over the others. In some rami as in the upper thoracic larger fibers up to 13 μ may be present.

These sensory myelinated fibers which are found in the white rami after section of the corresponding nerve roots proximal to the spinal ganglia take their origin from nerve cells in these ganglia. In the second paper of this series we have shown that there was no reason for assuming that there were sensory cells in the sympathetic ganglia which sent their axons into the dorsal roots or spinal ganglia (p. 333). Langley has shown that

Section of the inferior splanchnics, the lower lumbar sympathetic chain, or of a white ramus does not as a rule cause degeneration of any medullated fibers in the central ends of the nerves. Sometimes a few degenerated fibers may be followed for a short distance, but these appear to belong to small gray bundles and to pass off to peripheral tissues.

When we come to the study of the sympathetic trunk we shall find that while some of the fibers of a white ramus end in the nearest ganglion, a larger proportion of the fibers run up or down in the trunk for longer or shorter distances. That is to say, a white ramus is in no special sense associated with its own segmental ganglion. The gray rami, on the other hand, are in a very special sense the branches of the corresponding ganglia.

Gray rami communicantes. The physiological experiments of Langley ('91 a, '94) on pilomotor, vasomotor, and secretory fibers show that the majority of these postganglionic fibers take origin from the cells of that ganglion to which the gray ramus is attached, but in some cases a minority of the fibers are connected with cells in an immediately adjoining ganglion. On the histological side this arrangement is indicated by the fact

that a gray ramus plunges directly into a ganglion, its fibers being lost in the fiber complex; while in the case of the white rami it is easy to see that a large part of the fibers do not enter the ganglion, but pass along its surface to join the trunk above or below.

While the gray rami are composed in by far the greater part of unmyelinated fibers, each contains at least a few myelinated fibers and some contain a very considerable number. Langley ('96 a) has shown that the number of such fibers has been greatly underestimated. The seventh lumbar gray ramus of the cat may contain more than 300. According to Edgeworth ('92), the branches from the stellate ganglion to the cervical nerves in the dog contain a few small myelinated fibers, but no large ones. In commenting on Edgeworth's paper Langley ('92) states that he has always found some large myelinated fibers in the gray rami of the lower cervical and fourth, fifth, sixth, and seventh lumbar nerves. The number of small myelinated fibers is in general proportional to the size of the gray ramus, i.e., to the number of unmyelinated fibers it contains (Langley, '96 a). He states that the myelinated fibers range in size from 1.8 to 10μ and the variation in number affects almost entirely the small ones, the most constant form being the fiber of medium caliber. The number of myelinated fibers varies considerably in different mammals, there being many more in the cat than in the rabbit (Langley, '00). Müller ('09) demonstrated the presence of myelinated fibers in the gray rami of man.

In the rami to the first three cervical nerves from the superior cervical ganglion we found that the number of myelinated fibers varied greatly in different specimens. Most of these fibers were less than 3.3μ in diameter, although occasionally larger fibers up to 6 or 7μ were found, also in one case a single fiber measuring 10μ . We have examined sections of the ramus vertebralis of the stellate ganglion in one cat and found that it contained about the same proportion of myelinated fibers as the other gray rami. There were no fibers as large as 6μ . All of the thoracic gray rami contain a few myelinated fibers. These are for the most part small, but a few large fibers were found in the upper thoracic gray rami. We cite some enumerations which may be regarded

as typical. In one cat the sixth thoracic gray ramus contained one myelinated fiber 6.6μ in diameter and three others much smaller. The seventh was fused with the white ramus, and it was difficult to be sure which myelinated fibers belong to it. The eighth contained 3, the ninth 20, the tenth 27, the eleventh 14, the twelfth 6, and the thirteenth 16, all under 4μ in diameter.

What is the function of these myelinated fibers and from what cells do they arise? Many are postganglionic fibers arising from the cells of the ganglia of the sympathetic trunk. The observations to be found in the literature showing that postganglionic fibers in some instances acquire myelin sheaths have been given on page 323. As already mentioned, Gaskell showed that as a gray ramus reaches its spinal nerve it divides into two fascicles, one of which is directed peripherally. This peripheral branch receives its share of the myelinated fibers. These being directed toward the periphery can scarcely be other than postganglionic fibers. It is reasonable to suppose that many of those which turn centrally are of the same nature (Langley, '92 a).

In 1896 Langley made a careful study of this problem. After a variety of experimental lesions involving degeneration of fibers of various origin in different experiments, he counted and measured the normal and degenerated fibers in the gray rami of the lumbar and cervical nerves. We quote his conclusions:

The great majority of these (myelinated) fibers arise from sympathetic nerve cells in the corresponding sympathetic ganglion. In some cases, but not always, a few arise from sympathetic cells in an adjoining ganglion. No efferent fibers run from the spinal cord to the sympathetic by way of the gray rami. In some cases, but not commonly, a few efferent medullated fibers, passing to the sympathetic by the white rami, leave the sympathetic by the gray rami. These are to be considered as fibers on their way to aberrant sympathetic nerve cells lying in the gray rami before they reach the spinal nerves. The afferent medullated fibers of the gray rami are of various sizes, 2μ , 4μ , 6μ , and in some cases 8 to 12μ . These are few in number and rapidly diminish (especially those of more than 4μ in diameter) in passing from the lower lumbar to the coccygeal rami. Most of (these) afferent fibers join the sympathetic by white rami (only to leave again by the gray), but there is some evidence that a few, especially the larger ones may run to the sympathetic by the gray rami.

In spite of the presence of a few myelinated sensory fibers in the gray rami "no reflex of any kind has been obtained by stimulating them" (Langley, '00). This may be due to their small number, or it may be as Langley ('92 a) has intimated, to the fact that these large afferent fibers are not fibers of general sensibility.

STRUCTURE OF THE THORACIC PORTION OF THE TRUNCUS SYMPATHICUS

In order to understand the structure of the sympathetic trunk it is necessary to think of it as a ganglionated nerve which receives preganglionic myelinated fibers from the various white rami and through which these fibers are distributed to ganglia more or less remote from the point where the fibers enter the trunk (fig. 4). Above the sixth thoracic ganglion the trunks consist chiefly of ascending preganglionic fibers from the upper white rami destined to end in the upper thoracic, stellate, and cervical ganglia. Below the tenth thoracic ganglion it consists chiefly of descending preganglionic fibers from the lower thoracic and lumbar white rami to the more caudal ganglia of the trunk and to the splanchnic nerves. From the sixth to the ninth ganglia it contains both ascending and descending preganglionic fibers. The lowest known origin of ascending fibers to the superior cervical ganglion is from the seventh thoracic white rami and consists of pilomotor fibers for the face and neck. Fibers ascend to the stellate ganglion from white rami as low as the ninth. The highest fibers running to the splanchnic nerve come from the fifth or possibly the fourth. Fibers from a given white ramus may be distributed to from five to ten successive ganglia of the sympathetic trunk, though the branches of an individual preganglionic nerve fiber would be distributed to a smaller number. These statements are based on Langley's ('92 a, '00, '03 a) work on the cat. In more general terms this distribution of the fibers of the white rami has been known for many years and was well stated by Gaskell ('86). According to him, the white rami from the second to the fifth thoracic nerves, inclusive, in the dog are directed upward, below the fifth they are directed mainly

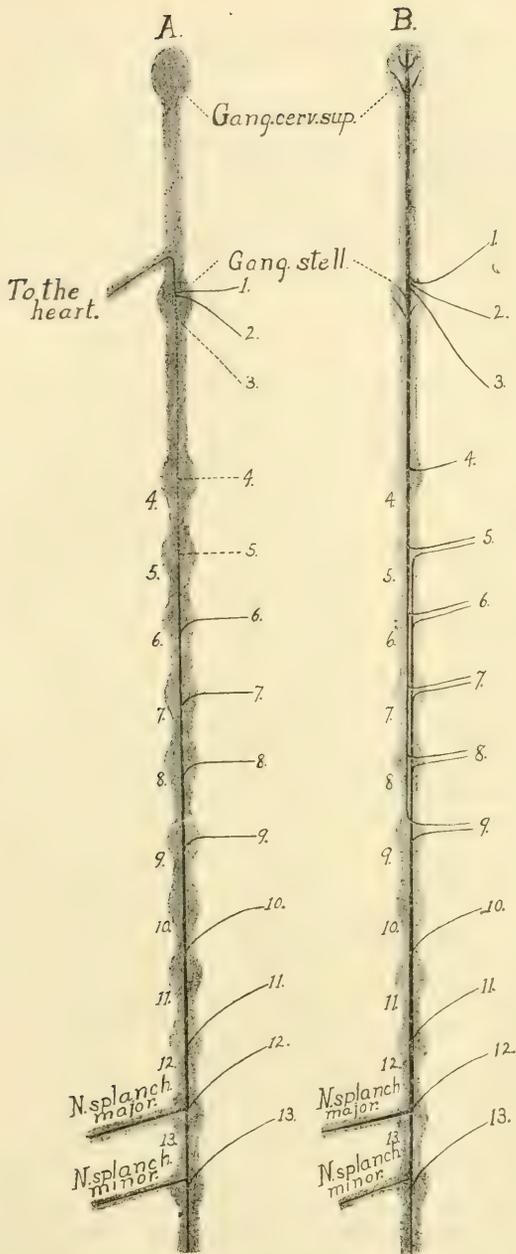


Fig. 4 Diagram illustrating the course of the fibers from the thoracic white rami through the sympathetic trunk in the cat. A. The course of the afferent fibers. B. The course of some of the more important groups of preganglionic fibers, those terminating in the thoracic ganglia below the stellate are not indicated.

TABLE 1

Connections of the spinal nerves with the vertebral ganglia, so far as these supply the skin, except that of the head and the anogenital region in the cat with an anterior arrangement of the spinal nerves—after Langley-Schafer's Physiology, vol. 2, p. 634

SPINAL NERVE	SYMPATHETIC GANGLIA	SPINAL NERVE
IV	G St.....	IV
V	G St.....	V
VI	G St.....	VI
VII	G St 4, 5, 6, 7, 8, 9.....	VII
VIII	G St 4, 5, 6, 7, 8, 9, 10.....	VIII
IX	(G St) 4, 5, 6, 7, 8, 9, 10, 11.....	IX
X8, 9, 10, 11, 12, 13.....	X
XI12, 13, 1, 2, 3.....	XI
XII13, 1, 2, 3, 4 (5) (6) (7).....	XII
XIII1, 2, 3, 4 (5) (6) 7 (1).....	IXII
I2, 3, 4 (5) (6) 7, 1, 2.....	I
II3, 4 (5) (6) 7, 1, 2, 3.....	II
III4 (5) (6) 7, 1, 2, 3 Coc..	III

downward. This is associated with the course of the fibers of which they are composed which pass not only into their segmental ganglia, but also upward into the cervical ganglia, downward into the lumbar and sacral ganglia and outwards into the collateral ganglia. Müller ('09) has shown that the preganglionic fibers in man have a similar distribution. The connections of the spinal nerves with the ganglia of the sympathetic trunk so far as these supply vasomotor, pilomotor, and secretory fibers to the skin has been worked out in detail by physiological methods and is expressed in table 1. This shows that these preganglionic fibers from the nerves above the seventh thoracic are directed upward from the nerves below the tenth downward and from the seventh to the tenth, inclusive, both up and down.

With the exception of the cervical and stellate ganglia, which contain other elements also, the ganglia of the sympathetic trunk may be regarded as aggregations of postganglionic pilomotor, vasomotor, and secretory neurones whose axons are distributed through the corresponding gray rami and spinal nerves. As we have stated before, the fibers of a gray ramus arise from the associated sympathetic ganglion, though a few fibers may

come from the next higher or next lower ganglion. The ganglia and gray rami are therefore more nearly segmental than the white rami. As we shall see, few if any postganglionic fibers, arising in the ganglia of the sympathetic trunk, pass by way of the splanchnic nerves to the abdominal viscera.

With these facts in mind we are prepared to understand the observations which follow and which show that the sympathetic trunk is a well myelinated nerve.

The sympathetic trunk caudad to the sixth thoracic ganglion has the structure shown in figure 5. It consists like other portions of the thoracic trunk of two fascicles which, though not sharply separated from each other by connective-tissue septa, maintain their identity throughout, and in cross-sections of the stained nerve are easily distinguished from each other because of their markedly different fiber content. The larger fascicle, well myelinated, presents in cross-section a round outline and occupies the greater part of the area of the cross-section. The other, which makes up but a small part of the area, is composed almost exclusively of unmyelinated fibers, and is flattened out like a crescent upon the surface of the larger bundle. For convenience of reference and until its nature is better known we will speak of this bundle as the crescent. The larger, more rounded, area will be referred to as the oval.

When followed in serial sections the crescent of unmyelinated fibers is seen to enter the ganglion at either end of the internodal segment and become lost in the ganglion. The crescent contains a very few fine myelinated fibers, and has in fact the structure of a gray ramus. The fibers of the larger well myelinated bundle, the oval, run in part into the ganglion at either end of the internodal segment, but in even larger part pass by along the side of the ganglion. Every internodal segment of the thoracic sympathetic trunk presents this separation into two fascicles—and in every case where serial sections of an internodal segment, including the ganglia at both ends, were examined the crescent was found to be continuous from ganglion to ganglion.

The same structure was described as a peripheral fascicle of unmyelinated fibers in the cervical sympathetic trunk. As

the fascicle was followed caudad from the superior cervical ganglion it was seen to give off very small bundles of fibers which left the trunk as gray branches, bringing about a gradual reduction in the size of the fascicle. One set of serial sections of the entire cervical portion of the sympathetic trunk was prepared,



Fig. 5 The sixth thoracic internodal segment of the sympathetic trunk in the cat. Two fascicles may be recognized, one appearing in the cross-section as a large oval well myelinated field, the other as a crescentic field with few myelinated fibers. Osmic acid. $\times 425$.

and in this preparation it was found that in tracing the crescent downward it decreased in size and finally disappeared. It is obvious, therefore, that in the upper cervical region a fascicle similar to the crescent consists of postganglionic fibers which accompany the trunk for a certain distance before being given off

in gray branches. In the thoracic region one cannot often see this fascicle of the trunk give off branches. It appears rather to serve as a commissural cord joining two successive ganglia together.

There are three possibilities concerning the nature of the fibers of this fascicle: 1. It may consist of commissural fibers arising from the cells of one ganglion and running to another. Against this assumption is all the evidence presented by Langley to show that such commissural neurones do not exist. The most important evidence in this connection is that based on degeneration experiments. Langley has shown ('03 b) that after degeneration of the lower thoracic and lumbar spinal roots, the lower part of the sympathetic trunk is in the same condition as after injection of nicotine. Stimulation between the ganglia has either no effect or only such effect as could be interpreted as due to post-ganglionic fibers. The literature on this question was considered at some length in the second paper of this series on page 320. In the paper by Dr. Johnson this question is again considered, and what seems to be conclusive evidence is presented that no commissural fibers exist in the sympathetic trunk of the frog. In view of these facts, it does not seem probable that the crescent is composed of commissural fibers.

2. The crescent may consist of fibers belonging to gray rami which ascend or descend in the trunk for a short distance. From what has been said about the crescent in the cervical region and from the fact that, as we have already stated, the fibers of a given gray ramus may come in part from the ganglion next above or next below, it seems obvious that some at least of the fibers of the crescent must be of this nature. Since, however, gray ramus fibers do not ascend or descend in the trunk for more than one segment and since such fibers are not numerous nor constantly present, it seems doubtful if they can account for the large number of fibers constantly present in the crescent.

3. A third possibility is that the crescent is formed by unmyelinated terminal branches of preganglionic fibers. There is some evidence that these fibers may lose their sheaths before terminating. This evidence has been summarized by Langley ('00) as follows:

By the degeneration and by the nicotine method, it can be shown that in the cat fibers run from the upper lumbar white rami to the sacral and coccygeal ganglia without passing through nerve cells. In the rabbit the nicotine method only has been tried; it gives the same results. We may then conclude that in the rabbit there are preganglionic fibers, stretching from the upper lumbar white rami to the sacral coccygeal ganglia. But since the sympathetic in the sacral and coccygeal region of the rabbit contains very few medullated fibers, it follows that the preganglionic fibers in this region must be non-medullated, and as they are medullated in the white rami they must become non-medullated in passing down the sympathetic chain. In other words, preganglionic fibers may become non-medullated some distance from their termination in the vertebral ganglia.

But after all has been said it must be admitted that we are not in possession of a satisfactory explanation of the bundle of unmyelinated fibers which we have provisionally called the crescent and we do not know what the source of its fibers may be.

As seen in figure 5, the myelinated fibers which constitute the larger oval field are of various sizes. The small fibers 1.5 to 3.5μ in diameter are by far the most numerous. They have the size and appearance of white rami fibers with somewhat thicker sheaths than is usual on postganglionic fibers of the same caliber. The larger fibers are rather conspicuous but are not present in great numbers. They will be recognized as the large fibers of the white rami which, as we have seen, take their origin from the dorsal root ganglia.

Sections stained with osmic acid through successive internodal segments from the sixth thoracic downward to the origin of the first splanchnic nerve show no great change in structure. There is obvious a rather considerable increase in area of the oval myelinated fascicle without any regular increase in the area of the crescent. The most noticeable feature is, however, the absolute and relative increase in the number of large myelinated fibers. A comparison of figures 5 and 6 will show that they are relatively much more numerous in the eleventh thoracic internodal segment than in the sixth. And the area of the cross-section at the eleventh is much greater than at the sixth. This increase in area is caused by the large number of fibers descending in the trunk to enter the splanchnic nerves. All of the large fibers of

the lower eight thoracic white rami turn downward toward the splanchnic nerves, and accumulate in the trunk. It is probable that many of them branch on their way down. Langley ('00) states that the large fibers of the sympathetic system occasionally divide. In this case the branches are of somewhat less diameter than the parent fibers. He does not state how these observations were made, but most of his histological observations were made on teased preparations. As evidence that division of the large

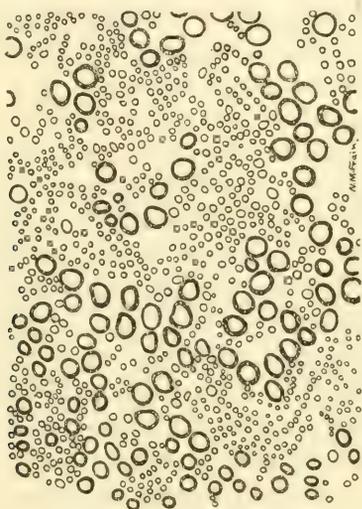


Fig. 6 A small part of a section of the eleventh thoracic internodal segment in the cat. Osmic acid. $\times 425$.

fibers occurs in the sympathetic trunk we may mention the results of the enumeration of the large fibers in the lower thoracic white rami and in the trunk just above the origin of the first splanchnic nerve. Only fibers 6μ or greater were counted. The total number of large fibers in the lower eight thoracic white rami was 864. In the trunk just above the origin of the first splanchnic nerve there were 464, i.e., a little more than half as many as in the rami. Since, as we shall see, all or practically all of the large fibers from these rami turn downward in the trunk, and since none or almost none are given off in any of the other

branches of the truncus, and since being sensory fibers, it is not likely that they terminate in the ganglia, the simplest explanation of these numerical results would be that through branching about half of them became reduced in size below a diameter of 6μ .

In serial sections of the sympathetic trunk with the white rami attached it is easy to trace the course of the myelinated fibers from the latter. In one cat longitudinal serial sections of the trunk at the level of the entrance of the sixth white ramus were prepared from osmic acid material, also similar sections of the trunk at the level of the seventh white ramus. These rami joined the trunk at the level of the lower end of the corresponding ganglia and could be seen to divide into two bundles, a smaller ascending and a larger descending bundle. The majority of the fibers do not plunge directly into the ganglion, but seem to run by on its surface. This is especially evident in case of the descending bundle which can be followed into the trunk below the ganglion. It is very easy to follow the large medullated fibers and to see that practically all of these in the sixth and seventh white rami turn downward past the ganglion into the internodal segment.

An instructive set of preparations was obtained from another cat in which the seventh thoracic ganglion and the associated rami were cut into transverse serial sections. The white ramus on reaching the ganglion divided into two parts: the smaller of the two joined the myelinated portion of the truncus on the surface of the ganglion; the other part turned downward in a well-defined fascicle separated from the ganglion by a connective-tissue septum and could be traced downward for a considerable distance along the side of the seventh thoracic internodal segment before it joined with the trunk. So far as could be determined all the large fibers of this white ramus turned downward in this fascicle. Such a separate-descending fascicle is of course atypical, but this ramus serves to indicate in a diagrammatic way the course taken by the fibers of the white rami on entering the trunk. Of course the corresponding fibers of the upper thoracic white rami turn upward instead of downward.

At the point where the first and largest splanchnic nerve is given off, which is usually near the thirteenth thoracic ganglion, the size of the trunk becomes abruptly reduced, and it is obvious, when serial sections are studied, that a large part of its myelinated fibers run into this nerve.

The sympathetic trunk cephalad to the sixth thoracic ganglion is characterized by the small number of large myelinated fibers which it contains. The peripheral crescent-like bundle of unmyelinated fibers is seen here as well as in lower segments and can be traced continuously from one ganglion into another. Above the fourth thoracic ganglion the trunk sometimes breaks up into two or three fascicles which run parallel to one another to

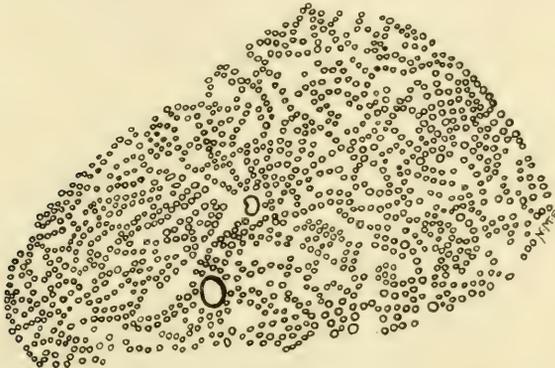


Fig. 7 One of three fascicles composing the sympathetic trunk above the level of the fourth thoracic ganglion in the cat. Osmic acid. $\times 425$.

reach the stellate ganglion. A cross-section of such a fascicle just above the level of the fourth thoracic ganglion is seen in figure 7. The crescent of unmyelinated fibers was joined with one of the other two fascicles of which the trunk was composed. The fascicle which is seen in cross-section in figure 7 contained no bundle of unmyelinated fibers large enough to be recognized in osmic acid preparations. With the exception of two larger fibers, it was composed of myelinated fibers of uniformly small size. The other fascicles of the trunk were also characterized by the paucity of large and medium-sized myelinated fibers.

In studying the white rami we have found reason for believing that the large and medium-sized fibers of the sympathetic system are afferent. There are also small myelinated afferent fibers, but these are not readily distinguished from the preganglionic efferent fibers. It will be evident from what has been said that the large and medium-sized myelinated afferent fibers are present in varying numbers in different parts of the thoracic sympathetic trunk. Between the stellate ganglion and the sixth thoracic ganglion they are few in number. Caudal to the sixth ganglion there is a steady increase in these fibers with the accession of each successive white ramus until the point of origin of the greater splanchnic nerve is reached through which nerve a large part of these fibers run toward the viscera (fig. 4 B). We shall now see that unmyelinated afferent fibers from the white rami are distributed in the same way as these myelinated sensory fibers which we have been studying.

Above the level of the fourth thoracic ganglion there are very few unmyelinated fibers in the trunk except for the well-defined bundle which we have referred to as the crescent. The fine myelinated fibers of which the rest of the cross-section is composed are almost free from an admixture of unmyelinated fibers. These are also not very numerous in the oval of the seventh internodal segment. In the lower thoracic segments the oval well myelinated portion of the section does not consist entirely of myelinated fibers, but, as is shown in figure 8, it contains also very large numbers of unmyelinated axons. These are grouped in small bundles which lie among the myelinated fibers. The distribution of the three kinds of fibers, large myelinated, small myelinated, and unmyelinated, is not uniform throughout the cross-section. The large myelinated fibers are much more numerous in some parts of the field than in others (fig. 5). They also show a tendency to be arranged in bundles which are separated from each other by the small myelinated fibers. Now it is in and about these bundles of large myelinated fibers that the greatest number of the unmyelinated axons are found. The grouping of these with the large myelinated sensory fibers suggests that they also may be afferent in function. The data thus

far presented would not exclude the possibility that these unmyelinated fibers might be preganglionic fibers that had lost their myelin sheaths, but in the paper which follows we will present evidence to show that they are afferent fibers and arise from the cells in the spinal ganglia.

Since there are few large myelinated and unmyelinated fibers

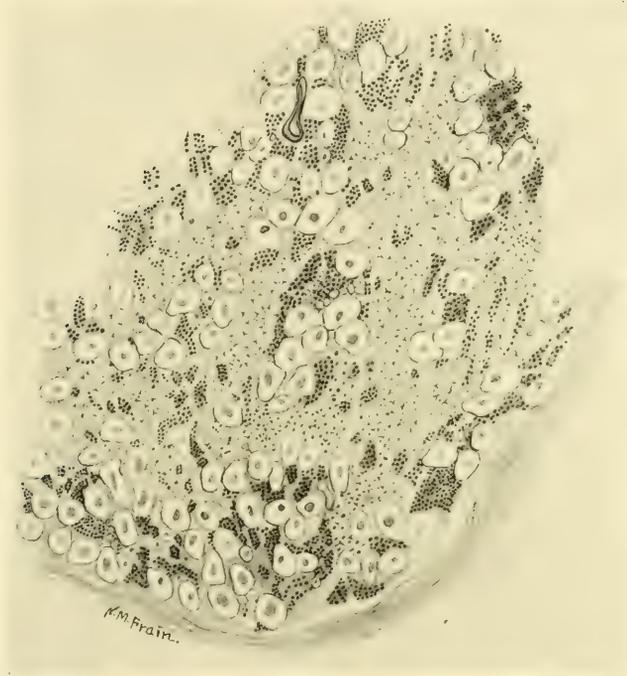


Fig. 8 A part of a section through the tenth thoracic internodal segment in the cat. Pyridine silver. $\times 425$.

in the sympathetic trunk below the stellate ganglion and practically none in the cervical part of the trunk, we must conclude that the sensory fibers which reach the stellate ganglion by way of the first three white rami run out again through the branches of the stellate or the inferior cervical ganglion. These branches have been studied in only one cat. The cardiac branch of the stellate ganglion, while consisting chiefly of unmyelinated fibers, contained a somewhat larger number of myelinated fibers than

the internal carotid nerve. These were all under 4.5μ except two, which measured 6μ . Large myelinated fibers were found in both limbs of the subclavian ansa which joined to form a single trunk just below the middle cervical ganglion. A cardiac branch given off by the trunk in this position contained a considerable number of fibers between 4.5 and 7μ . We counted forty-eight that measured approximately 6μ . Aside from the presence of these larger fibers, this nerve had the same structure as the cardiac branch of the stellate ganglion. These observations indicate that the large myelinated fibers pass through the stellate ganglion, run in both limbs of the ansa, and leave through the cardiac branch coming from the middle cervical ganglion or from the ansa subclavia. This is in keeping with the work of Edgeworth ('92), who found that the large myelinated fibers in the dog could be followed in the stellate ganglion through the ansa subclavia and middle cervical ganglion, whence they were distributed to the heart and lungs. This question deserves thorough study. As is indicated in figure 4 B, the sensory fibers from the lower eight thoracic rami run downward in the trunk and out through the splanchnic nerve. In the segments just below the stellate ganglion there are few large myelinated and unmyelinated sensory fibers, as is indicated in the diagram by the dotted line.

THE GREATER SPLANCHNIC NERVE

At another time we expect to take up the more detailed consideration of all the splanchnic nerves of the cat, but the present paper would not be complete without some account of the structure of the first and largest of the series, the greater splanchnic nerve. A study of serial sections through the trunk at the point of origin of this nerve shows clearly that it is formed by the separation of a large part of the oval well myelinated fascicle from the rest of the trunk. The nerve has the same structure as this oval fascicle and consists of large and small myelinated and unmyelinated fibers in the same proportion and with the same arrangement as in that fascicle.

Usually in pyridine silver preparations it is possible to see that there are somewhat larger accumulations of unmyelinated fibers near the periphery or directly under the perineurium. These do not constitute well-defined fascicles such as one would expect to find if any large number of postganglionic fibers were present. They are probably of the same nature as those scattered through the nerve.

In two out of ten normal greater splanchnic nerves examined we found evidence of postganglionic fibers in the form of a well-defined and fairly good-sized fascicle composed chiefly of unmyelinated fibers. Preparations of the first lumbar segment of the sympathetic trunk and the greater splanchnic nerve taken

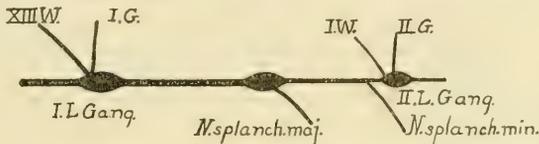


Fig. 9 Diagram of the upper lumbar portion of the sympathetic trunk of a cat in which there was an accessory ganglion at the origin of the greater splanchnic nerve. XIII. W., white ramus to the XIII thoracic nerve; I. G., gray ramus to the I lumbar nerve; I. W., white ramus of the I lumbar nerve; II. G., gray ramus to the II lumbar nerve.

from Cat 8 were especially instructive. Figure 9 shows that in the first lumbar segment of the trunk there was a ganglion, not connected with the spinal nerves by rami, located at the point of origin of the greater splanchnic nerve. The entire portion of the sympathetic trunk shown in the figure was cut in serial sections. A study of these sections shows that no branches, even of microscopic size, are given off from the trunk at the level of this ganglion except the splanchnic nerve. As this nerve leaves the trunk it carries with it a rather large bundle of peripherally placed unmyelinated fibers which closely resembles the crescentic area described in the trunk. It seems probable that this unusual bundle of fibers takes origin from the cells in this aberrant ganglion.

The observations so far recorded lead one to conclude that the greater splanchnic nerve is composed chiefly of preganglionic

autonomic fibers and visceral afferent fibers. In the majority of the specimens studied (eight out of ten) it was not possible to demonstrate any group of fibers that could be identified as post-ganglionic. We shall see that these conclusions agree with those of Langley. The statements which appear in the citation below will be found scattered through several pages of text (Schäfer's *Physiology*, vol. 2, pp. 644, 646, 648):

By dissection, it is easy to see that a large proportion of the splanchnic nerve fibers arise from the white rami communicantes, running in the sympathetic chain for a variable distance. In the cat and dog the fibers of the great splanchnic nerve can be traced upwards in the sympathetic chain as far as the sixth thoracic ganglion. And there is good reason to believe that all the splanchnic fibers are the direct continuation of the fibers of the white rami. It can easily be shown in the rabbit that the very great majority of the fibers running from the spinal cord to the abdominal viscera end in the prevertebral ganglia. After injection of a small amount of nicotine in the rabbit, the nerve roots, the splanchnics proper, and the inferior splanchnics have either no effect or a mere trace on the blood vessels or abdominal and pelvic viscera; but all the normal effects can be readily obtained by stimulating the fibers given off by the prevertebral ganglion. It has long been known that the major splanchnic contains a considerable number of non-medullated fibers, and it is in large part this fact which has led to the unquestioned belief that the ganglia of the sympathetic chain send fibers to the solar ganglia or to the abdominal viscera. If, then, the view which I have given above be accepted, namely, that very few if any fibers pass from the cells of the vertebral ganglia to the splanchnic nerves, we must take the non-medullated fibers to be preganglionic fibers which have lost their medulla.

According to Langley, the majority of the efferent fibers of the greater splanchnic terminate in the solar ganglion, though a few may pass on to more distal ganglia. He also admits the possibility that occasionally a few postganglionic fibers arising from cells in the ganglia of the trunk may run through the splanchnic to the coeliac plexus. The physiological experiments on which his conclusions are based are found in the papers by Langley and Dickinson ('89), Langley ('96 b), and Bunch ('97).

It will be seen that our histological results are in agreement with those obtained by physiological experimentation. We have seen reason to believe that the unmyelinated fibers in the splanchnic which Langley thought might be preganglionic fibers that had lost their sheaths, are instead afferent fibers. More convincing

evidence on some of these points will be presented in the paper which follows.

CONCLUSIONS

We shall make no attempt to summarize the detailed observations presented in the preceding pages, but will merely state a few general conclusions that seem warranted by the facts already given.

The segmental character of the sympathetic trunk is evident in its ganglia and gray rami. The fibers of each gray ramus arise chiefly, and sometimes exclusively, from the cells of its own segmental ganglion and are distributed through its associated spinal nerve. When two or more segmental ganglia are fused together the resulting compound ganglion gives rise to gray rami running to the corresponding spinal nerves. Except for compound ganglia like the cervical and stellate, the ganglia of the trunk are best designated by the number of the spinal nerve with which their gray rami are associated. The white rami have a restricted origin from the first thoracic to the fourth lumbar spinal nerves, inclusive, and their fibers are distributed through the sympathetic trunk to ganglia at higher and lower levels. A white ramus is in no special sense associated with its own segmental ganglion.

The gray rami contain in addition to the unmyelinated also a few, mostly fine, myelinated fibers. The latter are for the most part postganglionic. No preganglionic fibers run from the spinal cord to the sympathetic ganglia by way of these rami.

The white rami consist of myelinated fibers ranging from 1.5 to 13 μ , though fibers of more than 10 μ are rare except in the first two white rami and most of the large fibers have a diameter of about 6 or 7 μ . The majority of the myelinated fibers are small, measuring 1.5 to 3.5 μ . Most of these are preganglionic. The afferent components include myelinated fibers of all sizes, some of the very smallest as well as those of medium and large size, and also unmyelinated axons. The number of the large myelinated fibers varies greatly in the different white rami. They were found to be most numerous in the seventh to the tenth,

from which they run through the sympathetic trunk and the splanchnic nerves to the viscera.

The sympathetic trunk is to be looked upon as a series of more or less segmentally arranged ganglia bound together by fibers from the white rami. Above the sixth thoracic ganglion these fibers are chiefly ascending, below the tenth descending, but between the sixth and tenth both ascending and descending fibers are present. In addition to these fibers from the white rami, which make up the larger part of the cross-section of the trunk in the form of a large well myelinated oval field, there is also present throughout the thoracic sympathetic trunk a small well-defined bundle consisting chiefly of unmyelinated fibers. This in cross-sections appears flattened out like a crescent against the larger oval well myelinated field. Some of the fibers in the crescentic field are postganglionic, ascending or descending to reach adjacent gray rami. Others may be preganglionic fibers that have passed through one or more ganglia, giving off collaterals and losing their myelin sheaths.

In the upper part of the thoracic sympathetic trunk the oval well myelinated field is composed almost exclusively of fine myelinated preganglionic fibers, with very few large myelinated and unmyelinated afferent fibers. In the lower thoracic segments there are in addition to the preganglionic components also afferent fibers, both myelinated and unmyelinated, which increase steadily in number from the sixth internodal segment toward the origin of the greater splanchnic nerve.

The greater splanchnic nerve of the cat usually leaves the trunk at or just below the level of the thirteenth thoracic ganglion. It is formed by the separation of a large part of the oval well myelinated fascicle from the rest of the sympathetic trunk and is composed of fine myelinated preganglionic fibers, destined to end in the coeliac ganglion, and of both myelinated and unmyelinated afferent fibers. Occasionally it also contains a bundle of postganglionic fibers arising from cells in ganglia of the sympathetic trunk.

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AN EXPERIMENTAL ANALYSIS OF THE SYMPATHETIC TRUNK AND GREATER SPLANCHNIC NERVE IN THE CAT

S. W. RANSON AND P. R. BILLINGSLEY

Anatomical Laboratory of the Northwestern University Medical School¹

TEN FIGURES

A consideration of the facts presented in the preceding paper makes it clear that much could be learned through the study of the sympathetic trunk and splanchnic nerves after a variety of experimental lesions leading to the degeneration of nerve fibers arising from the spinal cord and spinal ganglia. We have five experiments to record, and since no two were just alike it will be best to consider each separately. The operations were performed under rigid asepsis. The general technique of exposing the spinal cord and nerve roots has been given in another place (Ranson and v. Hess, '15). After time had been allowed for degeneration, the lesion was verified at autopsy and the affected portion of the sympathetic trunk with its rami communicantes and the greater splanchnic nerve was removed and prepared for microscopic examination by fixation in osmic acid or by the pyridine silver technique. So far as was possible the material was cut into serial sections. The details of the five experiments follow.

Cat XI. Died seven days after the left sympathetic trunk was cut below the ninth thoracic ganglion and the ninth thoracic to the first lumbar spinal nerve roots cut proximal to the spinal ganglia as shown in figure 1. Examination of the gray rami of the tenth, eleventh, and twelfth thoracic nerves, showed that the few fine myelinated fibers which they normally contain were not in the process of degeneration. That is to say, these are not

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preganglionic efferent fibers coming from the spinal cord (page 421). The white rami of these three nerves showed marked changes. Most of the small myelinated fibers were undergoing degeneration, but there were a few which in cross-section appeared as sharply contoured black rings. These were apparently normal as were also all of the large myelinated fibers. In the trunk

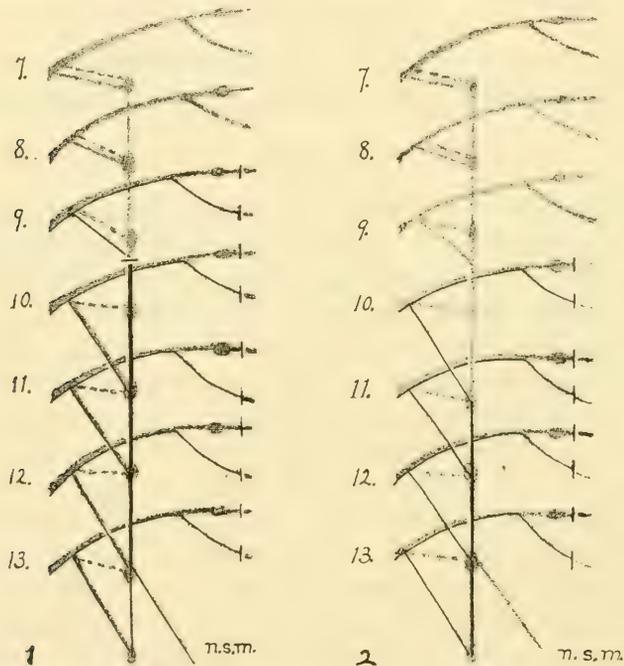


Fig. 1 Diagram of the thoracic sympathetic trunk with the corresponding spinal nerves and rami communicantes to illustrate lesions produced in cats IX and XII. The course of the degenerated fibers is indicated in black. N.S.M. = N. splanchnicus major.

Fig. 2 Diagram of the thoracic sympathetic trunk with the corresponding spinal nerves and rami communicantes to illustrate the lesions produced in cat VII. The course of the degenerated fibers is indicated in black. N.S.M. = N. splanchnicus major.

above the level of the tenth ganglion, i.e., between the lesion and the next lower ganglion, the oval field described in the preceding paper (fig. 5, page 426), was largely degenerated. Nearly all of the fine myelinated fibers were represented by

myelin globules, though a very few of them retained a normal appearance. There was very little degeneration of the large fibers, and, since the fibers present at this point must nearly all have been cut away from their cells of origin, we must interpret this result as showing that sufficient time had not elapsed for the degeneration of the large fibers. It has been shown by Van Gehuchten and Molhant ('10) that the speed of degeneration in myelinated fibers is inversely proportional to their size. In parts of the crescentic field the scattered fine myelinated fibers were normal, in other parts of this same field they were all degenerated.

A cross-section of the trunk below the tenth ganglion showed most of the scattered fine myelinated fibers in the crescentic field to be normal in appearance, indicating that few of them took origin above the cut. The oval field had the same appearance as in the section described above. The tenth white ramus could be seen in longitudinal section as it entered the trunk. The majority of its fine myelinated fibers had their myelin broken up into globules, giving them a beaded appearance. Its large fibers and a few of the small ones were normal.

Sections of the greater and lesser splanchnic nerves showed that most of the fine myelinated fibers were degenerated, while the large fibers were all or nearly all normal. These results were confirmed by a study of teased preparations of the twelfth inter-nodal segment of the trunk and the greater splanchnic nerve. In these teased preparations it was possible to see that a few large fibers were also in the early stages of degeneration.

Cat VII, killed thirty-three days after section of the roots of the left tenth, eleventh, twelfth, and thirteenth thoracic and first lumbar nerves proximal to the spinal ganglia as indicated in figure 2.

Sections of the trunk below the entrance of the tenth white ramus showed a circumscribed area of degeneration at the surface of the trunk. In this area there were two large and a considerable number of small normal myelinated fibers. This degenerated area was taken to represent the tenth white ramus, although enough sections were lost from the series at this level to prevent our tracing that ramus directly into the degenerated area.

The white ramus of the eleventh thoracic nerve contained myelinated fibers of all sizes in about equal proportions. These were scattered fairly evenly throughout the cross-section and were separated by a large amount of degenerative material (fig. 3). It was obvious that the preganglionic fibers had degenerated as the result of the section of the ventral root. The fibers which remained were afferent and arose from the cells in the spinal ganglia. These afferent myelinated fibers were of all

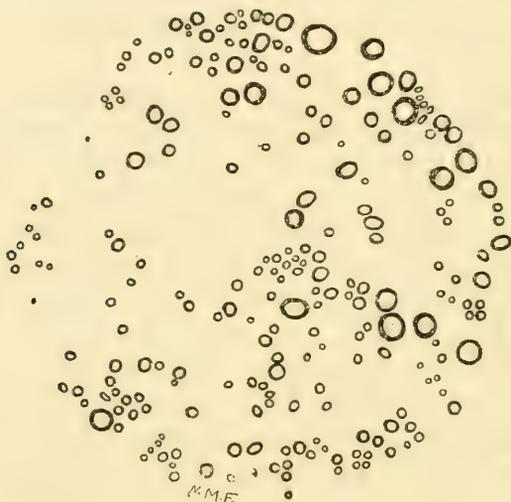


Fig. 3 Eleventh thoracic white ramus of the cat after the degeneration of all the preganglionic efferent fibers. All of the remaining fibers are afferent. Osmic acid. $\times 425$.

sizes, as is shown in the illustration, but as a rule there are relatively more large ones than in this ramus.

In the serial sections the degenerated eleventh white ramus could be traced into the trunk above the level of the twelfth thoracic ganglion (fig. 4 a). Here it occupied a position superficial to that occupied by the degenerated fibers from the tenth (fig. 4 b). The rest of the oval field was occupied by large and small myelinated fibers and was normal in appearance. Only a small part of this is shown in the illustration.

A little farther down in the trunk the fibers derived from the tenth and eleventh white rami formed a single well-defined bundle which because of the degeneration was easily distinguished from the normal part of the trunk. This degenerated bundle could be traced through the trunk beyond the origin of the first splanchnic nerve. None of the degenerated fibers seemed to go



Fig. 4 From the eleventh thoracic internodal segment of the sympathetic trunk of cat VII, showing the partially degenerated fascicles derived from a) the eleventh and b) the tenth white ramus. Osmic acid. $\times 260$.

into the greater splanchnic nerve, which was normal in appearance and seemed to receive all or nearly all of the undegenerated oval well myelinated portion of the trunk. In this case all of the fibers of the greater splanchnic nerve came from the white rami above the tenth. In one instance it received a few fibers from the tenth white ramus (Cat XIV) in another (Cat XVI) all of its fibers came from above the ninth.

Above the level of the eleventh ganglion there was some evidence of degeneration, and this could be followed up as far as the tenth. The evidence of an ascending degeneration was, however, by no means as clear as that for a descending degeneration.

The gray rami of the eleventh, twelfth, and thirteenth thoracic nerves were normal, containing a few fine myelinated fibers. No axon stain was made. The white ramus of the tenth nerve was not well stained, that of the eleventh nerve has already been described and figured. The twelfth white ramus contained a fair number of medium and small-sized fibers, but no large ones. Most of the normal fibers in the thirteenth white ramus were also of medium and small size. It is clear that in these rami of this cat the afferent fibers were for the most part of medium and small size. We regard the paucity of large fibers as somewhat atypical.

The point which stands out most clearly as a result of this experiment is that the majority of the fibers of the tenth and eleventh white rami turn downward in the trunk, forming a well-defined fascicle near its surface which can be traced in the trunk beyond the origin of the great splanchnic nerve. At least in the upper part of this course the fibers from the two rami remain separate, those from the eleventh lying superficial to those of the tenth. This lamination of the fibers in the trunk in flattened bundles, corresponding to the white rami from which they come, explains why it is easy to follow these fibers by dissection through the trunk to the splanchnic nerve, as is claimed by Langley ('00).

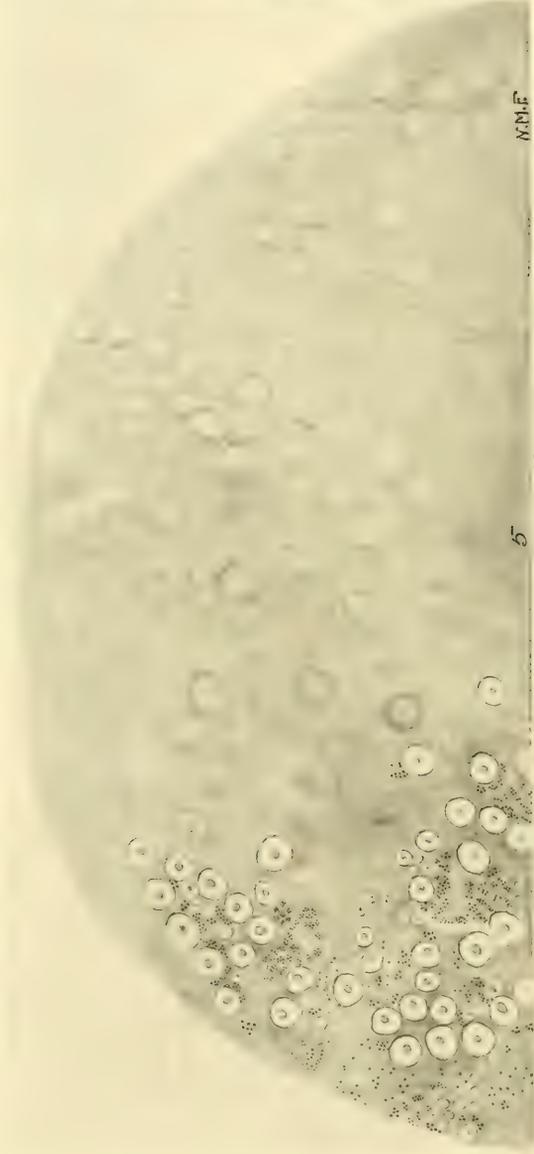
The degeneration of the preganglionic fibers in the lower thoracic white rami enables us to isolate the myelinated sensory fibers and to see that these include fibers of all sizes. These can be seen not only in the rami themselves, but also in the degenerated fascicles representing these rami in the trunk.

Cat XII. The sympathetic trunk was cut on the left side at the level of the ninth internodal segment and the roots of the left ninth, tenth, eleventh, twelfth, and thirteenth thoracic and first lumbar nerves were cut proximal to the spinal ganglia, as shown in figure 1. The cat was killed thirteen days after the operation.

The gray rami of the tenth, eleventh, twelfth, and thirteenth thoracic nerves were normal, containing the usual small number of fine myelinated fibers, except that in the tenth there were four or five fine fibers which did not appear normal. The white rami of these nerves were in large part degenerated, although scattered through each there were a considerable number of myelinated fibers of all sizes. The proportion of large and small fibers did not seem to be constant. These undegenerated fibers might, so far as the data given by this experiment is concerned, have had their cells of origin in the spinal ganglia or in the ganglia of the sympathetic trunk. Other experiments will show that the cells were located in the spinal ganglia.

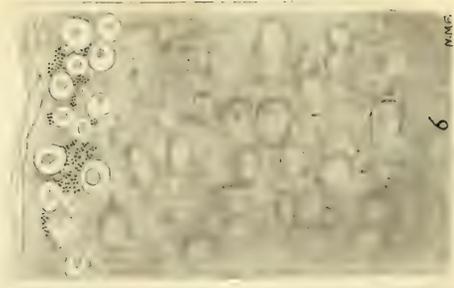
The part of the trunk including the tenth thoracic ganglion and internodal segment was fixed in osmic acid and cut into serial sections. Just below the tenth ganglion all the fibers in the trunk were degenerated. Many of the larger myelinated fibers were still seen in process of degeneration. A little lower down a very small branch was seen entering the trunk, probably an accessory white ramus from the tenth nerve, which contained eleven myelinated fibers chiefly of medium size. These could be followed down in the trunk as a small compact fascicle for some distance, but became lost just above the point where the tenth white ramus entered the trunk, at which point the serial sections were imperfect, but it probably joined with the fibers from this ramus as it was not recognizable as a separate fascicle below the point where this ramus entered. Below the point of entrance of the tenth white ramus there was a well-defined fascicle of about the size of the ramus, composed of myelinated fibers of all sizes rather widely separated from each other. This fascicle from which the bulk of the fine myelinated fibers had disappeared could be followed downward at the surface of the trunk throughout the series of sections which did not include the entrance of the eleventh ramus.

The twelfth thoracic ganglion and adjacent portions of the trunk were prepared by the pyridine silver technique. Most of the fibers in the trunk were degenerated, but the crescent could be recognized and contained a great many normal fibers, the



5

N.M.F.



6

N.M.F.

Fig. 5 From the twelfth thoracic intermodal segment of the sympathetic trunk in cat XII which had suffered lesions as indicated in figure 1. At one side of the degenerated trunk is seen a group of normal fibers derived from the tenth and eleventh white rami. Pyridine silver. $\times 425$.

Fig. 6 From the greater splanchnic nerve of cat XII. Pyridine silver. $\times 425$.

staining of these fibers was not very satisfactory, however. On one side of the trunk there was a rather large area containing scattered normal myelinated fibers, many of which were of large size. This area represented the contribution of the tenth and eleventh white rami, and the myelinated fibers in this area were the afferent fibers from these rami. Among these normal myelinated afferent fibers were considerable numbers of unmyelinated fibers, also of normal appearance and showing a marked tendency to arrange themselves in groups, as seen in figure 5. Throughout the rest of the trunk all the fibers, both myelinated and unmyelinated, were degenerated. The fibers in this completely degenerated area had their cells of origin located above the point of section of the trunk, and from what has already been said in this and the preceding paper we know that they entered the trunk by way of the white rami above the tenth. The tenth and eleventh white rami contributed the fibers found in the area which is only partly degenerated, and since the roots of the corresponding spinal nerves were cut proximal to the spinal ganglia the only normal fibers which these rami could contribute would be afferent with cell bodies located in the spinal ganglia. We are therefore justified in interpreting as afferent all the fibers in this area, including large and small myelinated and unmyelinated fibers.

We have both osmic acid and pyridine silver preparations of the greater splanchnic nerve. This was almost completely degenerated. There was, however, at one side a small group of normal myelinated fibers. These could be seen in both osmic acid and pyridine silver preparations. In the latter, as shown in figure 6, there were also some normal unmyelinated fibers to be seen mingled with the others. The rest of the splanchnic was completely degenerated except for a very small bundle of unmyelinated fibers on the other side of the cross-section. In connection with this bundle there were some nerve cells and the fibers of this group were probably to be regarded as postganglionic, arising from the cells of a small ganglion in the course of the splanchnic. The bundle of myelinated and unmyelinated fibers was clearly a continuation of a part of that found in the trunk and illustrated in figure 5.

Serial sections of the trunk including the first lumbar ganglia and the origin of the second splanchnic nerve, stained with osmic acid, were examined. In the trunk below the thirteenth thoracic ganglion and the origin of the greater splanchnic nerve the majority of the fine myelinated fibers had degenerated. There were present, however, normal myelinated fibers of all sizes rather widely separated from each other by degenerated material. These were the afferent fibers of the tenth, eleventh, and twelfth white rami. The lesser splanchnic had the same structure as the thirteenth thoracic internodal segment.

Cat XIV. Killed thirty-two days after section of the roots of the tenth distal, and those of the eleventh thoracic nerve proximal, to the spinal ganglia (fig. 7). In osmic acid preparations of the trunk including the tenth, eleventh, and twelfth thoracic ganglia, the tenth white ramus could be seen entering the trunk. It contained six or eight normal fine myelinated fibers, but except for these was completely degenerated. It could be traced down the trunk as a sharply defined fascicle occupying a superficial position. In addition to the half-dozen fine myelinated fibers that could be traced in along with the tenth ramus this degenerated area became invaded by a few fine myelinated fibers that worked their way into it from the normal part of the trunk.

The white ramus of the eleventh nerve could also be traced into the trunk. It contained a small number of large fibers and a somewhat greater number of medium-sized and small fibers. These normal fibers were separated by a considerable amount of unstained material representing the degenerated preganglionic fibers. These normal and degenerated fibers of the eleventh white ramus could be followed down the trunk where they could be seen to occupy a position adjacent and partially superficial to the fibers from the tenth ramus.

The bundles from the two degenerated rami presented a marked contrast. That of the tenth contained only a few fine myelinated fibers, that of the eleventh a much greater number of all sizes. The latter are easily accounted for as afferent fibers with their cells of origin in the eleventh thoracic spinal ganglion.

The half-dozen fine fibers traced from the tenth ramus are more difficult to understand. It must be admitted that such fibers are just what one would find if sensory fibers arising in the sympathetic ganglia pass back along the white rami to end in the spinal ganglia (p. 333-334). They might also be accounted for as postganglionic fibers accompanying the white ramus (p. 412-418).

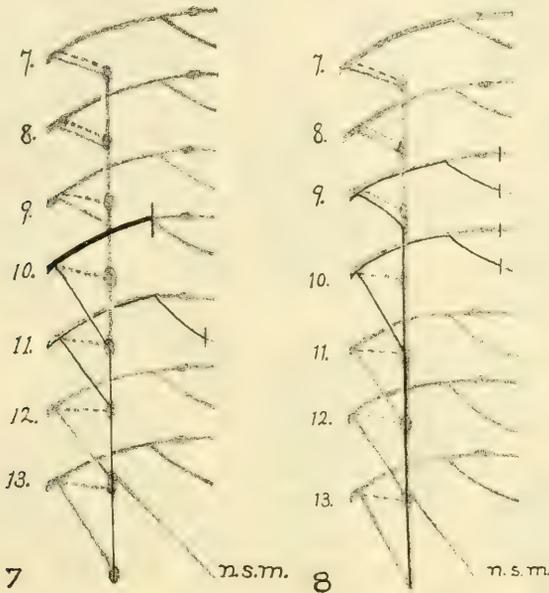


Fig. 7 Diagram of the thoracic sympathetic trunk with the corresponding spinal nerves and rami communicantes to illustrate the lesions produced in cat XIV. N.S.M. = N. splanchnicus major.

Fig. 8 Diagram of the thoracic sympathetic trunk with the corresponding spinal nerves and rami communicantes to illustrate the lesions produced in cat XVI. N.S.M. = N. splanchnicus major.

Osmic acid preparations of the greater splanchnic nerve showed a very restricted area of degeneration, almost the entire nerve being of normal appearance.

Cat XVI. Killed twenty-two days after section of the roots of the ninth and tenth thoracic nerves proximal to the spinal ganglia (fig. 8). The trunk including the ninth, tenth, and

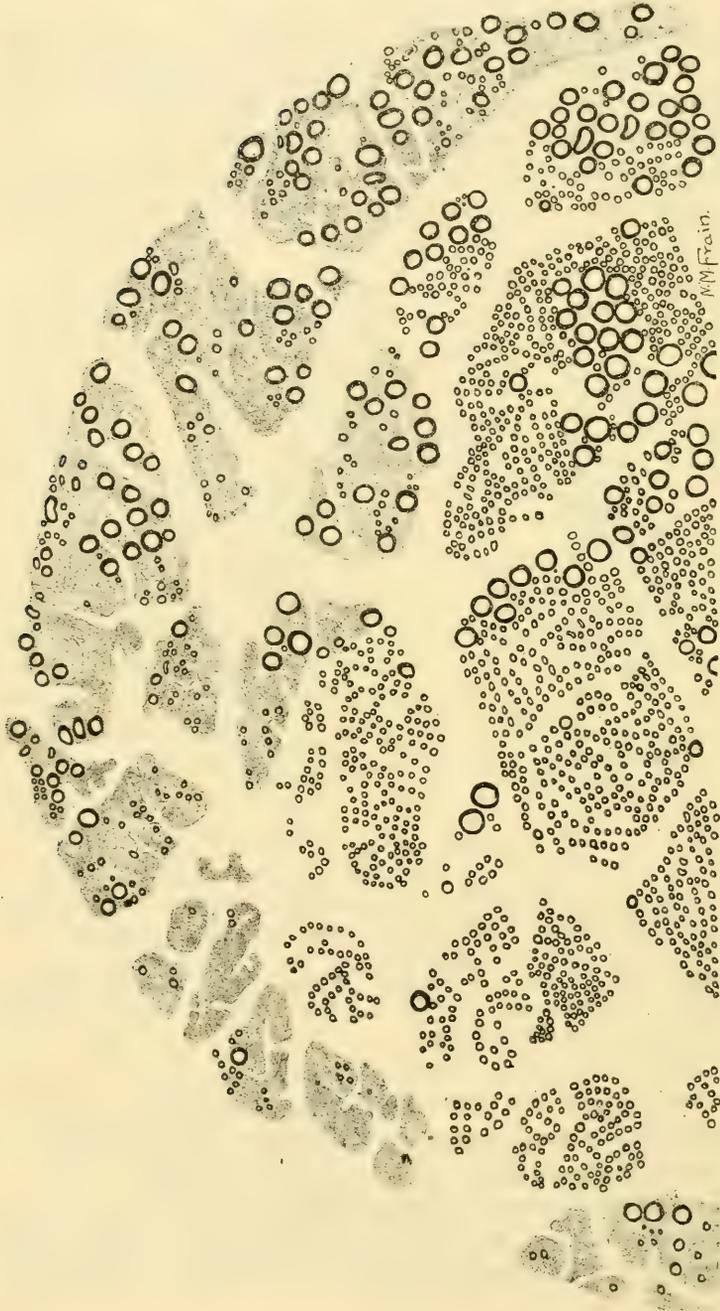


Fig. 9 From the eleventh thoracic internodal segment of the sympathetic trunk in cat XVI. A superficial, crescentic fascicle from which the fine preganglionic fibers have disappeared represents the contribution of the ninth and tenth white rami. It contains afferent fibers only. Osmic acid. $\times 425$.

eleventh thoracic ganglia, stained with osmic acid, was cut into serial sections. In these it was possible to identify the ninth white ramus which contained a considerable number of normal myelinated fibers, of which the greater number were large. The fibers from this ramus could be followed as a superficial bundle down the trunk to the point where the tenth ramus entered. This contained in addition to the degenerated preganglionic fibers a considerable number of normal myelinated fibers, and of these there were rather more small than large ones. As each ramus entered it lay close to the crescentic field of unmyelinated fibers and the area of the tenth was immediately adjacent to that of the ninth. A little farther caudad it was no longer possible to separate the two areas, the two together being spread out over nearly half the circumference of the trunk as shown in figure 9. In this figure the degenerated bundles are indicated by the stippled background. The myelinated fibers in these bundles are afferent, and it will be seen that they are of all sizes and there are about as many of one size as of another.

Pyridine silver preparations of the twelfth thoracic internodal segment were especially instructive (fig. 10). The greater part of the trunk was normal and was characterized by the presence of great numbers of small myelinated fibers. Large myelinated and unmyelinated fibers were also in evidence. On one side there was seen a condensation of the unmyelinated fibers which represents the crescentic field normally present at all levels of the thoracic sympathetic trunk. Another area, rather sharply limited, from which the majority of the fine myelinated fibers had disappeared, contained myelinated fibers of all sizes in about equal proportion and also unmyelinated axons. The background presented a peculiar reddish-yellow tone which we have found characteristic of degenerated fascicles stained by this method. It is obvious that the fine myelinated fibers had degenerated and that this is the same fascicle that is seen in figure 9. A comparison of the two figures will show that the areas occupied by the degenerated fibers have undergone great shrinkage in passing through the steps of the pyridine silver technique, and because of this the large myelinated and unmyelinated fibers



Fig. 10 From the twelfth thoracic internodal segment of cat XVI. a) Normal portion of the oval well myelinated fascicle. Large and small myelinated and unmyelinated fibers derived from the white rami above the ninth; b) normal fasciculi of unmyelinated fibers; c) fascicle representing the ninth and tenth white rami containing afferent myelinated and unmyelinated fibers. Pyridine silver. $\times 425$.

are more closely grouped together in figure 10. Since this partially degenerated fascicle could be traced to the white rami of the ninth and tenth thoracic nerves, the roots of which had been cut proximal to the spinal ganglia, it is clear that the normal fibers remaining in this fascicle were not preganglionic autonomic fibers. They must either have been afferent, with their cells of origin in the spinal ganglia, or they must have been directed from the sympathetic ganglia toward the spinal ganglia or spinal cord. The complete degeneration of the greater part of the trunk at the level of the twelfth thoracic internodal segment after section of the trunk below the ninth thoracic ganglion in Cat XII, as illustrated in figure 5, shows that these fibers do not take origin from the sympathetic ganglia.

The partially degenerated fascicle from the ninth and tenth white rami made no contribution to the greater splanchnic nerve, but was continued along the trunk into the lesser splanchnic. Osmic acid and silver preparations of the greater splanchnic showed that this nerve was entirely normal, while similar preparations of the lesser splanchnic showed that it had the same structure as the partially degenerated fascicle in the trunk.

SUMMARY

Section of the thoracic spinal nerve roots proximal to the spinal ganglia results in a degeneration of all of the preganglionic autonomic fibers in the corresponding white rami, but leaves the afferent fibers intact. The white rami studied were the ninth, tenth, and eleventh. The fibers from these partially degenerated rami could be traced caudad in the trunk, those from each ramus forming a well-defined fascicle. It is this arrangement which makes it possible to trace the fibers of the splanchnic nerve by dissection to the white rami as high as the sixth. The afferent fibers, which alone remained in these partially degenerated rami and the corresponding fascicles of the trunk, included myelinated fibers of all sizes and many that were unmyelinated. They took origin from the cells of the spinal ganglia. In one case after section of the tenth thoracic nerve distal to the spinal ganglion we found a half-dozen normal myelinated fibers in the corre-

spending white ramus, but these may have belonged to a small gray ramus accompanying it.

When the sympathetic trunk was cut caudad to the ninth thoracic ganglion all the fibers degenerated in the oval well myelinated field in the twelfth thoracic internodal segment, except in a fascicle derived from the tenth and eleventh white rami, which entered the trunk caudad to the cut. The fibers in this oval field, therefore, come from the spinal cord and spinal ganglia by way of the white rami; at least this experiment proves that none of them in the twelfth thoracic internodal segment come from the ganglia of the sympathetic trunk below the ninth, and under the circumstances there is no reason to suppose that they might come from those situated farther cephalad. In this experiment the greater splanchnic nerve was degenerated except for a small bundle of fibers that could be traced into it from the fascicle representing the white rami of the tenth and eleventh nerves, and a very small number of unmyelinated fibers obviously associated with a small group of ganglion cells located in the course of the nerve. It is clear that in this case the splanchnic nerve received no fibers from the ganglia of the sympathetic trunk below the ninth, and there is every reason to believe that all of its fibers, except those arising from the small ganglion located in its course, came from the spinal cord and spinal ganglia (p. 434-436). Exclusive of an occasional well-defined bundle of obviously postganglionic fibers found in two out of ten normal specimens of the greater splanchnic nerve, the unmyelinated fibers of this nerve are derived from spinal ganglia by way of the white rami. The number of rami from which this nerve may receive fibers seems to vary, but it usually does not contain any from those below the ninth.

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THE OLFACTORY ORGANS OF DIPTERA

N. E. McINDOO

Bureau of Entomology, Washington, D. C.

FIFTY-FIVE FIGURES

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INTRODUCTION AND METHODS

The results herein recorded are a continuation of the writer's investigation concerning the morphology of the olfactory pores. Up to date, including the present results, these organs have been carefully studied in Hymenoptera, Coleoptera, Lepidoptera, and Diptera. The chief object of the present investigation is to determine whether the olfactory pores are better adapted anatomically than the antennal organs to receive olfactory stimuli.

The investigators who have performed experiments on flies with mutilated antennae have concluded that these appendages bear the olfactory organs, regardless of whether or not the antennal organs are anatomically fitted to receive olfactory stimuli. Since these investigators failed to study sufficiently the behavior of the insects investigated, it is possible that the responses observed misled them in determining the seat of the olfactory organs.

In 1857 Hicks discovered porelike organs on the wings and halteres of flies, and claims that they are similar in structure and probably have the same function, that of smell. He was able to trace a nerve to each group of organs, the one going to the halter being the larger. The same author ('59) found these organs in *Hippobosca equina* and *Tipula oleracea*, and in 1860 discovered them on the legs of various insects, including Diptera. In the same year Leydig described and figured the same organs on the halteres of *Calliphora (Musca) vomitoria* and *Eristalis tenax*. Each one of the foregoing authors was able to trace nerves to these pores, but they could not understand the internal anatomy of them.

Graber ('82) described and figured these organs on the wings and halteres of several Diptera, and called them chordotonal organs, because he thought the peripheral ends of the sense cells were sensory chords.

Lee ('85) described and figured in detail these structures on the halteres of *Calliphora vomitoria*, but he, like the preceding authors, failed to understand their internal anatomy.

The paper of Weinland ('90) is the most comprehensive one dealing with the sense organs found on the halteres, and as a whole it is the best, although he did not clearly understand the anatomy of these structures. He gives a good review of the literature pertaining to the halteres, and according to him the earliest writers (beginning in 1711) said that these appendages served in maintaining the equilibrium of the insect while flying; hence the Latin name, *halteres* and the English translation, *balanciers*. About a century later experiments proved that flies with amputated halteres could fly, although not as well,

and consequently the preceding view has long since been abandoned. Another old view was that the halteres aid in respiration. Hicks and Lee regarded the structures as olfactory organs, while Leydig and Graber thought they were auditory in function. Weinland determined that the halteres in vibrating rapidly perform a number of different movements, and chiefly for this reason he thinks that the organs borne by them bring about the perception of movements, thereby steering the flight of the insect. He asserts that since the antennae bear the olfactory organs, the organs on the halteres certainly do not perform the same function.

Nagel ('94), in commenting on the probable function of the halteres, thinks that the first four preceding views have been abandoned, but he is a strong advocate of Weinland's view.

The paper of Prashad ('16) seems to be the most recent one concerning the sense organs on the halteres, and this author studied only the halteres of the mosquito, *Ochlerotatus pseudo-taeniatus* Giles. He evidently did not have access to most of the literature on this subject and consequently has added little knowledge concerning these organs. He thinks that each organ has an external opening and found two scalpel groups of pores on each halter, while the present writer found only one scalpel group on each halter of mosquitoes belonging to other genera.

McEwen ('18) has just recently observed the sense organs on the wings of *Drosophila ampelophila*. He determined "that these organs had nothing to do with the response to light" (pp. 85 to 87), but performed no experiments using odor stimuli.

To obtain material for the study of the disposition of the olfactory pores, dried museum specimens were largely used. These specimens were obtained of Messrs. C. T. Greene and C. H. Popenoe through the courtesy of Dr. L. O. Howard. Mr. Greene is furthermore to be thanked for verifying the identification of all the species used. Fresh material was fixed in the modified Carnoy's fluid, and was embedded in celloidin and paraffin. The sections were cut three and five microns in thickness, and were stained in Ehrlich's hematoxylin and eosin. All the drawings were made by the writer and all are original except figures 50 to 55; these represent the antennal organs of flies

and mosquitoes, and were copied from Hauser, vom Rath, and Nagel. The drawings were made at the base of the microscope with the aid of a camera lucida.

THE OLFATORY PORES

Before making a study of the anatomy of the organs, called the olfactory pores by the writer ('14 a), the distribution and number of them were first investigated.

Disposition of pores in Musca domestica

Owing to an abundance of material and to the economic importance of the house fly, the olfactory pores of this insect have been studied and drawn in detail, and it is hoped that such work will encourage experimentation along practical lines.

a. Pores on legs. Seven groups of pores lie on each leg and the disposition of them is as follows: nos. 1 to 4 on the inner surface of the leg (fig. 1) and nos. 5 to 7 on the outer surface; nos. 1, 2, and 5 being on the trochanter, nos. 3 and 6 on the femur, and nos. 4 and 7 on the tibia. Nos. 1 and 2, consisting of 5 and 8 pores, respectively, always lie on the anterior margin of the leg, while no. 3, composed of 11 pores, lies on the posterior margin. Nos. 4 and 7, when present, may lie on either or both margins of the leg and the number of pores in each group varies from one to three. No. 5, consisting of 3 pores, usually lies near the posterior margin, while no. 6, composed of 1 pore, lies near the anterior margin.

b. Pores on wings. Six groups and several scattered pores lie on each wing and the disposition of them is as follows: Nos. 8 to 11 and scattered pores *a* to *c* lie on the dorsal surface of the wing (fig. 2), while nos. 12 and 13 and the scattered pores *d* and *e* lie on the ventral surface. No. 8, consisting of about 24 pores, lies at the proximal end of the propterygium (*Pr*), while nos. 9 to 13 lie on the subcostal (*Sc*) vein in about the positions as indicated by the numbers in figure 2. The number of pores in each of these groups varies slightly, but the average number in each is about as follows: no. 9 has 50 pores; no. 10, 12 pores; no. 11, 10 pores;

No. 12, 9 pores, and no. 13, 18 pores. The scattered pores vary considerably in number and position and they are located about as follows: 1 at *a* on the base of the humeral vein; 2 always present at *b* on the distal end of the first radial vein; 1 at *c* on the radiomedial vein; 1 at *d* on the proximal end of the first radial vein; and 1 at *e* on the fourth radial vein.

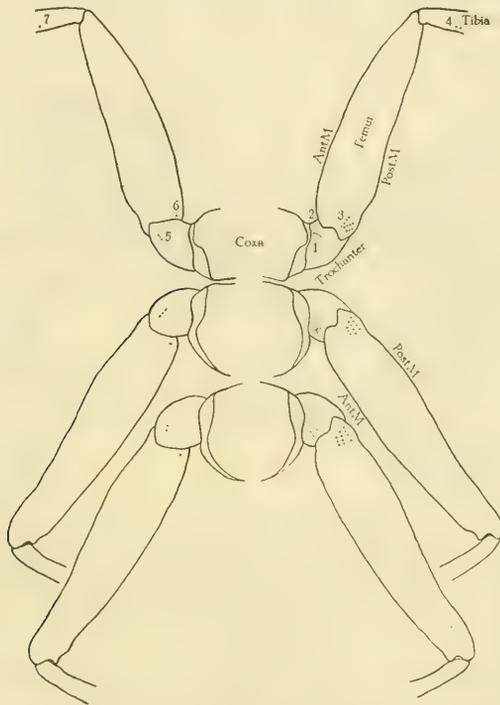


Fig. 1 Portions of legs of house fly (*Musca domestica* ♂), showing location of groups nos. 1 to 7 of olfactory pores. The drawings at the right represent the inner surface and those at the left the outer surface. *AntM* and *PostM* stand for anterior and posterior margins. $\times 20$.

c. Pores on halteres. Five groups and 1 isolated pore lie on the base of each halter (fig. 3); nos. 14 to 16 and the isolated pore at *f* being found on the dorsal surface and nos. 17 and 18 on the ventral surface. The pores lie on plates whose outlines are similar in shape to the contours of the groups of pores themselves;

hence, the pores in nos. 14 and 18 have been called scalpel organs because each group lies on a plate shaped like a scalpel. No. 15 lies on the basal plate, consequently its pores have been called basal organs. No. 16 lies on the anterior end of the basal plate, while no. 17 on the opposite side of the halter lies on the proximal end of the scalpel plate; the pores in these two groups are like in structure, and since their structure is like that of those on the wings they have been called Hicks' organs. In the following pages it is shown that the scalpel and basal organs are unlike in structure and also neither one of these two types is exactly like the Hicks' organs. The isolated pore at *f* is found on only about

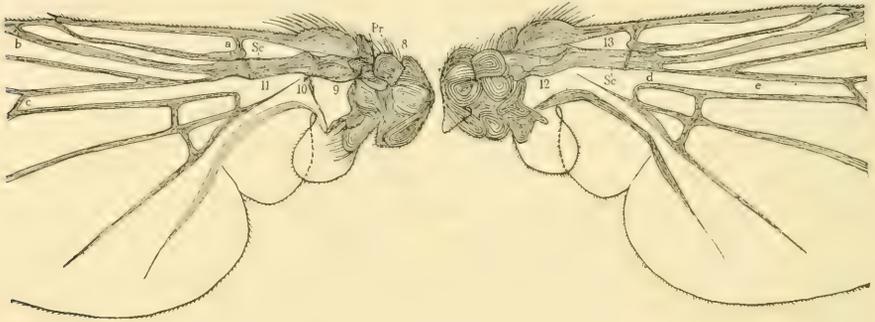


Fig. 2 Portion of left wing of *Musca domestica* ♂, showing location of groups nos. 8 to 13 of olfactory pores on protergyium (*Pr*) and on subcostal vein (*Sc*) and the scattered pores at points marked *a* to *e*. The drawing at the left represents the dorsal surface and the one at the right the ventral surface. $\times 20$.

one-half of the halteres of the house fly, and it has been called an undetermined type by Weinland.

Considering the twenty halteres belonging to five males and five females, the numbers of pores in the groups are as follows: In no. 14 they vary from 74 to 110 with 92 as an average; in no. 15, from 70 to 96 with 88 as an average; in no. 16, from 10 to 11 with almost 11 as an average; in no. 17, from 3 to 8 with 7 as an average, and in no. 18, from 74 to 110 with 93 as an average.

Disposition of pores in other species

In making a comparative study of the disposition of the olfactory pores in Diptera, 47 species, belonging to 38 genera and representing 21 families, were used. In most cases only one specimen of each species was employed, and whenever a portion of an appendage or an entire appendage was missing or was badly mutilated in being prepared for study, the supposed number

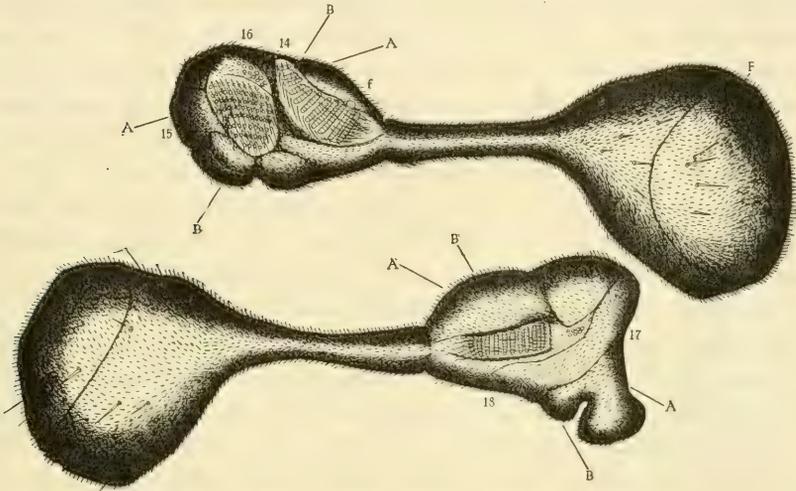


Fig. 3 Right halter of *Musca domestica* ♂, showing location of scalpel pores (nos. 14 and 18), basal pores (no. 15), Hicks' pores (nos. 16 and 17) and the undetermined type (*f*). The upper drawing represents the dorsal surface and the lower one the ventral surface. The upper margin of each drawing represents the anterior surface and the lower margin the posterior surface. *F*, one of the folds caused during preparation of halter. $\times 100$.

of pores on this portion or entire appendage was regarded the same as the number found on the corresponding portion or entire appendage on the opposite side of the body. Since the pores on only one specimen for each species were counted, the total number of pores recorded cannot be a fair average. Besides this error, there is also another small probable error for each species, because a few of the pores were probably overlooked, and often, as on the tibiae, it was impossible to distinguish the

olfactory pores from hair sockets. As a rule, only the legs, wings, and halteres were examined, although in several instances the chitinous parts of the reproductive organs and the mouth parts were also examined, but usually no olfactory pores were seen on them. The sex of the species, except in a few cases, was not determined.

a. Pores on legs. The disposition of the pores on the legs is more similar to that of those on the legs of Hymenoptera (McIndoo, '14 b) than to those on the legs of Lepidoptera or Coleoptera (McIndoo, '15, '17). Pores were found on each trochanter and femur examined, but sometimes none was seen on a tibia and not one was ever observed on a tarsus. The distribution of them is similar to that of the house fly, already described. The total number of them varies considerably, depending on the number of groups present and the size of the species. The groups are usually conspicuous and the one on the femur is quite characteristic; it consists of two or three rows of pores variously arranged, depending on the genus examined.

b. Pores on wings. The disposition of the pores on the wings is more similar to that of those on the wings of Lepidoptera than to those on the wings of Hymenoptera or Coleoptera. In Lepidoptera the pores are well grouped, while in Diptera they are poorly grouped and consequently not much reliance can be placed upon the number of groups recorded; for this reason the variation in the number of groups need not be discussed. Lepidoptera have more isolated pores than have Diptera, and in the former order they may extend along the full length of the veins, while in Diptera they are never found farther than two-thirds the distance from the base of the wing. The propterygium (fig. 2, *Pr.*) was often lost during the preparation of the integument, but group No. 8, was usually found on it whenever this part of the wing was present. This is the first time for this group to be reported.

c. Pores on halteres. As already mentioned on page 462, there are four types of pores on the halteres, although the undetermined type, consisting of large isolated pores, should be called isolated Hicks' pores. The groups of Hicks' pores are seen only with

much difficulty and doubtless many of them were overlooked. The writer is the only observer who has seen a group of them on either side of the halter. Since the number of pores on the halteres has never been tabulated, the following table is presented. A reference to this table will show the minor variations in these pores better than a description of them, therefore only the more important variations need be pointed out. The Hicks' groups were found on 75 per cent of the halteres; a basal group on each halter, except in one species (no. 2); one or two scalpel groups on each halter; and the undetermined pores on 45 per cent of the halteres examined. One basal group (excepting no. 2) was invariably present on each halter, while two scalpel groups were observed on each halter examined, except in the three mosquitoes (nos. 3 to 5) and two of the wingless forms (nos. 13 and 48); only one scalpel group was seen on each halter of these five species.

d. Pores on abnormal species. To determine what effect environmental conditions has had upon the disposition of the olfactory pores, seven species were selected for this purpose. Table 3 (p. 470) shows to what families they belong and the number of their olfactory pores in comparison with the pores of the normal species. In table 2 they are arranged according to the degree of degeneracy of the wings and halteres and they shall be described accordingly.

The sheep tick (45 *Melophagus ovinus*) is much compressed; has no signs of wings and halteres; its legs are short and the segments are wide; the entire integument is thick and tough. Olfactory pores were found only on the trochanters and femora; their distribution is normal, but their number is reduced. The bat tick (48 *Nycteribia bellardii*) is also much compressed and has no compound eyes; its wings are totally wanting and its halteres are unusually small. The disposition of the pores on its legs is normal, but on the halteres the pores are comparatively few; the scalpel type being reduced to only one group per halter (table 1). The so-called wingless female of the snow-fly (2 *Chionea valga*) copulates on the surface of the snow and it seems to be abnormal in four ways; 1) The number of pores on

TABLE 1

Number of organs in the four types of olfactory pores found on the halteres of Diptera

NUMBER AND NAMES OF SPECIES	TYPE							Total Number of pores
	*Nos. 15 and 17 Hicks'		No. 15 Basal		Nos. 14 and 18 Scalpel		Undetermined	
	Number of groups	Number of pores	Number of groups	Number of pores	Number of groups	Number of pores		
1. <i>Tipula</i> sp.....			2	90	4	134	6	230
2. <i>Chionea valga</i> ♀.....					4	26	2	28
3. <i>Culex pipiens</i>			2	130	2	152	4	286
4. <i>Aedes vexans</i>			2	156	2	138	4	298
5. <i>Corethra cinctipes</i>			2	160	2	132	6	298
6. <i>Mycetophila punctata</i>			2	158	4	189	3	350
7. <i>Sciaria inconstans</i>	2	10	2	140	4	176	4	330
8. <i>Macrosargus decorus</i>	3	45	2	272	4	552	1	870
9. <i>Tachydromia</i> sp.....	2	6	2	72	4	200	4	282
10. <i>Rhamphomyia abdita</i>			2	152	4	384		536
11. <i>Psilopus</i> sp.....	2	20	2	130	4	438		588
12. <i>Aphiochaeta</i> sp.....			2	65	4	209	4	278
13. <i>Pulicifora borinquensis</i> ♀.....			2	64	2	72	4	140
14. <i>Calobata antennipes</i>	2	10	2	128	4	292		430
15. <i>Piophila casei</i>	2	18	2	140	4	231		389
16. <i>Tritoxa flexa</i>	4	16	2	65	4	191		272
17. <i>Anacampta latiuscuta</i>	4	34	2	138	4	307	6	485
18. <i>Euxesta notata</i>	2	12	2	145	4	277		434
19. <i>Dacus cucurbitae</i>	2	14	2	168	4	332		514
20. <i>Milichiella lacteipennis</i>	2	20	2	140	4	311		471
21. <i>Drosophila busckii</i>			2	108	4	180		288
22. <i>Drosophila amœna</i>	2	12	2	100	4	212		324
23. <i>Drosophila funebris</i>	2	12	2	108	4	236	2	358
24. <i>Paralimna decipier</i>	2	4	2	96	4	209		309
25. <i>Paralimna appendiculata</i>	2	4	2	120	4	216	2	342
26. <i>Ephydra gracilis</i>	2	12	2	100	4	192	2	306
27. <i>Chlorops coxendix</i>			2	74	4	182		256
28. <i>Tetanocera plumos</i>	4	36	2	194	4	358		588
29. <i>Helomyza tineta</i>	4	22	2	160	4	340		522
30. <i>Scatophaga stercoraria</i>	2	18	2	150	4	302		470
31. <i>Scatophaga furcata</i>	4	22	2	150	4	300		472
32. <i>Homalomyia canicularis</i>	2	20	2	166	4	306		492
33. <i>Hylemyia simpla</i>	2	24	2	166	4	276		466
34. <i>Phorbia brassicae</i>	4	39	2	144	4	319		502
35. <i>Phorbia fusciceps</i>	2	22	2	140	4	340		502
36. <i>Coenosia</i> sp.....	2	16	2	140	4	248		404

TABLE 1—Continued

NUMBER AND NAMES OF SPECIES	TYPE							Total number of pores
	*Nos. 15 and 17 Hicks'		No. 15 Basal		Nos. 14 and 18 Scalpel		Undetermined	
	Number of groups	Number of pores	Number of groups	Number of pores	Number of groups	Number of pores		
37. <i>Musca domestica</i> ♂.....	4	35	2	183	4	387	1	606
38. <i>Musca domestica</i> ♀.....	4	35	2	166	4	350	1	552
39. <i>Sarcophaga plinthopyga</i>	2	18	2	140	4	316		474
40. <i>Sarcophaga lambens</i>	2	32	2	*168	4	334		534
41. <i>Sarcophaga helicis</i>	4	48	2	186	4	326	4	564
42. <i>Sarcophaga</i> sp.....	4	36	2	146	4	292		474
43. <i>Sarcophaga</i> sp.....	4	34	2	150	4	334		518
44. <i>Olfersia americana</i> ♂.....			2	60	4	242	2	304
45. <i>Melophagus ovinus</i> ♀.....	†							
46. <i>Lipoptena depressa</i> ♂.....	2	10	2	68	4	122		200
47. <i>Hippobosca struthiniosis</i> ♂.....	2	16	2	120	4	304	2	442
48. <i>Nycteribia bellardii</i> ♂.....			2	6	2	36	2	44
Variation.....	{ 0—	0—	0—	0—	2—	26—	0—	28—
	{ 4	48	2	272	4	552	6	870

* These numbers refer to those in figure 3, showing the same types on the halteres of the house fly.

† Halteres totally wanting.

the legs is slightly more than might be expected; 2) the wing is nothing more than a little pad, about as long as the base of the halter, but it bears no pores; 3) the halteres seem normal in size, but the pores on them are comparatively few in number, the Hicks' and basal groups being absent; 4) the ovipositor seems to bear 21 small pores, but they are not recorded in the tables. The chitinous parts of the genital organs of all the abnormal species and of a few of the normal species were examined, but no olfactory pores were observed on them except as above stated. The so-called wingless female phorid (13 *Pulicifora borinquensis*) is the smallest specimen examined. The wing is padlike, about the size of the halter and it bears 7 pores. The number of pores on the halter appears to be reduced. The deer tick (46 *Lipoptena depressa*) has vestigial wings which are unusually thick

at the base. The number of pores on them is greatly reduced. The two remaining parasitic species, the fowl tick (44 *Olfersia americana*) and the ostrich tick (47 *Hippobosca struthiniosis*), are winged and apparently are normal, unless one considers the number of their pores slightly reduced.

TABLE 2
Number of olfactory pores found on abnormal species

NUMBER AND NAME OF SPECIES	NUMBER OF PORES ON			Total number of pores
	Legs	Wings	Halteres	
45. <i>Melophagus ovinus</i> ♀.....	162	A	E	162
48. <i>Nycteribia bellardii</i> ♂.....	178	A	F44	222
2. <i>Chionea valga</i> ♀.....	391	B	28	419
13. <i>Pulicifora borinquensis</i> ♀.....	168	C14	140	322
46. <i>Lipoptena depressa</i> ♂.....	144	D75	200	419
44. <i>Olfersia americana</i> ♂.....	168	154	304	626
47. <i>Hippobosca struthiniosis</i> ♂.....	180	167	442	789
Variation.....	144—	00—	00—	162—
	391	167	442	789

The following is an explanation of letters A to F in the above table: *A*, totally wingless; *B*, wing about as long as base of halter; *C*, wing about size of halter; *D*, wing much reduced, about same length as that of the short tarsus; *E*, halteres totally wanting; and *F*, halteres unusually small and peduncles threadlike.

e. Generic, specific, individual, and sexual variations. As already stated, the variations between the olfactory pores of Hymenoptera, Coleoptera, Lepidoptera, and Diptera are large and in regard to both disposition and structure of the pores they are characteristic for each order. The variations among the families depend upon the families compared; for example, the disposition of the pores in Tipulidae and Muscidae is very different, but in Muscidae and Sarcophagidae only slightly different. The generic characteristics are slight variations in the disposition of the pores, while the specific variations are based almost solely upon the total number of pores present. The individual and sexual variations are distinguishable only by comparing the total number of pores present.

A reference to tables 1 and 3 shows that the variations found pertain to the number of groups on the halteres and to the variations in number of pores on the legs, wings, and halteres. Exclud-

ing the wingless forms (nos. 13 and 48), the mosquitoes (nos. 3 to 5) differ from all the other Diptera examined in that each halter bears only one scalpel group instead of two. While the legs and wings of these mosquitoes are long and slender, the halteres are short and stout; relative to the other species examined, the reverse is generally true. The number of pores on the halteres of mosquitoes is considerably less than the average number on the halteres of flies, but they appear to be considerably larger. Tipulidae is the only family which bears more pores on the legs than on either the wings or halteres. As a rule, the smaller species bear fewer pores than the larger ones, but there are many exceptions; for example, *Tritoxa flexa* (no. 16) is one of the largest specimens examined, yet its total number of pores is among the lowest recorded. Among the genera the total number of pores may vary slightly, as in the mosquitoes (nos. 3 to 5) and in Anthomyiidae, or considerably, as in Mycetophilidae and Empididae; but among the species the total number usually varies only slightly, as in nos. 24 and 25, 30 and 31, 34 and 35, but occasionally a larger variation may be found, as in nos. 21 to 23 and 39 to 43.

The olfactory pores on five females and five males of *Musca domestica* were carefully counted to determine the individual and sexual variations. For the females the number of pores on the legs vary from 165 to 175 with 186 as an average; on the wings, from 219 to 274 with 252 as an average; on the halteres, from 530 to 570 with 552 as an average. For the males the number of pores on the legs vary from 168 to 180 with 172 as an average; on the wings, from 232 to 257 with 248 as an average; on the halteres, from 564 to 625 with 606 as an average. Thus, as an average a female bears 972 pores and a male 1026 pores.

The mouth parts and antennae of many specimens were examined, but no olfactory pores were seen on them. Other parts of the integuments besides those discussed were also often examined, although no olfactory pores were found on them, except on the ovipositor already mentioned (p. 467) and occasionally two or three pores on the thorax near the base of the wing. These were not carefully recorded and do not appear in the tables.

TABLE 3

Number of olfactory pores on legs, wings, and halteres of Diptera

FAMILY	NUMBER AND NAME OF SPECIES	NUMBER OF PORES ON			Total number of pores
		Legs	Wings	Halteres	
Tipulidae.....	1. <i>Tipula</i> sp.....	380	252	230	862
	2. <i>Chionea valga</i> ♀ Harr.....	391	B*	28	419
	3. <i>Culex pipiens</i> L.....	208	170	286	664
Culicidae.....	4. <i>Aedes vexans</i> Meig.....	194	192	298	684
	5. <i>Corethra cinctipes</i> Coq.....	220	160	298	678
Mycetophilidae.....	6. <i>Mycetophila punctata</i> Meig.....	225	343	350	918
	7. <i>Sciaria inconstans</i> Fitch.....	160	138	330	628
Stratiomyidae.....	8. <i>Macrosargus decorus</i> Say.....	272	408	870	1550
Empididae.....	9. <i>Tachydromia</i> sp.....	186	60	282	528
	10. <i>Rhamphomyia abdita</i> Coq.....	148	192	536	876
Dolichopodidae.....	11. <i>Psilopus</i> sp.....	168	163	588	919
Phoridae.....	12. <i>Aphiochaeta</i> sp.....	159	74	278	511
	13. <i>Pulicifora boringuensis</i> ♀ Wheeler	168	C14	140	322
Micropezidae.....	14. <i>Calobata antennipes</i> Say.....	138	161	430	729
Sepsidae.....	15. <i>Piophila casei</i> L.....	124	154	389	667
	16. <i>Tritoxa flexa</i> Wied.....	90	111	272	473
Ortaliidae.....	17. <i>Anacampta latiuscuta</i> Loew.....	151	222	485	858
	18. <i>Euxesta notata</i> Wied.....	166	184	434	784
Agromyzidae.....	19. <i>Dacus cucurbitae</i> Coq.....	182	192	514	888
	20. <i>Milichiella lacteipennis</i> Loew.....	128	124	471	723
Drosophilidae.....	21. <i>Drosophila busckii</i> Coq.....	160	98	288	546
	22. <i>Drosophila amoena</i> Loew.....	173	110	324	607
	23. <i>Drosophila funebris</i> Fabr.....	180	117	358	655
Ephydriidae.....	24. <i>Paralimna decipier</i> Loew.....	168	138	309	615
	25. <i>Paralimna appendiculata</i> Loew...	173	126	342	641
Chloropidae.....	26. <i>Ephydra gracilis</i> Pack.....	164	183	306	653
	27. <i>Chlorops coxendix</i> Fitch.....	177	138	256	571
Sciomyzidae.....	28. <i>Tetanocera plumos</i> Loew.....	174	202	588	964
Helomyzidae.....	29. <i>Helomyza tineta</i> Walk.....	172	197	522	891
	30. <i>Scatophaga stercoraria</i> L.....	170	214	470	854
Scatophagidae.....	31. <i>Scatophaga surcata</i> Say.....	173	208	472	853
	32. <i>Homalomyia canicularis</i> L.....	195	198	492	885
	33. <i>Hylemyia simpla</i> Coq.....	178	241	466	885
Anthomyidae.....	34. <i>Phorbia brassicae</i> Bouche.....	174	236	502	912
	35. <i>Phorbia fusciceps</i> Zett.....	177	240	502	919
Muscidae.....	36. <i>Coenosia</i> sp.....	178	223	404	805
	37. <i>Musca domestica</i> ♂ L.....	172	248	606	1026
	38. <i>Musca domestica</i> ♀ L.....	168	252	552	972

TABLE 3—Continued

FAMILY	NUMBER AND NAME OF SPECIES	NUMBER OF PORES ON			Total number of pores
		Legs	Wings	Halteres	
Sarcophagidae..	39. <i>Sarcophaga plinthopyga</i> Wied.....	174	198	474	846
	40. <i>Sarcophaga lambens</i> Wied.....	170	204	534	908
	41. <i>Sarcophaga helicus</i> Towns....	179	218	564	961
	42. <i>Sarcophaga</i> sp.....	180	194	474	848
Hippoboscidae..	43. <i>Sarcophaga</i> sp.....	186	202	518	906
	44. <i>Olfersia americana</i> ♂ Leach.....	168	154	304	626
	45. <i>Melophagus ovinus</i> ♀ L.....	162	A	E	162
	46. <i>Lipoptena depressa</i> ♂ Say.....	144	D75	200	419
Nycteribiidae....	47. <i>Hippobosca struthionis</i> ♂ Jansen	180	167	442	789
	48. <i>Nycteribia bellardii</i> ♂ Rondani..	178	A	F44	222
Variation		90— 391	00— 408	00— 871	162— 1550

* For explanation of letters A to F, see p. 468.

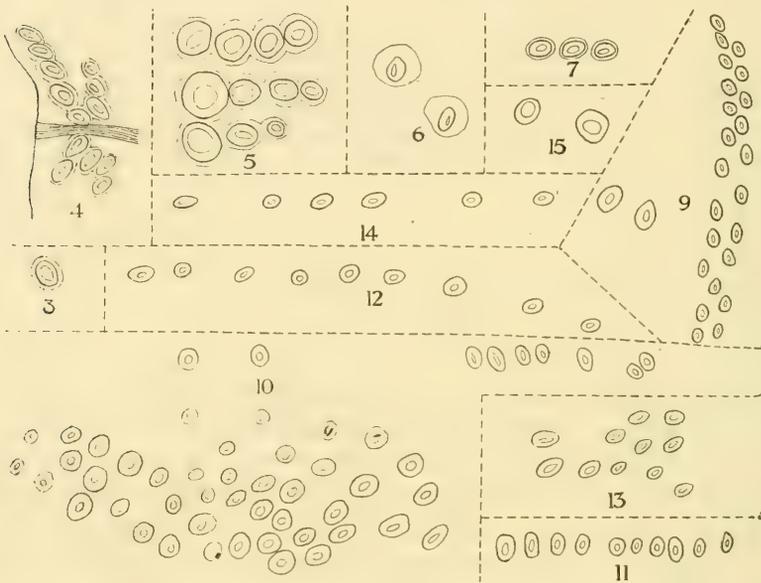
Structure of pores in Musca domestica

The preceding pages deal with the disposition of the olfactory pores, and now a discussion of their anatomy will be given.

a. *External structure.* As already stated, the pores in groups nos. 16 and 17 on the halteres (fig. 3) have been called Hicks' organs, and since their structure is like that of those on the legs and wings, all of these pores may be regarded as belonging to the Hicks' type. Since their anatomy does not differ materially from that of those in the other orders of insects, discussed in other papers by the writer, a reference to figures 4 to 15 may suffice at this place.

Under a high-power lens the scalpel groups (nos. 14 and 18) and the basal group (no. 15) look somewhat as shown in figures 16 and 17. They may be compared with the Hicks' type (nos. 16 and 17). It is to be noted that the scalpel group no. 14 consists of 11 rows and no. 18 of 10 rows. From a superficial view the rows appear to be flat, but sections will show that the pores are linked together and stand in ridges, projecting far above the surrounding integument. The summit of each ridge is beautifully sculptured, and a row of stout hairs (fig. 16, *Hr*¹)

arises between each two rows of pores. These rows of hairs are only prolongations of the chitin and therefore should be called pseudohairs; their only function is probably to protect the rows of pores. The apertures (*PorAp*) of the pores are invariably long, narrow slits, while sculptured markings replace the pore walls and pore borders in the Hicks' type. The two halves

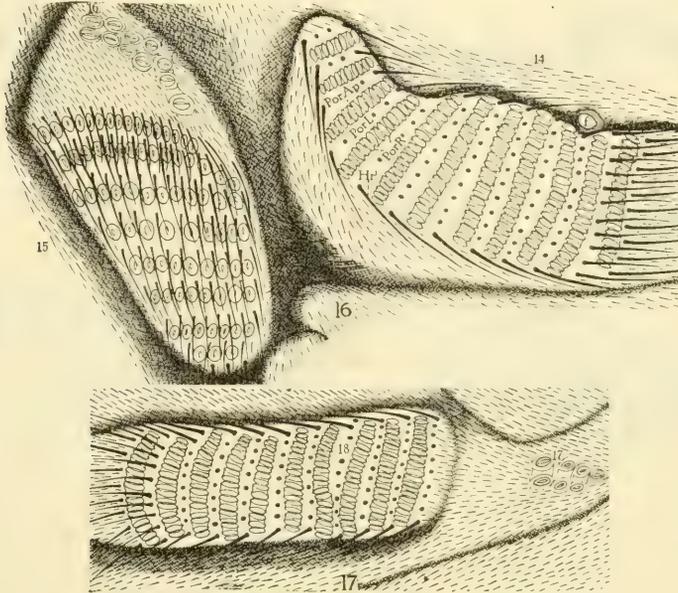


Figs. 4 to 15 External view of olfactory pores in *Musca domestica* ♂, showing variation in size. Fig. 4, groups nos. 1 and 2 (fig. 1); fig. 5, group no. 3; fig. 6, group no. 4; fig. 7, group no. 5; fig. 8, group no. 6; fig. 9, group no. 8 (fig. 2); fig. 10, group no. 9; fig. 11, 10 of 12 pores in group no. 10; fig. 12, 9 of 10 pores in group no. 11; fig. 13, group no. 12; fig. 14, 6 of 18 pores in group no. 13; fig. 15, scattered pores at *b*. $\times 500$.

(*PorR*), surrounding the aperture, are similar in position to the pore wall, but do not correspond to it; this structure may be called the pore ridge. The portion, marked *PorL*, may be called the pore link, because it unites the pore ridges; in position it is similar to the pore border, but it is quite different in structure.

The structure of the basal type of pores is similar to that of the Hicks' type, excepting pore borders are not present and a row of

pseudohairs arises between each two rows of pores. Each basal group consists of about eight rows of pores which are usually smaller than the scalpel pores; the pseudohairs in this group are also smaller than those in the scalpel group. The Hicks' pores are never protected by pseudohairs.

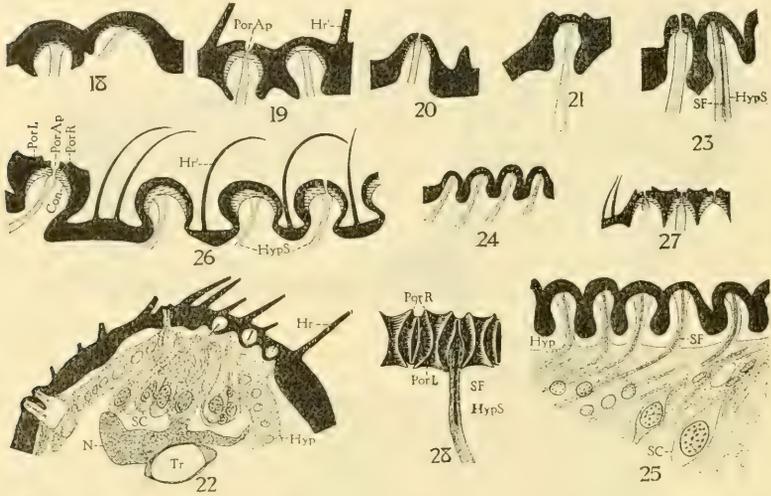


Figs. 16 and 17 External view of scalpel pores (nos. 14 and 18), basal pores (no. 15), Hicks' pores (nos. 16 and 17), and the undetermined type (*f*) on base of right halter of *Musca domestica* ♂ (fig. 3). All of the pseudohairs (Hr^1) in group no. 15 are represented, but only a few of those in groups nos. 14 and 18 are shown, the bases of the remainder being represented by black dots. $\times 500$.

b. Internal structure. As in Lepidoptera, the olfactory pores of Diptera may be called dome-shaped structures. All of the pores on the legs (fig. 18) and most of those on the wings (fig. 19) are typical dome-shaped structures, while the remainder on the wings (figs. 20 and 21) and all of those on the halteres (figs. 23 to 27) are modifications of the typical structure. It will be noted that the internal structure of each type of pore is identical to that of any other type and it is also similar to that of the

olfactory pores in other orders of insects; therefore, it is the external structure that really determines the various types.

A hypodermal strand (figs. 23, 26, and 28, *HypS*), running from the hypodermis (fig. 25, *Hyp*) to the chitinous cone (fig. 26, *Con*), is always present. In this strand may be observed the



Figs. 18 to 28 Sections showing internal anatomy of olfactory pores of *Musca domestica*. Fig. 18, from trochanter; figs. 19 to 21, 3 variations on wing; fig. 22, portion of cross-section of wing ($\times 500$); fig. 23, largest Hicks' pores; fig. 24, smallest, and fig. 25, largest basal pores, both rows being cut lengthwise; fig. 26, 4 rows of largest scalpel pores cut crosswise and 1 cut lengthwise; fig. 27, a row of smallest scalpel pores cut lengthwise; and fig. 28, from an oblique section of a scalpel row of pores, only their external view and nervous connection having been drawn. The sense fiber (*SF*) and hypodermal strand (*HypS*) are taken from a deeper focus. Attention is called to the sense fiber ending at the center of the pore aperture. *Con*, chitinous cone; *Hr*¹, pseudohair; *Hyp*, hypodermis; *N*, nerve; *PorAp*, pore aperture; *PorL*, pore link; *PorR*, pore ridge; *SC*, sense cell, and *Tr*, trachea. $\times 1000$.

sense fiber (figs. 23, 25, and 28, *SF*), but it is easily overlooked owing to the minute size of these organs. The sense cells in the legs and wings (fig. 22, *SC*) are spindle-shaped as usual, but in the halteres (fig. 25, *SC*) they are more than spindle-shaped and assume almost a spherical shape (fig. 29, *SC*). A pore aperture (figs. 19 and 26, *PorAp*) was seen only occasionally

and then never distinctly; it would never have been regarded as an opening had not the writer seen many good examples of it in the olfactory pores of other insects. These pores are the smallest ones ever examined by the writer, and this fact easily explains why other observers have never seen the pore apertures. The sections were studied under a magnification of 1900 diameters, and with the aid of a camera lucida the drawings made represent a magnification of 3000 diameters before reduction; and they were reduced to 1000 diameters.

As already stated, the pores on the legs, wings and groups nos. 16 and 17 on the halteres belong to the Hicks' type, while group no. 15 belongs to the basal type and nos. 14 and 18 to the scalpel type. A glance at figures 19 to 25 shows that the structure of the basal type (figs. 24 and 25) is like that of the Hicks' type (figs. 20 and 23), and the only difference (not shown in these figures) between these two types is that a row of pseudohairs (fig. 16) lies between each two rows of pores in the basal group. Pseudohairs (figs. 19 and 20, *Hp¹*) also protect some of the pores on the wings, but they are never arranged in rows as they are on the halteres.

The size of the pores in any type varies considerably. This is shown by comparing the smallest and largest basal pores (figs. 24 and 25) and the largest and smallest scalpel pores (figs. 26 and 27). The scalpel type differs from the other types in the following three particulars: 1) The domes lie totally above the surrounding chitin; 2) the bottoms of the domes are considerably constricted, while in the basal and Hicks' types on the halteres the domes are projected about one-half their height above the surrounding integument and their bases are constricted little or not at all, and 3) the tops of the domes are beautifully sculptured and assume a more or less flat surface. One pore (fig. 21) on the wing, resembling a scalpel pore, was found, while several (fig. 20) on the wing are identical to those in the Hicks' and basal groups on the halteres.

Sections passing longitudinally through the rows of basal pores show the pores as drawn in figures 25 and 29 (*BPor₁*), while sections passing transversely through the rows show the pores as

drawn in figure 29 ($B\text{Por}_2$). Figure 26 represents a section passing transversely through four rows and longitudinally through one row of scalpel pores. In the latter pore, as well as in figures 27, 28, and 29 ($S\text{Por}_1$), the pore ridge ($\text{Por}R$) and pore link ($\text{Por}L$) can be identified. Figure 29 represents an oblique longitudinal section through the base of the halter in the direction of AA in figure 3. The large nerve (N) is very conspicuous; it spreads out fanlike and connects with the masses of sense cells

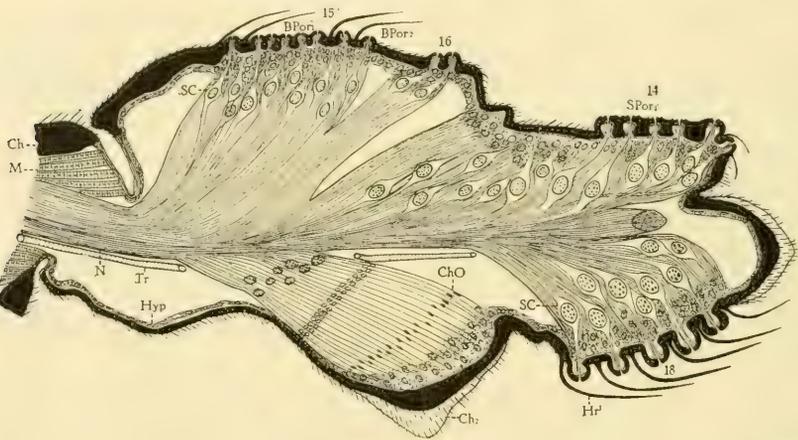


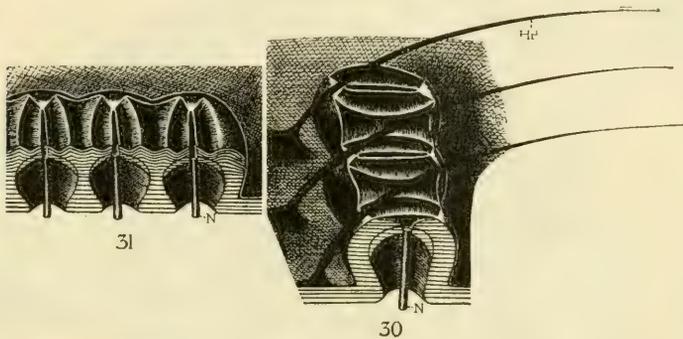
Fig. 29 Longitudinal section ($\frac{2}{3}$ diagrammatic), cut in direction of line AA in figure 3, through base of halter of *Musca domestica*, showing internal anatomy, scalpel pores (nos. 14 and 18), basal pores (no. 15) and Hicks' pores (no. 16). The chordotonal organ (ChO) is only in its approximate position and was copied from Lee ('85). One row each of basal pores ($B\text{Por}_1$) and scalpel pores ($S\text{Por}_1$) cut lengthwise, and 3 rows of basal pores ($B\text{Por}_2$) and 5 rows of scalpel pores (no. 18) were cut crosswise. Ch , internal view of chitin; Ch_2 , external view of chitin; M , muscle; N , nerve; SC , sense cell, and Tr , trachea. $\times 500$.

(SC). A trachea (Tr), muscles (M) and a chordotonal organ (ChO) are also present. Both Lee and Weinland have studied the chordotonal organ, but the present writer has paid little attention to it, hoping later to make a special study of this type of sense organ. In figure 29 it is represented in only its approximate position as drawn by Lee.

Figures 30 and 31 are schematic drawings of a portion of a row in a scalpel group, showing the pores both in perspective and in

section. In figure 30 the row was cut crosswise, passing longitudinally through the slitlike aperture, whereas in figure 31 the row was cut lengthwise, passing transversely through the slitlike aperture.

Figure 32 is a drawing, showing a portion of the base of the halter in perspective and in section, it was cut crosswise in the direction of line *BB* in figure 3. The muscle (*M*) and chordotonal organ (*ChO*) are drawn in only their approximate positions as represented by Weinland; their points of attachments are incorrect. The scalpel pores (nos. 14 and 18) and a few basal pores (no. 15), shown both in perspective and in section, lie on



Figs. 30 and 31 Schematic drawings of a portion of a scalpel row on halter of *Musca domestica*, showing the row in perspective and in section. In figure 30, the row was cut crosswise, longitudinally through the slitlike aperture, while in figure 31 the row was cut lengthwise. The nerve (*N*) is drawn in perspective, and strong pseudohairs (*Hr*¹) bend over the pores, protecting them well.

curved plates, and it is noted that the surface of the base of the halter is very rough, being made up of minute hills and hollows.

In Weinland's drawings it is noted that the nerve does not run beyond the olfactory pores on the halter, but the trachea runs into the peduncle and stops there. A cross-section of the knob of a halter somewhat resembles a double convex lens; it contains masses of cells which are certainly not sensory, but probably they are the remains of the early hypodermis. The surfaces of the knobs of prepared halteres bear a few true hairs, and they are generally smooth excepting the folds (fig. 3, *F*), caused by preparing the specimens.

Structure of pores in other species

Since the structure of the pores in the house fly has been described in detail, only the more important variations concerning the structure of the pores in other Diptera will be mentioned and attention will be called to the various figures.

a. External structure. On the legs of one or two specimens the pore walls are diamond-shaped instead of being round and oblong.

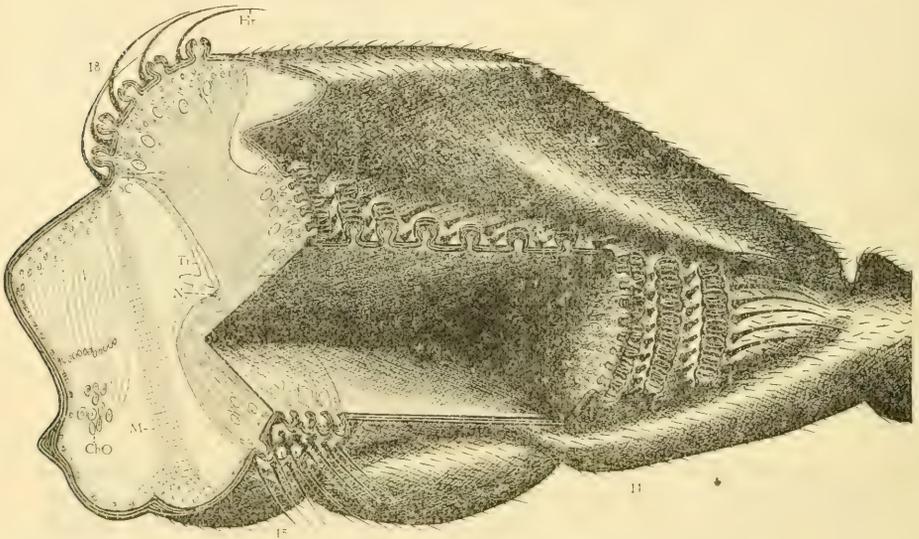


Fig. 32 Portion of base of right halter of *Musca domestica*, cut across in direction of line *BB* in figure 3, showing halter, scalpel pores (nos. 14 and 18), and basal pores (no. 15) in perspective and in section. The chordotonal organ (*ChO*) and muscle (*M*) were copied from Weinland ('90) and were drawn in only their approximate positions.

and the pore apertures in several instances are long, more or less slit-shaped, and resemble the slits in the lyriform organs of spiders (McIndoo, '11); such is particularly true on the trochanters of *Tipula* (fig. 33). The pores on the tibiae of *Sarcophaga* (fig. 34) are very large and striking. The pore wall is surrounded by three areas of differently colored chitin; the inner one is real light in color; the middle one is a little darker, and the outer one, having a soft appearance, is still darker.

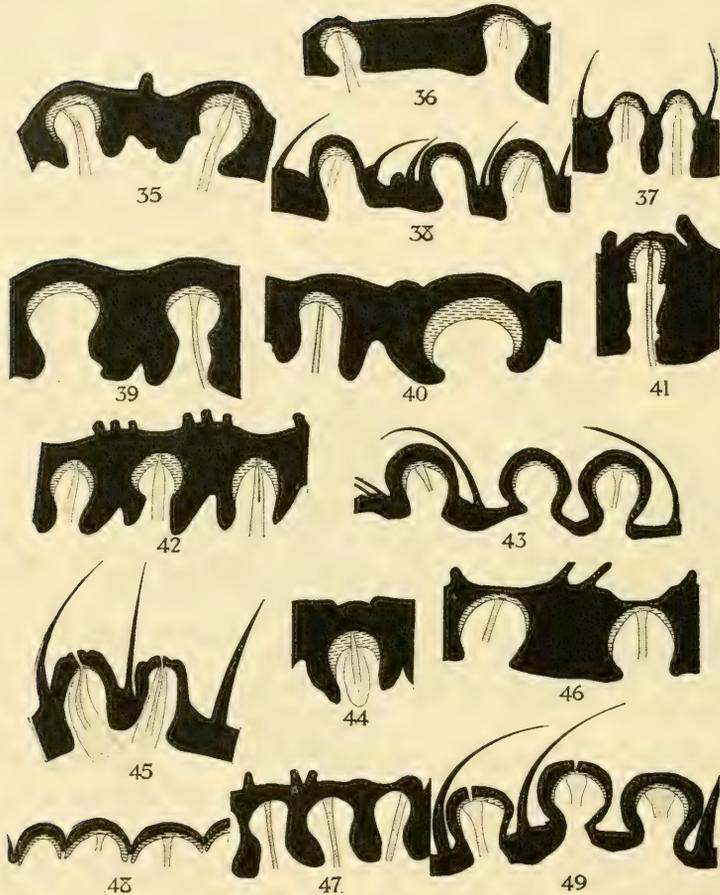
b. Internal structure. A reference to figures 35 to 49 shows that the size of the pores usually varies according to the size of the insect studied; thus the average size of the pores in the robber fly (figs. 39 to 43) is greater than that of the pores in the flesh fly (figs. 44 to 49), although the pores on the halteres of both flies are about equal in size. While the pores on the legs are always dome-shaped, many of those on the wings (figs. 42 and 46) and a few on the halteres (fig. 47) are not dome-shaped. Many of those on the wings (fig. 45) of *Sarcophaga* project far above the surrounding chitin and their tops slightly resemble those of the scalpel pores on the halteres. A study of these pores shows a complete series of variations, ranging from the Hicks' type to the scalpel type, and perhaps each type is still in the trans-



Figs. 33 and 34 External views of olfactory pores of other flies. Fig. 33, a group from trochanter of *Tipula*, showing slitlike pore apertures, and fig. 34, a group from tibia of *Sarcophaga plinthopyga*, showing 3 areas of chitin around pore wall. $\times 500$.

itional stage. Morphologically the scalpel type is the most highly developed, but physiologically it is probably little or no better developed than any other type of pores.

All of these results indicate that while the hind wings of Diptera have been gradually reduced in size, consequently gradually diminishing their flying ability, their sensory function has been greatly increased, and now they bear the highest type of olfactory pore yet found. The latter statement is supported by the fact that in Hymenoptera, the hind wings bear about one-half as many pores as do the front wings; in Lepidoptera the hind wings do not bear quite as many pores as do the front wings, while in Diptera the halteres bear about as many pores as do the wings and legs combined, or close to one-half the total number of pores found.

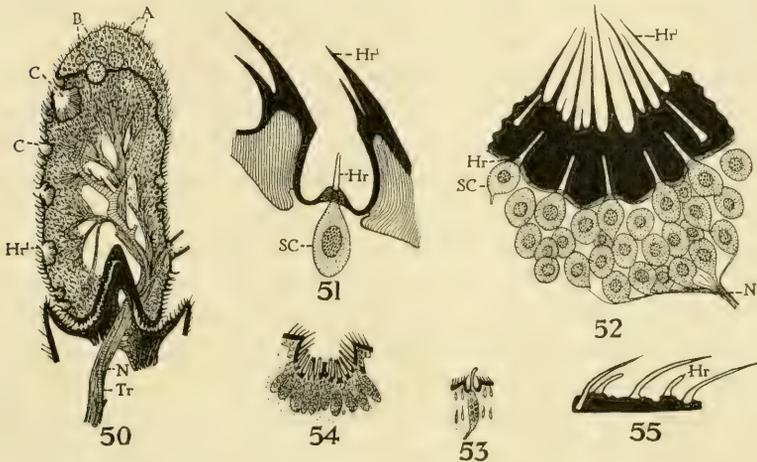


Figs. 35 to 49 Sections showing variations in internal anatomy of olfactory pores of other flies. Figs. 35 to 38, from crane fly (*Brachypremna dispellens* Walk.); fig. 35, from trochanter; fig. 36, from wing; and figs. 37 and 38, from halter, fig. 37 being basal type and fig. 38 being scalpel type. Figs. 39 to 43, from robber fly (*Erax aestuans* L.); fig. 39, from trochanter; fig. 40, from femur; figs. 41 and 42, from wing, and fig. 43, scalpel type from halter. Figs. 44 to 49, from flesh fly (*Sarcophaga* sp.); fig. 44, from trochanter; figs. 45 and 46, from wing, and figs. 47 to 49, from halter. $\times 1000$.

THE ANTENNAL ORGANS

Several investigators have studied the morphology of the antennal organs in Diptera, but since certain drawings of Hauser ('80), vom Rath ('88), and Nagel ('94) best illustrate the various types of antennal organs, the following discussion will be taken only from these three works.

The antennae of Diptera are usually short, generally consisting of only a few segments, which bear so-called olfactory pits.



Figs. 50 to 55. Structure of antennal organs of Diptera; figs. 50 to 52, copied from Hauser ('80); figs. 53 and 54, from vom Rath ('88); and fig. 55, from Nagel ('94). Fig. 50, longitudinal section through third or last antennal segment of *Cyrtoneura stabulans* Fll., showing internal anatomy of segment and the compound olfactory pits (C) in section. $\times 75$. The tip of the segment is not sectioned, thus showing the simple (A) and compound olfactory pits (B) from a superficial view. Fig. 51, section of a simple olfactory pit, and fig. 52, part of a section of a compound olfactory pit; $\times 750$. Fig. 53, section of simple olfactory pit with projecting hair; $\times 150$. Fig. 54, section of compound olfactory pit on palpus; $\times 100$. Fig. 55, 2 olfactory hairs (Hr) on antenna of a mosquito (*Culex pipiens* ♂); $\times 500$.

Not all of the segments bear such pits, but the distal or last one is usually well provided with them. Sometimes, however, olfactory pits are never present on any segment, as in the mosquitoes. The olfactory pits are divided into simple and com-

pound ones. From a superficial view, a simple pit looks like a small circle (fig. 50, *a*) with a dot at its center, while a compound pit resembles a large circle (*B*) which contains radiating lines and two or more dots. Sections through these pits show that a single hair (fig. 51, *Br*) arises from the bottom of a simple pit and two or more hairs (fig. 52, *Hr*) from the bottom of a compound pit (fig. 50, *C*). The mouth and sides of each pit are well protected by pseudohairs (*Hr'*). A sense cell (*SC*) lies directly beneath each sense hair and a nerve fiber runs from each sense cell to the nerve (figs. 50 and 52, *N*). An idea of how well the distal segment is innervated may be had by looking at figure 50.

Sometimes the hair in a simple pit projects out of the mouth of the pit (fig. 53), indicating that the primary function of such a hair is that of touch. All types of transitional forms of simple and compound pits have been found, and besides being present on the antennae, the compound pits are sometimes found on the palpi (fig. 54). Mosquitoes do not seem to have olfactory pits; Nagel has found two types of hairs on their antennae, and he calls the short, stout ones (fig. 55, *Hr*) olfactory organs. A male mosquito has only a few of these hairs, while a female has many. All flies seem to have olfactory pits, but some of them do not have the compound ones, and a few of the latter flies bear only one simple pit on each antennal segment.

SUMMARY

The disposition of the olfactory pores on the legs of Diptera is more similar to that of those on the legs of Hymenoptera than to those on the legs of Lepidoptera or Coleoptera, but those on the wings of Diptera are more similar to those on the wings of Lepidoptera than to those on the wings of the other two orders. The disposition of the pores on the halteres is entirely different from that of those on the hind wings of the other orders examined. In Hymenoptera the hind wings bear about one-half as many pores as do the front wings; in Lepidoptera the hind wings do not bear quite as many pores as do the front wings; while in Diptera the halteres bear almost one-half the total number of pores found. Excluding the abnormal forms, the total number of

pores found in the four orders examined varies as follows: For Hymenoptera, from 463 to 2608 with 1286 pores as an average; for Lepidoptera, from 514 to 1422 with 850 pores as an average; for Diptera, from 473 to 1550 with 772 as an average; and for Coleoptera, from 273 to 1268 with 724 pores as an average.

As in Lepidoptera, the olfactory pores of Diptera are dome-shaped and their internal anatomy is very similar to that of those in the other three orders, but the sense cells in the halteres are more spherical than usual.

For description the pores have been divided into four types as follows: The Hicks' type includes all of those on the legs, wings, and a few of those on the bases of the halteres. This type also includes all of those found in the other three orders examined. The other three types are found on the bases of the halteres. The undetermined type really belongs to the Hicks' type, while the basal type is very similar to the Hicks' type; nevertheless, the basal and scalpel types are quite unique and are found only on the halteres. While the basal pores stand in rows resembling the shape of mountain ranges, each row of the scalpel pores may be likened to an inverted urn-shaped ridge whose summit is more or less flat and is beautifully sculptured. Deep depressions lie between the rows in each type and a row of strong, protective pseudohairs stands in each depression. Morphologically, the scalpel type is the most highly developed, but physiologically it is probably little or no better developed than any other type of pore.

This study indicates that while the hind wings of Diptera have been gradually reduced in size, consequently diminishing their flying ability, their sensory function has been greatly increased.

Compared with the antennal organs, the olfactory pores are better adapted anatomically to receive olfactory stimuli, because the peripheral ends of their sense fibers come in direct contact with the external air, while those in the antennal organs are covered with hard chitin.

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REMARKS ON VON MONAKOW'S "DIE LOKALISATION IM GROSSHIRN"¹

F. H. PIKE

Department of Physiology, Columbia University

Every now and again a work appears which lays the axe at the root of some of our ancient and honorable scientific assumptions which have survived so long and for years have been so often and so vehemently repeated that they have acquired a certain sacredness and become a part of the dogmatic and uncritical part of our teaching. Verily, the axe hath other uses than those to which it is put by politicians or administrators, and it would seem a pity that a notable work in which certain long-cherished assumptions are put to the test of modern knowledge should escape being brought to public notice. My object is not to give a formal review of the book, but to discourse informally upon some of its unusual features, and particularly those which have to do with the fundamental conceptions of the function of the central nervous system.

One point in which von Monakow departs from the traditional views is his attitude toward the segmental theory of the nervous system and its necessary attendant hypothesis of shock. Without pausing just here to give a detailed discussion of his views, we may say that he rejects the segmental theory and limits the effects of shock in so far as they are incompatible with the theory of cerebral localization. It will conduce to the clearness of the discussion to give first a brief account of the older view of the segmental theory of the central nervous system and

¹ Die Lokalisation im Grösshirn und der Abbau der Funktion durch kortikale Herde, von Dr. med. C. von Monakow, Professor der Neurologie und Direktor des hirnanatomischen Institutes sowie der Nerven-Poliklinik aus der Universität in Zürich. Mit 268 Abbildungen im Text und 2 Tafeln. Wiesbaden. Verlag von J. F. Bergmann, 1914.

then take up more in detail the examination of von Monakow's argument against these views and in favor of cerebral localization.

The classical statement of the segmental theory and of the general hypothesis of shock is due largely to Goltz. I made this statement from the point of view of the physiologist rather than that of the anatomist. I should perhaps utter a warning here that the phenomena of shock, as Goltz and others have described it, and as the term is used in this paper, are not to be confused with other phenomena of uncertain nature which have come to be included under the somewhat obscure but widely inclusive term shock as it is used by the surgeon or the clinician. A perusal of the first chapter of von Monakow's work will be sufficient to show the error that may arise from failure to differentiate several different kinds of shock.

Goltz assumed that all reflexes occurred through the lower levels of the central nervous system and especially through the spinal cord. This view has been restated many times. Perhaps its most concise statement in modern anatomical terms is that by Edinger ('08):

Since it is certain that the palaeencephalon persists quite unchanged even after a well developed neencephalon has been added to it, there is no ground for regarding those activities which we recognize as palaeencephalic in one class of animals as anything else or as otherwise localized in higher animals. *Furthermore* we may regard an entire series of activities as common to all vertebrates and we may then seek to ascertain how other activities are added to these when a new structure is added to the palaeencephalon. All sense impressions and movement combinations belong to the palaeencephalon. It is able to establish simple new relations between the two, but it is not able to form associations, to construct memory images out of several components. *It is the bearer of all reflexes and instincts.*

This has generally been regarded as a certainty, and despite the fact that he adduces no independent proof, Edinger's italics leave little doubt as to his own views on the subject. But Goltz himself regarded it as an assumption, and no actual proof of its general truth has been forthcoming in the four decades and more since its enunciation. In view of the wide currency

of the general idea of shock as applied to the central nervous system it may not be out of place to give here Goltz's statement in his own words, as translated by Loeb ('00):

No one will assume, that that piece of the spinal cord which is separated from the brain in so short a time (i.e., a few days or weeks) acquires entirely new powers as a reflex organ; we must assume that these powers were only suppressed or inhibited temporarily by the lesion of the spinal cord.

Goltz's statement of the segmental theory was that each level or division of the central nervous system had essentially the same functions in all vertebrates (Goltz, '92). The reason why a man or a dog will not recover as completely as a frog or a turtle after loss of the cerebral hemispheres is not because the cerebral hemispheres have any more highly developed motor function in the higher forms, but because the effects of shock are so much more permanent and more severe in the higher forms than in the lower.

It may be remarked in passing that Magendie (1816), many years before Edinger, had with great clearness stated the mechanism of instincts in neurological terms. An abstract of his views follows:

We may distinguish, in those attitudes and movements which are intended to express our intellectual and instinctive acts, and which are included under the generic term 'gestes,' between those which are bound up with organization and, as a consequence, are present in all men, in whatever condition, and those which have arisen and reached their perfection in a social state.

The former are intended to express the most simple condition, the internal sensations as joy, pain, grief and the like, as well as the animal passions, through cries and the voice. One may observe them in the idiot, the savage, the blind from birth, as well as in the civilized man enjoying all moral and physical advantages. These are native or instinctive responses.

But while Edinger's statement of the relations was probably at variance with the known facts at the time it was made, and certainly is at variance now, the generality of Magendie's expression made it conform, not only to the facts of his time, but also gave it a lease of life which endures to the present day.

Von Monakow's views on cerebral localization and on the duration and severity of the effects of shock are at variance with those of Goltz, perhaps more widely than he realizes. For the substantiation of Goltz's views depends upon either, 1) the direct proof of the activity of the spinal cord in the reflexes in the manner which Goltz supposed it to act in the uninjured animal or, 2) the independent proof that the reflex or other activities of the regions of the nervous system lying below the level of the transection or the injury are merely depressed for days or years, as the case may be, and that no quantitative change occurs in the impulses passing over any given synapse in the lower regions of the nervous system leading to increased activity after the injury, as compared with the amount of activity before the injury occurred. The experimental evidence now available does not substantiate Goltz's conclusions on either of these points.

Von Monakow recognizes that, if Goltz's view of shock is to be accepted, the idea of cerebral localization must be abandoned, just as Goltz insisted. And if localization is true, one must set some limits to the effects of shock. This he does in his theory of diaschisis, which will be discussed a little later. But if we set any limits to the omnipotence of shock, we raise the question whether shock is a necessary conception in the explanation of the phenomena following injury to any portion of the central nervous system; and, considering shock as a purely depressive effect, whether the limits set may not become vanishingly small. If the limits do become small, the gap between von Monakow's position and Goltz's position must become even wider than it now is.

It is still necessary to make some assumptions in discussing the organization of the nervous system. Aside from the assumption that the effect of shock is merely temporary and that the cells in the levels below the lesion regain all their former functions in time, von Monakow ('10) makes certain others concerning the organization of the mechanisms of the spinal cord as well as those of higher levels. The account is best given in his own words.

From the experiments of Sherrington and others as described, it follows that in the spinal cord of higher mammals and, as my own observations show, apparently even of man, there must be present elements other than the direct receptor and effector cells themselves which retain a stimulus for a longer period than these (i.e., than the direct receptors and effectors). Included therein are found nerve cell elements which are excited by individual incoming fibers, facilitated through the summation of stimuli by others and again inhibited by still others. Single nerve cells in the spinal cord apparently return to a condition of rest after a short period of excitation, immediately after the completion of the specialized function assigned to their neurone complex, and again become receptive to new stimuli. Other cells, however, undoubtedly remain in a condition of excitation for a longer period—minutes or more—after the stimulus coming to them has been interrupted. In other words, we find in the spinal cord elements extremely variable in their duration of charge, both positively and negatively (mnestic elements) such as I have long postulated in the brain, with brief, intermediate or long duration of charge (Ladung). There must also be present here well organized groups of neurones which are effective, that is, which can discharge, only by means of a complex summation of stimuli each (action) in a qualitatively different manner and a different duration; and among them are groups which form the connecting links of a chain of acts released in succession, and which remain functional throughout the course of a reflex movement; they carry the 'kinetic melody' as the notes of a chord accompanying the tune.²

Von Monakow's views represent the growth of years. We may take as one starting point the view expressed in 1895 that, in a series of vertebrates, essentially similar nervous reactions involve more numerous and more widely scattered groups of cells and fiber tracts in the higher animals than in the lower. The logical development of this idea means abandoning the notion of sharply circumscribed centers particularly in the cerebrum, for various acts, which he does.

The issue is squarely joined, therefore, with two other opposing camps. There is, on the one hand, the issue between the adherents of the Goltzian view that the effects of shock may persist, undiminished if need be, for months or years, with its consequent negative view of cerebral localization, and the adherents of the view that shock, if present at all, is more or less

² I am indebted to Mrs. C. S. Winkin for assistance in the translation.

transient as one must hold if cerebral localization is to be substantiated. On the other hand, von Monakow opposes those who insist on "all the so-called centers in the bulb and cord (and particularly the cerebrum) with which the perverse ingenuity of investigators and systematic writers has encumbered the archives and text books of physiology." (Stewart, '00.)

A complete presentation of the evidence for and against the current ideas of shock and of the omnipotence of the circumscribed centers would require many pages, but some statement is necessary as a basis for a comparison of the various hypotheses and a general estimate of their validity

As already mentioned, Goltz's view, either in its original form or as restated by Edinger, that reflexes occur through the lower levels of the brain and the spinal cord exclusively, rests upon an assumption. Explicitly or implicitly, Goltz and his school assume that the cells and synapses of the isolated portion of the spinal cord never convey any greater quantity of energy, to use Hughlings Jackson's term, after isolation than they did before. Changes in isolated cells have been mentioned in the literature, e.g., Munk's term 'Isolationsänderung,' but those changes have more commonly been supposed to be retrogressive than otherwise. Sherrington's term 'isolation dystrophy,' although applied to a somewhat different condition of affairs, is an instance in point.

Senator ('98), however, admits that reflexes may be permanently absent in the human subject in cases in which no degeneration of, or damage to, the neurones of the supposed reflex arcs can be shown histologically. Basing his first conclusion, then, upon the fact that some of the reflexes return after a time in the isolated portion of the spinal cord, Goltz as previously indicated, found it necessary to make another assumption, to the effect that the reflexes were only temporarily suppressed or inhibited by the operation of transection of the spinal cord. This temporary failure of the reflexes had been called 'shock' by Marshall Hall, and Goltz spoke of 'Shockwirkung' in this connection. Goltz did not know what shock was, but was inclined to regard it as an 'Inhibitorische Fernwirkung' due to the

anatomical transection of the cord. And despite the fact that cutting a nerve produces but a relatively small and transient effect as compared with the effects of electrical stimulation, anatomical transection of the spinal cord is commonly said to be a terrific stimulus. Sherrington, however, shows that the effect of anatomical transection can be exerted but once, and concludes that the view of trauma qua trauma as the cause of spinal shock is not really tenable. It has been shown also that shock in the lower levels of the spinal cord may be produced by anaemia of its higher portion and of the brain without interruption of the circulation to the lower portion of the cord (Stewart et al., '06) or by freezing a segment of the spinal cord without excitation of the efferent motor pathway. Sherrington's view that the interruption of certain conduction pathways in the spinal cord favors the production of spinal shock derives much support from these results. The recent work of Ranson ('16) shows that the rupture of certain orally conducting pathways is effective in abolishing responses and that the rupture of the aborally conducting pathways may not be necessary, as Sherrington believed it to be. Ranson's results confirm, in a measure at least, my view that the shock effect is exerted upon the afferent pathway, since the efferent pathway is so obviously open, as judged by all the tests which one may apply.

The segmental theory of the central nervous system, as Goltz formulated it, does not accord with the facts of organic evolution, inasmuch as it makes no allowance for a change in function of the various levels of the system to correspond with the anatomical changes occurring in phylogenetic development. The argument for a shifting of function toward the anterior end of the central nervous axis (Steiner) and the development of cerebral localization is met by the statement on the part of the segmentalists that, if the effects of shock in the higher forms were not so severe, the lower levels of the nervous system of a man would manifest just as complete a recovery after injury to the higher levels as those of a frog. The increasing severity and permanence of the shock effects in higher animals, while freely admitted by Goltz, and even made a supporting point of his

hypothesis, are without any explanation on the basis of such an hypothesis. Goltz and his followers conclude that a cell in the lower levels of the central nervous system may never regain all its normal function after the injury to the higher levels.

Von Monakow departs from the fundamental assumption of the segmental theory—that all levels or segments have essentially the same function in all types of vertebrates—in his statement that more numerous and more widely separated groups of nerve cells and fibers are necessary for the successful execution of essentially similar movements in successively higher types of animals. This statement, as already noted, dates back to 1895. The anatomical and pathological evidence available twenty years and more ago was sufficient to shake his faith in the segmental hypothesis. To some of us it seems that all the additional anatomical, pathological, and experimental evidence which has accumulated since that time points toward cerebral localization as the logical and final development of the processes of evolution in the central nervous system. But, as I have already mentioned, and as I would particularly emphasize now, cerebral localization is an untenable view if all Goltz's postulates concerning spinal shock are to be granted. The emphasis is the more necessary since this part of Goltz's argument, which is essentially sound if his premises be granted, has been so frequently neglected or overlooked. Goltz considered the argument against cerebral localization to be just as cogent as his argument for the spinal cord as the great reflex mechanism, as a careful reading of his papers will show. He was much too careful and accurate a thinker to overlook any serious defects in the logic of his argument. Indeed it must be confessed that he was a far clearer and more logical thinker than many who have essayed this field since his day, or than many who have accepted his argument in part while rejecting the remainder of it. The task of these latter authors is more difficult than was Goltz's, for they must show, not only that one part of his argument is correct, but why the remainder, which is founded on exactly the same assumption as the other part and upon facts of exactly the same nature, is incorrect. I will freely admit

that intellectual evolutions of this sort are much too difficult for me to follow and, a fortiori, to execute. I cannot do less than to accord to Goltz here, from whom I differ on matters of interpretation, the same tribute he accorded to Le Gallois, from whom he differed on matters of interpretation. I do not question Goltz's facts any more than he questioned those of Le Gallois. And I should say of him, as he said of Le Gallois, that he was one of the clearest thinkers among the physiologists of his day. But just as the discovery of new facts compelled the revision of Le Gallois' interpretation, so I now believe that the discovery of new facts has compelled a revision of Goltz's interpretation. The limitation of the effect of shock to a degree which may in some measure be based upon anatomical or functional considerations is necessary. Whereas Goltz supposed that the cells in the regions below the level of injury might never regain all their former degree of activity, but might be permanently depressed or inhibited for the remainder of the life of the animal, von Monakow, while allowing a possible depression of function of the cells below the level of the lesion at the time of its occurrence, supposes that this depression is transient, and that, in time, the isolated cells may regain all their former functions. The minimal deficiencies of function remaining after some weeks or months subsequent to the injury afford a measure of the function of the injured or lost portions, particularly of the upper levels of the nervous system. In no case, so far as I have observed, does von Monakow suppose that the quantity of nervous energy, to use Hughlings Jackson's expression, flowing through any one of the remaining tracts is any greater after an animal's recovery from the injury than it was before the injury.

In his hypothesis of diascisis, von Monakow comes back to the view that it is the rupture of the aborally conducting, or efferent, paths which is the essential factor in shock. The lower lying neurone, after its separation from the higher, or after failure of the impulses which normally come down from the higher, supposedly suffers a temporary depression of function.

Von Monakow also attacks the idea of a vicarious assumption of the function of the injured portion of the central nervous

system by any remaining intact portion, declaring that it is not a useful conception in the explanation of the action of the nervous system normally or of the processes occurring in its recovery from injury.

If, by vicarious assumption, one means that some other cells and fibers which were never concerned directly or indirectly with the processes carried out by a second group when intact, assume a part of the function of the second group when the latter is injured, vicarious assumption becomes a mischievous as well as a useless hypothesis in the explanation of nervous processes. For, if one group of cells may take over a function with which it has had no previous connection, there is no localization of function in the proper sense of the term. If such be its meaning, the term vicarious assumption of function should be dropped from neurology.

The idea of compensation in the nervous system for injury to any of its parts should not, however, be disposed of so summarily. In order to show how such a compensation is susceptible of explanation in terms of nerve cells and fiber tracts without violating any of the postulates either of cerebral localization or of localization in the nervous system generally, I will ask leave to introduce here some conclusions to which I have been led from a study of certain processes of compensation for loss of particular afferent channels or central cells and fibers. To state the case intelligibly, it is necessary to give something of the general physiological basis of normal responses.

I have stated elsewhere my belief that the reactions of an animal generally occur in response to groups of afferent impulses of different kinds rather than to one single kind of afferent impulse. In looking over the field generally, I am more and more impressed with the number of responses in which afferent impulses from more than one source can be shown to participate. I am doubtful whether any single reflex response, particularly a response of the skeletal muscles, can be shown to involve afferent impulses from one source only.

In making these statements, I am fully aware that in the elicitation of certain reflexes under experimental conditions, one

nerve trunk only may be stimulated, and it may be urged that the reflex response occurs without the access of any other afferent impulses. Stimulation of a particular afferent nerve under constant conditions generally elicits a particular reflex response. Hermann embodied these facts in his statement of the law of specific response to stimulation. But the reflex response of a skeletal muscle involves other afferent impulses than those arising from stimulation of a given afferent nerve in a given manner, which may be regarded as the particular afferent impulses which elicit the response. Tschiriew showed that even the form of the curve of a single muscle twitch elicited by stimulation of the motor nerve to the muscle is modified by section of the afferent nerves from the muscle. Afferent impulses from the muscle itself are involved in its reflex response arising from stimulation of any other afferent nerve. And if the muscle is in situ, other, antagonistic, muscles are involved as well as the prime mover. The deportment of the antagonists is controlled by afferent impulses, arising in part in the antagonists themselves, and in part in other regions, such as the joints. The analysis of even the simplest reflex response in an intact animal shows that it is far from simple in the mechanism involved. One should not lose sight of all the other phenomena following the application of the one form of stimulus to a given limited area or location which is said to elicit the reflex. To lose sight of what follows is to get a very imperfect idea of even the simplest reflex response of a skeletal muscle. In general, it is the accessory afferent impulses, if one may so speak of them—the impulses arising from sensory fields other than the limited one to which a given stimulus is applied—which makes the reflex response biologically adequate, to use Edinger's phrase. That a reflex response may occur in the absence of some of the afferent impulses normally entering into its control does not affect the main statement. It is possible that under experimental conditions a reflex could be elicited which would involve afferent impulses from one and only one sensory field. But it is extremely doubtful whether such a condition ever arises in the intact animal. When we consider the liberation of one reflex

response by one preceding it, and when we consider also the considerable number of afferent impulses which may be involved in such a reflex response as the maintenance of an attitude of the body or a part of it, or in the maintenance of equilibrium, the actions become bewildering in their complexity.

The study of the specific reflex response to stimulation of a given afferent nerve and of the modifications of any given response which occur when any particular component of the afferent group is lacking are of importance not only from the point of view of the physiologist, but from the point of view of the clinician as well. One aid in diagnosis which the clinician employs is the study of the modification of typical motor responses which occurs when any particular afferent channel or channels are blocked. Considerably more precision of facts and ideas is necessary before this particular aid attains to its maximum usefulness to the clinician.

Other writers have also recognized this dependence of the normal response upon afferent impulses from various sources. Upon some such basis, if I get its significance correctly, must the idea of the integrative action,—a summing up of afferent impulses within the central system—of the nervous system be founded. I have expressed elsewhere the belief that the idea of the integrative action of the nervous system is one of the great principles of the physiology of the nervous system. It underlies all the work of Pawloff on conditioned reflexes. And all the work of Pawloff goes to show that it is in the cerebrum that the summing up of the afferent impulses so necessary for the finer sensory discriminations occurs. Instead of being an argument against cerebral localization, as I have once or twice seen intimated, it seems to me that Pawloff's work is an argument in favor of localization. The description in physiological terms of any response occurring through the nervous system must include an account of all the afferent impulses which enter into its inception and control, the central mechanism of this integration, and the efferent pathway. The relationships of the various afferent impulses concerned are not always obvious from the anatomical relations. Most of the instances in which

groups of afferent impulses from different sources are said to be concerned have involved more or less of a subjective element in the demonstration. It is, however, possible to get a purely objective demonstration of the fact that afferent impulses from at least two different sources are involved in postural activity, to use Sherrington's terminology, of the muscles which maintain the position of the head. If one otic labyrinth of a cat is extirpated, there is torsion of the head, the occiput being turned toward the injured side and the nose toward the sound side. If, after an interval varying from one hour to several months, the dorsal roots of the cervical nerves of the opposite side are divided, the torsion of the head disappears (Prince, '16). Subsequent experiments have shown that the processes of compensation are related to a considerable degree to the cerebral hemispheres (Prince, '17). There is a strong presumption, at least, that afferent impulses from divers peripheral sources are normally involved in the control of any motor reaction. All of these impulses of various kinds are necessary for the normal performance of such a motor act. There is also a strong presumption that when one of these afferent channels is blocked by accident or disease, certain of the other channels may, by an increase in the quantity of energy which passes over them, compensate, in part at least, for the loss of the impulses which formerly came in over the damaged pathway. What is commonly called vicarious assumption of function may be a reality in this sense and in this degree. But it is not necessary to postulate the participation in this process of compensation of any system or group of fibers which is not normally concerned in the control of the reactions in some degree. A more detailed account of this phase of the question will be presented in a forthcoming discussion of some unpublished experiments on the otic labyrinth. (See also Wilson and Pike, '12.)

I wish to say here, however, that the minimal deficiency of function would be an incorrect index of the actual function of such an organ as the otic labyrinth, as the index would be too low. I may remark in passing that Prince's results effectually dispose of the italicized portions of Edinger's remarks on the

localization of all reflexes. As the matter appears to me now, I would say that the loss of or injury to any given region of the brain may be compensated for, in part at least, by an increase in the quantity (without any change in the quality), to use a suggestion of Hughlings Jackson's, of the nervous energy passing over the other afferent pathways or through other central stations which are normally involved in the functions of the injured part. Compensatory processes of this general nature should be considered in arriving at an estimate of the normal function of any injured or lost portion of the central nervous system. And if, as I believe has now been definitely shown, these processes do enter into the problem of the interpretation of cerebral function, the minimal deficiency of function observable after a long period of recovery will be too low to serve as an accurate index of the normal function of the injured or lost part. Such a view is not in any way destructive of or antagonistic to von Monakow's argument for cerebral localization. As I see the problem, it strengthens von Monakow's general position inasmuch as it shows that normal cerebral function may be even greater than he imagines.

The view that more numerous and more widely separated groups of nerve cells and fibers are necessary for essentially the same sort of movement in higher animals than in lower and the view that afferent impulses from different sources are concerned in most of our neuromuscular reactions have a certain bearing on the hypothesis of circumscribed centers each having a definite and particular function. Von Monakow has taken the speech center as a test case and adduces evidence that the cerebral speech mechanism cannot be such a circumscribed center. Space does not permit a consideration of the evidence against such circumscribed centers urged by other physiologists (Leonard Hill).

There are other systems or mechanisms in which the hypothesis of a definite circumscribed center is no longer satisfactory. One would expect to find such a definite circumscribed region in the lower levels of the nervous system in the portions which have become highly organized, as Hughlings Jackson expresses it,

and whose responses to excitation occur in a definite regular manner time after time. The group of cells in the medulla oblongata which responds to increase in the concentration of the hydrogen ions in the blood by a respiratory impulse may be taken as a case in point. Probably there is such a definite group of cells from which arise impulses leading to movements of the respiratory muscles, and it is probable also that such impulses do not arise from any other group of cells. The evidence in favor of the normal participation in respiratory movements of accessory respiratory centers in the spinal cord does not appear to me to be conclusive. To this extent and in this sense, the respiratory center is a definite circumscribed center. But the question does not end here. The experimental evidence now at hand on respiratory movements alone is incompatible with the idea of such a circumscribed center as the complete controlling mechanism. Anatomically, the central respiratory mechanism is not very thoroughly known. Experimentally, it is a system of great neurological interest. This interest is heightened for the student of the speech mechanism by the fact that every afferent impulse involved in the control of respiration is involved also in the control of speech. And when we consider that speech involves respiratory movements, most certainly under cortical control, the idea of a circumscribed respiratory center becomes hopelessly inadequate to account for all respiratory movements that are possible in man. A complex mechanism consisting of groups of nerve cells more numerous and more widely separated in man than in the turtle becomes a necessary postulate.

The argument on shock may be summarized by saying that von Monakow in his theory of diaschisis has granted all that could reasonably be asked for shock, i.e., it is a temporary effect from which the cells recover fully, but never assume any greater function than their normal function in an intact nervous system.

One may be pardoned, perhaps, for suggesting that, before any hypothesis of shock as a consideration influencing our interpretation of the function of any level of the central nervous system is accepted, we find out just how necessary any such

hypothesis is. For any compensatory increase in the activity of the lower neurones must be subtracted from the supposed shock effect, and a corresponding amount must be added to the supposed function of the cerebral cortex, as determined by the criterion of a minimal deficiency of function. As the problem stands at present, there are three unknown quantities: 1) the exact function of the lower neurones, motor, sensory, commissural or association; 2) the amount of change of a progressive nature rather than retrogressive, which the lower motor neurones undergo after separation from the higher, and, 3) the exact function of the higher neurones. None of the quantities has been measured independently and directly, and the number of equations so far proposed is less than the number of unknown quantities. It seems idle, therefore, to introduce a fourth unknown quantity—the shock effect—or even a fifth, such as vicarious assumption of function, and to ascribe arbitrary limits to it, when the determination of its real value must await either a demonstration of its actual extent and potency or the solution of the equations involving the three other unknowns.

Certain considerations other than those already adduced may be brought forward in connection with the discussion of von Monakow's views. Diachisis, or shock, or whatever other name one may apply to the change which occurs in the lower levels of the central nervous system when they are separated from the higher, is a reversible change. I have already referred to Sherrington's statement that, when the shock effect has once been induced in the spinal cord by anatomical transection, a second transection below the first has no further effect. In this case the anatomical separation of one portion of the central nervous system once for all from the remaining portions would preclude any reciprocal action of one part upon the other. No possibility of a reversible reaction dependent upon a connection of the lower levels with the higher exists under such conditions. But when the function of the higher levels of the central nervous system is temporarily abolished, by tying off the arteries to the head, the lower part exhibits at first signs of shock similar to those seen after anatomical transection. There is, however, a

return of the reflex responses of the structures lying below the anaemic region of the spinal cord within a period of half an hour or an hour. Anatomical transection at this time is not attended by cessation of the reflexes. Just as in Sherrington's experiments, trauma qua trauma is not the necessary antecedent condition for the onset of spinal shock. But if the circulation to the head is restored and the animal is allowed to recover, a more or less normal deportment gradually returns. If anatomical transection of the cord is done on the following day, or even a few hours after re-establishment of the cerebral circulation, signs of shock appear immediately. The changes which occurred in the spinal cord leading to the return of the reflexes while the circulation to the head was interrupted were reversible, since, to all our tests, they did not greatly outlast the period of failure of cerebral and bulbar function.

There is one other point on which the doctrine of minimal deficiency of function comes into conflict with the conclusions drawn from the results of more acute experiments. Francois Franck and Pitres taught that in mammals tonic movements of the skeletal muscles originated from the lower motor cells (e.g., basal ganglia) and that the clonic movements originated from the higher motor neurones. Epilepsy and epileptiform convulsions (Hughlings Jackson) are of cortical origin. Gowers taught that a spastic paralysis indicated a lesion of the higher motor neurones, while a flaccid paralysis indicated a lesion of the lower motor neurones. Decerebrate rigidity (Sherrington) is due to the activity of lower motor neurones. Horseley reported some experiments from his laboratory in which absinthe was used to induce convulsions in cats. If the cerebral hemispheres were present along with the rest of the central nervous system, absinthe produced clonic convulsions. If the cerebral hemispheres were removed, absinthe produced tonic convulsions. If one cerebral hemisphere was removed and the other left intact, clonic convulsions appeared on the opposite side. So general has the belief in this hypothesis of the origin of tonic and clonic movements become that many have insisted that the pyramidal fibers exert an inhibitory action upon the lower

motor neurones. Concerning the truth of this latter statement, I must confess to a deep and enduring skepticism. Complications arise in such a scheme. If we follow out the types of movement that are present in various representatives of the vertebrate phylum, we find that even in such forms as the chimaeroid fishes in which higher motor neurones, as we know them in mammals, are lacking, clonic as well as tonic movements are possible. Moreover, in such forms, there is no sustained rigidity of the skeletal muscles: even without the supposed inhibitory action of the pyramidal fibers, the lower motor neurones do not normally develop any activity which results in a prolonged spastic condition of the muscles. If in the higher type of animals the pyramidal fibers exert an inhibitory influence, it seems equally clear that in the course of the evolution of vertebrates a change has occurred in the lower motor neurones, resulting in the development of some activity which must be inhibited. One must therefore admit a change in the function of the lower motor neurones in phylogenetic development if the hypothesis of the tonic inhibitory action of the pyramidal fibers is to be substantiated. Such a change in the function of the lower motor neurones seems improbable. It appears simpler to assume that as evolution has progressed there has been a separation in the types of movement represented by higher and lower motor neurones; and that in the higher animals, when the higher motor neurones are injured or destroyed, there may be a change in the amount of energy passing through—a quantitative but not a qualitative change—in the function of the lower motor neurones. As Dejerine ('14) shows, man is the only form in which a permanent spasticity of the skeletal muscles results from a purely cortical lesion. Goltz's decerebrated dog, in which although decerebration was not complete, no part of the motor area remained, did not exhibit any permanent spasticity. Complete decerebration in a dog is followed, usually within an hour, by marked decerebrate rigidity (Sherrington). The particular nerve cells which it is necessary to rupture in order to produce permanent spasticity have a different anatomical location in man as compared with the dog. Some change in the anatomical

site of the cells whose removal is necessary for the genesis of spasticity by the remaining cells of the central nervous system has occurred in the course of evolution from lower to higher vertebrates. The pyramidal fibers in a dog do not apparently exert the inhibitory effect on the lower motor neurones which they are said to exert in man.

Spinal shock, while of little direct interest to the present-day internist, has appealed to the clinical neurologists in days past, and from them has come the clinical counterpart of the laboratory expressions. That the necessity for some hypothesis or theory of shock is still felt among clinicians is shown by the fact that Mott ('16) has applied von Monakow's views in the attempt to explain some of the conditions arising in cases of shell shock. It is my opinion that the importance of a conception of the changes occurring in the nervous system as the result of injury will meet with more general recognition as the effects of war conditions are more generally and more critically studied. Two of the earlier attempts of clinicians to explain the effects of injury to or disease of the higher motor neurones are those of Gowers and Hughlings Jackson. Gowers formulated his ideas in terms of inhibition, but, in the opinion of some clinical neurologists, his hypothesis is unsatisfactory. Hughlings Jackson phrased his conceptions in terms of energy. He thought that if one level of the nervous system was damaged by disease about the same quantity of energy as passed through the whole central system before the injury passed through the remaining levels after the injury. Although he does not expressly say so, Jackson's view, particularly in the form in which it was expressed by Horsley ('07), postulates a quantitative change in the number or intensity of impulses going through the remaining nervous pathways. I can hardly see how the change in the amount of energy in the remaining levels of the central nervous system which he imagines to occur after the shutting out of one level can occur without such a quantitative change as has been shown to occur in some levels of the central nervous system. To all intents and purposes, the idea of a quantitative change in function must have been present in Jackson's mind. I do not

remember, either, that he used the term vicarious assumption of function. It is true that Jackson was not an experimentalist, but his powers of observation and of deducing from his facts a generalization which would hold them all together were extraordinary. In the matter of cerebral localization, he anticipated by several years the experimental work of Fritsch and Hitzig. The idea of a change of energy in the remaining levels of the central nervous system should, from its authorship, command at least a careful scrutiny. But aside from some of the fruitful suggestions of Luciani, I have seen little or no use made of the hypothesis by experimentalists, despite the fact that such a hypothesis might be given the rank of a fundamental assumption. I am strongly of the opinion at present that we have experimental proof that a given conduction pathway may carry a greater quantity of nervous energy after injury to another pathway associated with it in the control of a given response than it carries under the usual conditions.³

³ Prof. W. M. Bayliss, who has read the manuscript, has asked me just what the earlier statement of Jackson about the change in the quantity of nerve energy passing over a given pathway might mean in terms of the recent work of Lucas and Adrian on the nerve impulse. One may take as an example of such a change the crossing over of efferent impulses from the respiratory center at the phrenic nuclei. (Porter, *Journal of Physiology*, 1894-5, 17, p. 455). The reader must consult the original paper for the full description of the phenomena, as it is too long to give here in detail. When the spinal cord is hemisected above the level of origin of the phrenic nerve, we will say on the right side, the movements of the half of the diaphragm on that side cease. If the phrenic nerve of the opposite (uninjured or left) side is divided, the movements of the right half of the diaphragm begin again. The impulses which were passing down the left side of the cord now cross to the right side. As I see it, there is a change in the quantity of nervous energy passing over the commissural fibers and synapses from the left phrenic nucleus to the right. It is possible, even probable, that the increasing asphyxial condition which comes on after section of the left phrenic nerve leads to the excitation of more cells in the bulbar respiratory center and to the sending out of impulses over more efferent fibers than before. It is not necessary to postulate any increase in the intensity of the impulses coming over any one fiber. In view of Stirling's demonstration that the synapses have the power of summation of impulses, and Sherrington's experiments, as well as observations by G. N. Stewart and myself, pointing to the same conclusion, I think it probable that the principal change occurs in the passability of the synapses. In the compensations occurring after loss of the otic labyrinth, it does not seem possible that either more fibers are excited in any of the afferent systems entering

One reason for the neglect of Jackson's hypothesis may be that Jackson's conception is distinctly that of a physiologist, while clinicians generally have tried to interpret the nervous system without much reference to purely physiological data. The physiologist has generally given too little consideration to well established clinical data, and has often exercised too little critical discrimination with regard to widely current beliefs which were not necessarily in accordance with the facts. I find Jackson's views in general better suited to constructive work than Goltz's.

The odds in favor of any hypothesis of shock and against cerebral localization could scarcely be greater than von Monakow has granted. He has understated rather than overstated his case. To my mind, therefore, one of the fundamental questions in the physiology of the nervous system, and in fact the question that underlies practically all of our interpretation of the effects of lesions of the central nervous system today, is whether or not a nerve cell, or group of cells, perhaps forming a potential reflex arc, in any way increases quantitatively, after injury to a system connected with it, the work which it has been doing while all its connections are intact. Unless the possibility of such a quantitative change can be excluded, the whole hypothesis of shock must be modified. And if such a quantitative change can be shown in such an isolated (speaking relatively, of course) group of nerve cells, even von Monakow's conclusions must be modified in favor of a stricter view of cerebral localization than the one he now holds.

If von Monakow is right in his conclusions from anatomical data, and, as I have insisted elsewhere, they derive great support from the experimental data, Edinger's dictum becomes definitely obsolete, and takes with it all the obscurity and vagueness of the shock hypothesis, as well as, let us hope, some of its acrimony.

into the process of compensation or that impulses passing over these fibers are any more intense than before. There may be an increased sensitivity of some of the receptors, but it seems probable that the main thing is the change of resistance at the synapses.

On the basis of the all or none law, it is difficult to see how such a severe effect as has sometimes been supposed to result from transection of the spinal cord is possible.

But, if the rigid conceptions of the segmental system are to be substantiated and shock in all its pristine vigor is to remain with us, then must it be conceded that von Monakow has been pursuing a mirage and that the inferences from the great amount of fact collected in his volume are largely untrue. This I am loath to admit, since my own interpretations of experimental findings would be swept away with it. I may repeat that it is necessary to choose between the hypothesis of spinal shock and the segmental theory, on the one hand, and the theory of cerebral localization, on the other. The adherent of the theory of cerebral localization need not be unduly troubled by misgivings as to the security of his position until it has been shown beyond mere assumption that the things supposed to occur in shock actually do occur. So far as the experimental evidence goes at present, it is against Goltz's position rather than in favor of it. Whatever objections I may urge against von Monakow's position are to be regarded as constructive rather than destructive. Neither of us doubts the transient effect of shock nor the general truth of cerebral localization. I believe that the available evidence justifies a stricter view, a more rigid localization than the one he has propounded in his volume.

The doctrine of cerebral localization must be regarded as established, and the hypothesis of shock as Goltz formulated it must be discarded. Not only has there been no direct proof of the hypothesis of shock, but there is experimental proof of the main tenets of the theory of cerebral localization. There must be a corresponding revision of many of the chapters in our texts of physiology as they stand today.

The establishment of the theory of cerebral localization will bring us a step nearer to the realization of the prophetic vision of Magendie ('16b), which has been obscured for so many decades by the mass of detail accumulated by anatomists and experimentalists alike, both of whom have so far failed to accept the interpretation of the great French experimentalist.

One means by the term brain (*cerveau*), the organ which fills the cavity of the cranium and that of the spinal canal. To facilitate the study, the anatomists have divided it into three parts, the *cerveau*

(brain) properly speaking, the cerebellum, and the spinal cord. This division is purely scholastic. In reality the three parts form one and the same organ.

It is only when we regard the cerebrum as the great sensory and motor mechanism to which all the other parts contribute and from which they receive that we can rid ourselves of the idea—eminently fallacious, as I view it—of independent sensory or motor activities of other portions of the nervous system and begin to see all parts of the system acting as one system.

We are hearing much of the clearness of French thought in relation to scientific subjects at the present time. It is well that we are beginning to accord it the somewhat tardy recognition which it so nobly deserves. I am minded to emphasize the value of clear thinking in science and particularly in physiology, by a quotation from another source. In the German edition of Luciani ('07), but unfortunately omitted from the English edition, there is a fine sentence concerning another very prevalent fallacy—the view that the otic labyrinth has its main functional pathway through the cerebellum—but which is equally applicable to the popular status of shock to-day.

One cannot deny that the clearness and consistency of the book by leave something more to be desired, and its following among many clinicians and surgeons would be difficult for me to explain if I did not remember that great is the number of uncritical people among whom words of uncertain meaning have more weight than positive facts and clear, well considered explanations.

The plausibility of the words of uncertain meaning may be greater than that of the other type of exposition. How else may one account for the amazing vogue of fakirs and quacks? It may be remarked in passing that von Monakow inclines to the view that there is a cortical station for labyrinthine fibers in the cerebrum.

More recently, Luciani ('16), has warned against the confusion in thought which inevitably follows when one fails to recognize the essential unity of action of the central nervous system, but clings instead to the idea of separate, independent, and sharply localized centers in various divisions of the central

nervous system. As I have indicated elsewhere, some conception of a quantitative change in the amount of energy passing over a given nerve pathway after injury to another may have been present in Luciani's mind years ago.

Von Monakow's work will take its rank along with other classical monographs on the nervous system—Francois-Franck's "Lecons sur les Fonctions Motrices du Cerveau," Luciani's "Cervelletto" and Soury's "Le systeme nerveux centrale." It is to be hoped also that the various illuminating addresses and lectures which were published during the years when the larger volume was in preparation will be continued long after its publication.

The objection sometimes urged against works in the German language that American work does not receive proper consideration can scarcely be urged against von Monakow's volume. American anatomists, psychologists, clinical neurologists, and surgeons are mentioned in the index of authors. The small number of American physiologists whose work is cited may perhaps be taken as index of the lack of interest in this phase of physiology which has been manifested by American workers.

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WEIGHTS OF VARIOUS PARTS OF THE BRAIN IN NORMAL AND UNDERFED ALBINO RATS AT DIFFERENT AGES

C. A. STEWART

Institute of Anatomy, University of Minnesota, Minneapolis

ONE FIGURE AND THREE TABLES

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In connection with an earlier study of the changes in the relative weights of the various organs in underfed albino rats (Stewart, '18 b), the brain was observed to manifest a remarkable tendency toward continued growth in very young animals, even when increase in body weight was prevented. The work has been extended in the present investigation to a more detailed consideration of the growth of separate parts of the brain in severely stunted rats. In addition, a considerable number of observations was made on the weights of different parts of the brain in normal rats at various ages. This phase of the work, however, was discontinued when I learned that Prof. H. H. Donaldson, of The Wistar Institute of Anatomy, Philadelphia, had undertaken the latter problem upon an extensive scale. Fortunately, we had each selected the same brain subdivisions for consideration, so that direct comparison of our results is possible. Dr. Donaldson has kindly furnished me with a record of his data for

stock albino rats (presented in part in a Harvey Lecture, December, 1916) which in general are in agreement with my own observations upon normal animals. Only my own data are presented in this paper, however. This opportunity is taken to acknowledge my indebtedness to Prof. C. M. Jackson for valuable advice given during the course of the present experiments.

MATERIAL AND METHODS

In the present investigation the brains of 64 normal (31 males, 33 females, table 1), and of 29 test rats (19 males, 10 females, table 2) were used. Among the 64 normal rats are included 22 individuals which also served as the direct controls for the test rats. The rats used were all Albinos (*Mus norvegicus albinus*) from the colony in the Institute of Anatomy here.

The number and sex of the normal animals killed at the selected periods between birth and adult age are shown in table 1. Of the direct controls (table 2), 12 rats (8 ♂, 4 ♀) were killed at birth (average weight 4.7 to 5 grams), 9 rats (5 ♂, 4 ♀) at approximately 10 grams, and one male at 12 grams body weight.

The test rats were repeatedly starved by isolation from the mother for various periods as described elsewhere (Stewart, '18 b). In this manner 15 individuals (9 ♂, 6 ♀) were held approximately at birth weight for periods ranging from 5 to 18 days; and 13 rats (9 ♂, 4 ♀) were permitted to increase slightly in weight reaching approximately 10 grams at 3 weeks of age. In addition one male was weaned when 21 days old, body weight 10.5 grams, and was placed upon a limited diet of whole wheat (Graham) bread and whole milk. At 56 days of age this individual weighed only 12 grams.

It will be noted that the average final body weight is practically the same for the control and the test rats of each group (table 2). In comparing the data for the normal and the starved individuals, the slight differences existing in body weight have been disregarded. This seems justified since the error involved is small and cannot obscure the changes produced by the experimental conditions. Strictly speaking, however, a slight correction should be made as previously noted (Stewart, '18 b).

TABLE 1

Number and sex of rats, body weight and length, and weight of the brain with the percentage weights of its various subdivisions in normal rats at various ages

NUMBER, SEX, AND AGE OF RATS	GROSS BODY WEIGHT	BODY LENGTH	BRAIN WEIGHT	PER CENT OF BRAIN CERE- BRUM	PER CENT OF BRAIN STEM	PER CENT OF BRAIN CEREBEL- LUM	PER CENT OF BRAIN OLFACTO- RY BULBS
	grams	mm.	grams				
8 ♂, 4 ♀, Newborn.....	4.86	48.6 ¹	0.2086	64.4	29.3	3.65	2.51
1 ♀, 2 days.....	5.40	50.0	0.2640	62.4	30.3	4.28	3.12
1 ♀, 4 days.....	6.00	⁵	0.3545	67.6	25.6	5.64	1.31
1 ♀, 5 days.....	8.50	58.0	0.4400	68.6	22.5	5.43	3.47
1 ♂, 6 days.....	10.00	62.0	0.5135	69.4	22.4	5.36	2.75
1 ♂, 1 ♀, 8 days.....	9.80	62.0	0.6259	71.7	18.8	6.55	2.93
2 ♂, 1 ♀, 9 days.....	10.5	66.5 ²	0.6969	71.4	19.1	6.32	3.15
1 ♂, 1 ♀, 10 days.....	10.35	65.0	0.6699	71.2	18.8	7.33	2.65
1 ♀, 11 days.....	9.50	62.0	0.7451	70.1	18.7	8.06	3.14
1 ♂, 12 days.....	11.00	⁵	0.6838	70.9	19.3	7.01	2.79
1 ♀, 14 days.....	15.00	⁵	0.9994	69.2	17.6	10.2	3.04
3 ♂, 3 ♀, 21.3 days.....	23.2	86.0 ³	1.2800	67.1	16.2	12.8	3.69
1 ♀, 28 days.....	28.0	97.0	1.2087	65.1	16.6	13.5	4.47
1 ♀, 35 days.....	33.0	105.0	1.3500	65.0	16.9	13.7	4.33
1 ♂, 2 ♀, 42.6 days.....	53.2	126.3	1.4389	64.3	17.3	13.2	4.83
1 ♂, 2 ♀, 49.6 days.....	41.5	115.6	1.2026	63.1	18.3	14.3	4.15
1 ♂, 63 days.....	73.5	141.0	1.5856	63.7	17.8	14.2	4.62
3 ♂, 4 ♀, 70 days.....	96.1	149.0 ⁴	1.5962	63.6	18.0	13.9	4.58
1 ♂, 1 ♀, 114 days.....	142.5	176.0	1.6084	64.4	18.8	13.9	2.90
1 ♂, 1 ♀, 127 days.....	131.1	169.5	1.6839	61.4	19.4	14.1	5.01
2 ♂, 2 ♀, 143 days.....	164.7	182.5	1.7015	62.1	20.3	13.8	3.81
4 ♂, 4 ♀ { ♂ 357 days..	♂257.0	♂212.0	1.8100	60.8	21.8	14.6	2.92
{ ♀ 454 days..	♀213.0	♀197.0					

¹ Average of 10 individuals.

² Average of 2 individuals.

³ Average of 5 individuals.

⁴ Average of 6 individuals.

⁵ Not recorded.

The rats were killed either by chloroform or (in a few cases) by bleeding. The body (nose-anus) and tail lengths were immediately measured in the usual manner. The head was subsequently severed at a point immediately behind the foramen magnum. The brain was then carefully removed (care being exercised to preserve the cerebellar paraflocculi) and weighed in a closed container on balances accurate to 0.1 mgm.

The brain was next placed upon a moist plate of glass and its various parts dissected as follows. The olfactory bulbs were removed by a vertical incision at the point where they pass beneath the frontal lobes of the cerebrum. The cerebellum was then removed by severing its various crura or peduncles. Finally the cerebrum was separated from the brain stem by an incision immediately anterior to the superior colliculi passing through the anterior part of the crura cerebri. The cerebrum thus included the telencephalon (except olfactory lobes) and dien-cephalon, and the brain stem included the midbrain, pons, and medulla oblongata. The four brain subdivisions thus obtained were placed in a moist chamber and later carefully weighed in a closed container.

In all cases there is some difference between the total weight of the separate parts and the initial brain weight, due no doubt, either to evaporation from, or to fluid adhering to, the subdivisions weighed. Fortunately, however, the error is generally small and insignificant, especially as compared with the changes in weight that have occurred in the test rats. Based on the assumption that the error is probably distributed more or less proportionately among the various portions of the brain weighed, an attempt was made to correct the existing error in computing the percentage for each subdivision, by using the total weight of the separate parts rather than the original brain weight.

The observations in table 1 upon normal rats less than three weeks of age are grouped only in instances where there were two or more individuals of the same age. Later, when the brain growth is less rapid, the data have been averaged, grouping individuals differing a few (usually three or four) days in age. In the case of the eight adult rats only is there any considerable range in ages. Since the sexual difference in brain weight in animals of corresponding weight is comparatively small (Donaldson, '08, '09), the observations for males and females of each group have been combined. This is also justified by the relatively small number of observations, since the individual variations would obscure any existing difference according to sex.

In table 2 the data for the control groups and for the test rats are likewise grouped, only the averages being given. The original individual observations will be filed at The Wistar Institute of Anatomy and Biology (Philadelphia), where they may be consulted by those interested.

A preliminary report of the present investigation appeared in the Proceedings of the American Association of Anatomists, Minneapolis Meeting, December, 1917 (Stewart, '18a).

BRAIN

The weight of the entire brain (table 2) is considerably higher in the various groups of test rats than in the corresponding younger controls of the same body weight. In the fifteen individuals (9 ♂, 6 ♀) held at birth weight for various periods there is an increase from an average (sexes combined) of 0.2086 gram in the newborn controls to 0.4468 gram in the test rats, an increase of about 114 per cent. An inspection of the individual data in table 2 shows that the increase is greater in those rats held at maintenance for longer periods.

As may be observed in table 2, the body length also increases, although the body weight is held constant. The brain weight is also much greater in the stunted animals than in normal rats of the same body length, although the difference is not so great as when those of the same body weight are compared.

In the test rats weighing about 10 grams at 3 weeks the relative increase is less, amounting to approximately 33 per cent; while at 56 days with body weight at 12 grams the excess of brain weight in the test rats is about 30 per cent. In an earlier report (Stewart, '18 b) the brain in rats underfed from birth and weighing 10 grams at 3 weeks of age was found to exceed that in normal rats of corresponding body weight by about 60 per cent, which is considerably more than the excess obtained for a comparable group in the present series. In general, however, the results agree in showing a stronger growth tendency of the brain in the younger and smaller rats.

The increase in brain weight in spite of underfeeding with nearly stationary body weight is probably best shown in figure 1

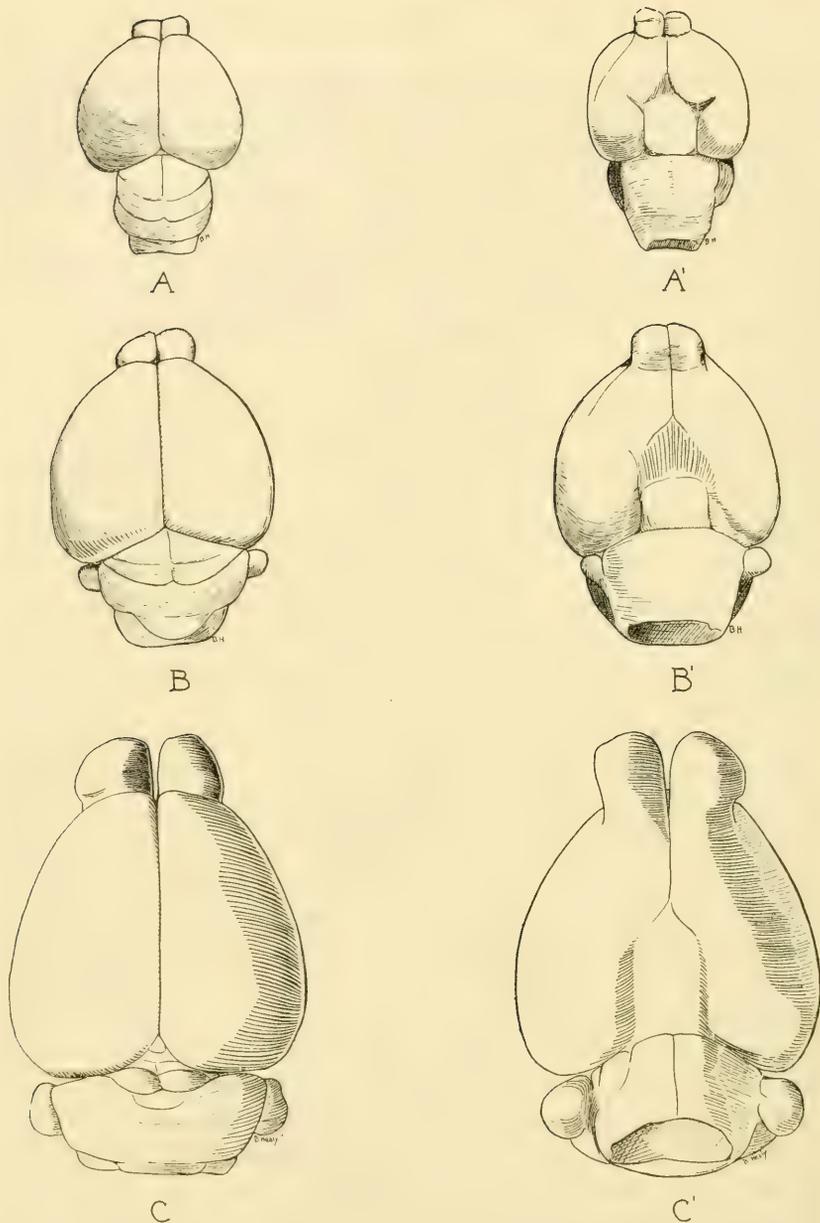


Fig. 1 *A* and *A'*, dorsal and ventral view, respectively, of brain of normal newborn rat. Body weight, 5.4 grams. Brain weight, 0.238 gram. $\times 3$.

B and *B'*, dorsal and ventral view, respectively, of brain of rat kept at birth weight by underfeeding for 20 days. Body weight, 5 grams. Brain weight, 0.506 gram. $\times 3$.

(Continuation of explanation of figures on page opposite.)

TABLE 2

Number, sex, weight, and length, with weights of the brain and its various parts in normal and underfed rats at different ages

NUMBER, SEX, AND AGE OF RATS	GROSS BODY WEIGHT	BODY LENGTH	BRAIN	CERE- BRUM	STEM	CERE- BELLUM	OLFACTORY BULBS
	grams	mm.	grams				
8 ♂, Control, newborn....	4.97	49.1 ¹	0.2106	0.1375	0.0622	0.0079	0.0055
1 Test ♂, 5 days.....	4.7	56.0	0.3653	0.2481	0.1085	0.0213	0.0151
1 Test ♂, 6 days.....	5.5	56.0	0.3872	0.2724	0.0940	0.0232	0.0118
1 Test ♂, 7 days.....	4.6	55.0	0.3743	0.2563	0.1027	0.0213	0.0150
1 Test ♂, 12 days.....	4.8	53.0	0.4711	0.3368	0.1014	0.0307	0.0154
1 Test ♂, 12 days.....	5.8	57.0	0.5348	0.3742	0.1143	0.0356	0.0246
1 Test ♂, 12 days.....	5.0	57.0	0.4790	0.3413	0.1134	0.0335	0.0192
1 Test ♂, 13 days.....	5.5	59.0	0.5404	0.3845	0.1334	0.0346	0.0242
1 Test ♂, 14 days.....	5.5	57.0	0.4920	0.3464	0.1062	0.0334	0.0220
1 Test ♂, 14 days.....	5.8	60.0	0.4571	0.3247	0.1053	0.0291	0.0180
Average, 10.6 days.....	5.24	56.7	0.4557	0.3205	0.1088	0.0292	0.0184
4 ♀, Newborn.....	4.65	47.5 ²	0.2046	0.1323	0.0611	0.0074	0.0048
1 Test ♀, 5 days.....	4.9	54.0	0.3603	0.2549	0.0999	0.0205	0.0149
1 Test ♀, 11 days.....	4.0	52.0	0.3728	0.2564	0.1033	0.0212	0.0154
1 Test ♀, 12 days.....	4.8	55.0	0.4434	0.3139	0.1018	0.0262	0.0180
1 Test ♀, 12 days.....	5.0	54.0	0.5079	0.3444	0.1068	0.0328	0.0204
1 Test ♀, 13 days.....	5.0	56.0	0.4019	0.2892	0.0872	0.0256	0.0142
1 Test ♀, 18 days.....	5.1	54.0	0.5212	0.3732	0.1180	0.0415	0.0216
Average, 12 days.....	4.8	54.1	0.4346	0.3053	0.1028	0.0280	0.0174
5 Control ♂, 9 days.....	10.2	63.0	0.6309	0.4589	0.1280	0.0396	0.0181
9 Test ♂, 22 days.....	10.4	67.8	0.8837	0.6169	0.1578	0.0956	0.0265
4 Control ♀, 9.5 days.....	9.6	63.3	0.6845	0.4830	0.1282	0.0497	0.0212
4 Test ♀, 22 days.....	9.6	65.9	0.8444	0.5894	0.1477	0.0896	0.0229
1 Control ♂, 9 days.....	12.0	69.0	0.7324	0.5304	0.1340	0.0556	0.0240
1 Test ♂, 56 days.....	12.0	77.0	0.9544	0.6312	0.1856	0.1210	0.0410

¹ Average of 7 individuals.

² Average of 3 individuals.

On comparison with the brain of the newborn rat (*A* and *A'*), it is evident that during underfeeding (maintenance) not only the brain as a whole, but also the olfactory bulbs and tracts, cerebral hemispheres, colliculi, cerebellum and flocculi, tuber cinereum, pons, and medulla continue to grow in young rats in spite of practically no change in body weight for 20 days. Comparison with the normal brain at 20 days (*C* and *C'*), however, shows that the growth of the various parts of the brain mentioned above, while considerable, nevertheless has been greatly retarded.

C and *C'*, dorsal and ventral view, respectively, of brain of normal rat at 20 days of age. Body weight, 17.5 grams. Brain weight, 1.047 grams. $\times 3$.

(*a*, *a'*, newborn control; *b*, *b'*, test rat). As compared with the control of the same body weight, not only the various subdivisions weighed, but also the olfactory tracts, tuber cinereum, corpora quadrigemina, and especially the para flocculi are evidently much larger in the starved rat.

Although considerable brain growth thus occurs during maintenance of constant body weight in young rats, nevertheless it occurs at a greatly retarded rate in comparison with the normal growth during the corresponding period of time. This is so well shown in figure 1 (*b*, *b'* and *c*, *c'*) that a lengthy discussion is unnecessary.

TABLE 3

Comparison of relative intensity of growth of various parts of the brain in normal and test rats

	PERCENTAGE BY WHICH THE WEIGHT OF THE VARIOUS PARTS OF THE BRAIN			
	At 11 days exceeds that at birth		At 3 weeks exceeds that in normal 10-gram rats	
	Normal	Test	Normal	Test
Cerebellum.....	696	272	274	113
Olfactory bulbs.....	351	240	144	30
Cerebrum.....	293	131	85	29
Brain stem.....	130	72	63	20

In older rats held at maintenance for various periods, investigators in general have noted practically no change in the brain weight. Thus Hatai ('08) found the brain weight in stunted rats to be practically identical with that for normal younger rats of the same body weight. In a large series of rats studied by Donaldson ('11), after maintenance from 30 to 51 days of age, the brain exceeded the calculated initial weight by only 3.6 per cent. Jackson ('15 a) and Stewart ('16) conclude that there is practically no change in the weight of the brain in rats held at maintenance for various periods starting at 3 weeks of age. Holt ('17) noted a slight increase in brain weight in under-sized rats fed upon an unsuitable diet of whole corn after the period of weaning.

Aron ('11) publishes data showing in a few instances the brain weight in greatly stunted dogs practically equal to that in normal heavier dogs of the same age. However, no observations were made concerning the initial brain weight at the beginning of the experiment and the extent of the brain growth which apparently occurred during the underfeeding is therefore uncertain.

It is interesting to note that Variot and Lassabliere ('09) found the growth of the brain in underfed infants to be retarded less than the growth in body weight, the brain thus increasing at the expense of other tissues of the body. This observation agrees with my own results for young albino rats.

During severe starvation a slight decrease in the weight of the brain was noted by Bechterew ('95) in puppies and kittens, and by Hatai ('04) in young rats. Acute and chronic inanition in adult rats causes but little if any loss in absolute brain weight (Jackson, '15 b). A very complete summary of the literature bearing upon the effect of inanition upon the brain is given by Jackson ('15 b).

CEREBRUM

If the percentages are calculated from the combined weight of the separate brain parts, it appears that the cerebrum (table 1) (telencephalon and diencephalon, excluding olfactory bulbs) during normal growth increases from an average of slightly more than 64 per cent of the entire brain at birth (sexes combined) to a relative maximum of approximately 71 per cent during the early part of the second week. Thereafter, although increasing in absolute weight, the cerebrum forms a progressively smaller proportion of the brain, decreasing to an average of approximately 67 per cent (sexes combined) at three weeks, and to about 61 per cent at one year and later. My results agree fairly well with those of Hatai ('15) for adult individuals of approximately similar body length, with those of Sugita ('17) for the rat during the first 150 days, and also with the unpublished data of Donaldson (personal communication). Slight differences appear which are presumably due partly to experimental error and partly to normal variability in the size of the brain segments.

In the stunted rats kept at birth weight for various periods, and also in those weighing approximately 10 and 12 grams at three and eight weeks, respectively, the weight of the cerebrum (table 2) considerably exceeds that of the normal younger controls of corresponding body weight. For the first group (sexes combined) there is an increase from an average of 0.1358 gram in the controls to 0.3144 gram in the test rats, an increase of more than 131 per cent. In the test rats at three weeks (22 days) the increase in the cerebrum is relatively less, amounting to approximately 29 per cent, and at eight weeks it has decreased to about 19 per cent.

As to relative proportions, the percentage weight of the cerebrum is slightly higher in the test rats kept at birth weight various periods than in the controls, the apparent increase being from an average of approximately 64 per cent of the combined weight of the separate parts in the latter to 67 per cent in the stunted individuals. The range in the test rats is from about 63 per cent to 69 per cent, increasing in general with the length of the experiment. If we now compare the corresponding change in relative proportion of the cerebrum during normal growth, it is evident that with the increase in brain weight from birth there is normally an increase in the percentage that the cerebrum forms of the entire brain, similar and practically equal to that noted in the brain of equal size in the stunted rats.

In the test rats weighing about 10 grams at three weeks, however, there is apparently a slight decrease (71 to 69 per cent) in the relative size of the cerebrum as compared with the controls of the same body weight. Likewise during normal growth there is a similar decrease in the percentage weight of the cerebrum while the brain weight is increasing from about 0.6500 gram to 0.8700 gram. At eight weeks of age the cerebrum in the test rats, though absolutely larger, is relatively smaller than in the control. This change likewise is probably associated with the usual tendency toward declining relative size of the cerebrum in normal brains of corresponding weight, although the difference in this case is greater than would be expected from the apparent change during normal growth.

In general, therefore, the data indicate that during the persistent growth of the brain, in very young rats stunted by underfeeding, the cerebrum (telencephalon and diencephalon) maintains the same relative size as in the normal brain of corresponding weight.

BRAIN STEM

The percentage weights (calculated from the combined weights of separate brain subdivisions) for the brain stem (including midbrain, pons, and medulla oblongata) show a relative decrease from an average of about 29 per cent of the normal brain at birth to about 16 per cent at three weeks. Subsequently the growth of the brain stem is more rapid than that of the brain as a whole, resulting in a gradual increase in relative weight to an average of about 22 per cent in the adult rats. The normal initial decrease and subsequent increase in the relative size of the brain stem is in agreement with the observations by Sugita ('17) and Donaldson (unpublished data). As compared with adult animals of corresponding body length, my results correspond fairly well with those obtained by Hatai ('15).

In the stunted rats held at birth weight for various periods, and also in the other groups of test animals, the weight of the brain stem (table 2) in all cases considerably exceeds that in the younger controls of the same body weight. In the first group there is an increase from an average of 0.0618 gram (sexes combined) for the controls to 0.1064 gram in the test rats, an increase of approximately 72 per cent. In the test rats at three and eight weeks of age, the increase in brain stem weight amounts to about 20 and 39 per cent, respectively.

As to relative proportions, the brain stem in the rats held at birth weight apparently decreases from about 29 per cent (in the controls) to about 22 per cent of the brain weight. In the test rats at 22 days the brain stem weight has further decreased to about 18 per cent, as compared with 19 per cent in the controls of similar body weight. In the test rat at 56 days, however, the brain stem has slightly increased to 19 per cent (18 per cent in the control).

In these cases, however, the relative size of the brain stem in the brain of the stunted rats corresponds approximately to that in normal brains of the same weight. The only exception is that of the single test rat in which the brain stem should be relatively slightly smaller than in the control, according to the change found in the normal brains of corresponding weights. The difference is slight, however, and may be obscured in this case by individual variation or experimental error.

On the whole, therefore, it appears that during the persistent growth of the brain, in very young rats stunted by underfeeding, the brain stem (midbrain, pons, and medulla) maintains approximately the same relative size as in the normal brain of corresponding weight.

CEREBELLUM

Calculations from the data obtained show that during post-natal growth the cerebellum (table 1) apparently increases rapidly from an average of about 3.7 per cent of the total weight of the separate parts of the brain at birth (sexes combined) to about 14 per cent at seven weeks of age, and maintains approximately this relative weight in the adult albino rat. In general these results agree fairly well with those obtained by Hatai ('15) (for adult rats of body length similar to that of my adult controls), by Sugita ('17) (from birth to 150 days of age), and by Donaldson (unpublished data).

In the rats underfed for various periods the cerebellum (table 2) shows a remarkable growth. In the individuals held at birth weight the cerebellum has increased from an average of 0.0077 gram in the controls (sexes combined), to 0.0287 gram, an increase of over 272 per cent. At three and eight weeks of age the increase in the test rats is approximately 113 and 118 per cent, respectively, as compared with the younger controls of the same body weight.

As to relative proportions, the cerebellum is in all cases found relatively much larger in the brain of the test rats, in comparison with that in control rats of the same body weight. If the percentage of the brain weight formed by the cerebellum in the test

rats (table 2) is compared with that in normal brains (table 1) of the same weight, however, the agreement is surprisingly close. It is therefore apparent that during the persistent growth of the brain in underfed young rats the cerebellum, like the segments previously considered, maintains approximately the same relative size as in the normal brain of corresponding weight.

OLFACTORY BULBS

Calculations from my data (table 1) indicate that the olfactory bulbs, although rather variable, in general increase from an approximate average (sexes combined) of 2.5 per cent of the total weight of the separate parts of the brain at birth, to about 3.7 per cent at three weeks, and probably reach a relative maximum of about 4.8 per cent at six or seven weeks of age. Subsequently their relative weight decreases in the majority of cases, reaching about 2.9 per cent in the adult. Attention should be called to the fact that the data indicate not only a relative decrease, but even an absolute loss in the weight of the olfactory bulbs in the older rats. In general my results agree with those obtained by Hatai ('15), Sugita ('17), Holt ('17), and Donaldson (unpublished data) for normal albino rats, the existing differences probably being due partly to normal variability and partly to experimental error.

In the stunted rats the olfactory bulbs greatly exceed those in the younger controls of the same weight (table 2). For the group held at birth weight there is an increase of nearly 240 per cent. For the other test animals at three and eight weeks of age the increase is less marked, amounting to 30 and 71 per cent, respectively.

The percentage that the olfactory bulbs form of the entire brain weight, especially in the case of the individuals kept at birth weight for various periods, averages higher than that for the newborn controls. According to my data, accompanying an increase in brain weight from approximately 0.2100 gram to 0.4500 gram there is normally a considerable increase in the relative weight of the olfactory bulbs, although apparently not so great as in the stunted rats with brains of corresponding weight.

Thus the olfactory bulbs appear relatively larger in the stunted rats than in normal rats of the same brain weight.

For the group fasting three weeks the relative increase is slight and inconstant. In the normal rats with corresponding brain weight (0.6309 to 0.8837 gram) the relative weight of the olfactory bulbs is likewise nearly stationary, though somewhat variable. This is in agreement with Holt ('17), who found the relative proportions of the olfactory bulbs to remain practically unchanged in rats undersized after four and eight weeks of feeding upon an unsuitable diet of whole corn.

The data for my rat underfed from birth to eight weeks indicate an apparent increase in the relative weight of the olfactory bulbs, which is in accordance with the general tendency toward an increase in the relative size of olfactory bulbs in normal rats with brains of corresponding weight. Miss Holt noted a tendency for the bulbs to increase in relative weight during prolonged defective feeding in rats weighing about 50 grams.

On the whole it therefore appears that during the persistent growth of the brain in underfed young rats the olfactory bulbs tend to maintain a relative size similar to that in the normal brain of corresponding weight. In the youngest and smallest group, however, they apparently become relatively hypertrophied and appear relatively larger than in normal animals with the same brain weight.

DISCUSSION

Quite uniformly the results of experiments have shown that the brain demonstrates a marked ability to grow when increase in body weight is prevented by underfeeding only in very young animals and at a time when the normal growth of the brain is very pronounced. There is, therefore, apparently a definite relation between the increase in size accomplished during starvation and the normal growth power possessed by the organ at the time when underfeeding is commenced. That this dependency upon the intensity of the growth impulse applies also to the various parts of the brain is evident upon comparison of the relative rapidity of growth of the various parts of the brain in young rats.

As is shown in table 3, in both the normal and test rats, the cerebellum manifests the strongest growth power, the olfactory bulbs, cerebrum, and brain stem following in the order mentioned. The perfect agreement in this respect between the control and test individuals can hardly be considered a mere coincidence, but more probably is the expression of inherent normal tendencies.

Furthermore, it has been pointed out that with the growth of the brain in the stunted rats, the various portions of the brain undergo practically the same changes in relative size as found in normal animals of the same brain weight. The olfactory bulbs which show an overgrowth (in the younger group) apparently form the only notable exception to this rule. In general, therefore, it appears that normal growth tendencies foreshadow the character and the amount of the changes that accompany growth of the brain during underfeeding. In other words, the growth of the brain in the stunted rats appears normal, so far as the changes in the size of the constituent parts is concerned.

The tendency for the different brain subdivisions to maintain largely the normal proportions during starvation is in marked contrast to the change in the relative weights produced among various organs of the body as to result of underfeeding. Jackson ('15, p. 152) also noted that in some cases (e.g., liver, alimentary canal) there is a certain degree of parallelism between the normal growth tendency and the behavior of organ weight in young rats when the body weight is held constant. Furthermore, the greatest number of organs showing growth during maintenance (constant body weight) occurs in very young rats during the normal period of most rapid growth (Stewart, '18). The above-mentioned principle therefore applies not only to the brain and its various subdivisions, but also to many other organs. However, there are certain exceptions to this rule, as pointed out by Jackson.

It is interesting to note that the marked growth of the brain in rats stunted by underfeeding occurs only at a period when the normal increase in size is still due partly to cell multiplication, especially in the cerebellum (Allen, '12). This is a phase of the inanition problem worthy of further investigation.

SUMMARY

1. The weights of various parts of the brain were studied in 64 normal rats at various ages, and also in 29 test animals, of which 15 individuals were held at birth weight by underfeeding for periods ranging from 5 to 18 days of age, 13 rats were permitted to increase slightly in weight reaching approximately 10 grams at 3 weeks, and one male weighed 12 grams at 56 days of age.

2. According to the data available, the cerebrum (excluding olfactory bulbs) increases from a normal average of slightly more than 64 per cent of the entire brain at birth, to a maximum of about 71 per cent during the early part of the second week, but subsequently forms a progressively smaller proportion of the brain, decreasing to an average of about 61 per cent in the adult.

The brain stem (including midbrain, pons, and medulla oblongata) decreases from a normal average slightly exceeding 29 per cent of the brain at birth to about 16 per cent at 3 weeks, but later increases reaching a relative weight of about 22 per cent in adult animals.

The cerebellum increases rapidly from an apparent average of 3.7 per cent of the entire brain at birth to about 14 per cent at 7 weeks of age, and thereafter.

The olfactory bulbs, while variable, in general increase from an average of about 2.5 per cent at birth to 3.7 per cent at 3 weeks, and probably reach a relative maximum of slightly more than 4.5 per cent at 6 or 7 weeks of age. Subsequently there is a gradual decrease in relative weight to about 2.9 per cent in the adult rat. The data indicate not only a relative decrease, but even an absolute loss in the weight of the olfactory bulbs in the older rats.

3. For the stunted rats the weight of the brain as a whole in the individuals held at birth weight for various periods averaged 114 per cent higher than that in the controls, whereas the excess in test rats weighing 10 grams at 3 weeks and 12 grams at 8 weeks of age was 33 and 30 per cent, respectively.

As shown in figure 1, the increase is shared not only by the various brain parts dissected and weighed, but also by the olfactory tracts, tuber cinereum, colliculi, and the paraflocculi.

Of the various parts of the brain, the weights of the cerebellum, olfactory bulbs, cerebrum, and brain stem exceed those for the control rats of corresponding weight in the order mentioned, the greatest change occurring in the individuals kept at birth weight for various periods. In this group of individuals the different parts of the brain in the order above listed show an increase of 272, 240, 131, and 72 per cent, respectively.

In the persistent growth of the brain in the young rats stunted by underfeeding, the various parts of the brain in general preserve approximately the same relative weight as in normal individuals of the same brain weight. The olfactory bulbs apparently form an exception to this rule, as they become abnormally large in the younger group of stunted rats. This apparent hypertrophy may be due, however, to experimental error.

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ON THE INCREASE IN THE DIAMETERS OF NERVE-
CELL BODIES AND OF THE FIBERS ARISING
FROM THEM—DURING THE LATER
PHASES OF GROWTH (ALBINO RAT)

HENRY H. DONALDSON AND G. NAGASAKA

The Wistar Institute of Anatomy and Biology

THREE CHARTS AND ONE FIGURE

In the later phases of growth some neurons increase not only in the diameter of the cell body, but also in the diameter of the fiber or fibers growing from the cell body. Moreover, in the case of the fiber, the increase occurs not only in the diameter of the axis cylinder, but, when myelinated, in the myelin sheath also.

In order to determine more precisely how this increase in diameter is distributed between the cell body and the fiber coming from it, we have undertaken to observe during the later phases of growth what takes place in two classes of neurons at the level of the seventh cervical segment of the spinal cord of the albino rat.

The neurons chosen for study were *a*) those with the largest cell bodies in the ventro-lateral group of the ventral horn and the ventral root fibers which were assumed to come from them, and, *b*) those with the largest cell bodies in the corresponding spinal ganglion together with the largest fibers in both the dorsal root and in the nerve just distal to the ganglion. This seventh segment of the spinal cord with ganglia and roots was removed from a series of twenty-four male albino rats which are listed in table 1.

As table 1 shows, these rats range from 17 to 360 days in age and from 18.7 to 316.3 grams in body weight.

As one object of the study was to determine whether the nerve fibers continued to increase in diameter after the cell bodies had

TABLE 1

Data on the twenty-four normal male albino rats used for this study

NUMBER	AGE	BODY WEIGHT	BODY LENGTH	TAIL LENGTH
	<i>days</i>	<i>grams</i>	<i>mm.</i>	<i>mm.</i>
I	17	18.7	86	61
II	17	18.7	88	61
III	26	25.2	97	74
IV	26	25.2	96	72
V	29	43.3	122	94
VI	29	42.8	120	88
VII	39	59.2	130	110
VIII	39	58.9	130	108
IX	49	81.0	148	132
X	49	82.0	147	126
XI	81	115.1	168	141
XII	81	114.5	163	140
XIII	85	120.3	185	150
XIV	85	117.0	185	155
XV	104	149.3	190	158
XVI	104	153.5	187	160
XVII	125	178.0	194	155
XVIII	125	180.8	195	159
XIX	130	233.1	212	185
XX	130	228.8	217	173
XXI	312	243.1	219	176
XXII	312	236.5	213	172
XXIII	360	316.3	234	178
XXIV	360	314.1	235	180

attained their full size, the examination was begun with rats 17 days of age, since at this time some of the cell bodies at least had reached nearly their full size.

TECHNIQUE

Each rat was tested while alive to make sure that it was quite normal in its reactions. Rats thus selected were killed with chloroform, and the body weight, body length, and tail length recorded, as in table 1. The rat was then completely eviscerated, as this makes the subsequent dissection easier. The spinal canal was next opened so as to expose the seventh cervical segment with its nerves, and both segment and nerves were removed.

To obtain all the data desired, two rats of like age and size were required. From the left side of one, the two spinal roots, the ganglion, and a short part of the nerve were removed together. These were extended to the normal length on a bit of cardboard and fixed for twenty-four hours in 1 per cent osmic acid. From the same rat the seventh cervical segment, with the right roots, ganglion, and nerve attached, was removed and fixed in Bouin's fluid for twenty-four hours, according to the procedure described by Sugita ('17).

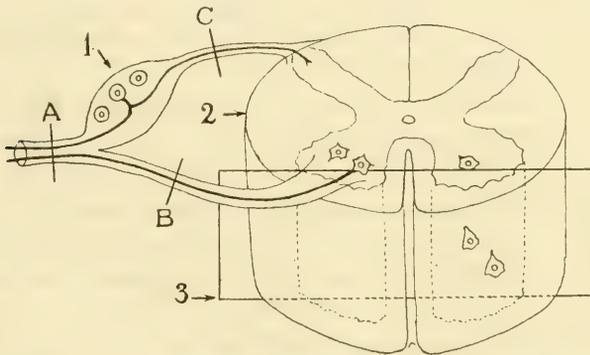


Fig. 1 A scheme of the seventh cervical segment of the spinal cord. Levels of the nerve-fiber sections: At A, section of seventh nerve; at B, section of ventral root; at C, section of dorsal root. 1. The spinal ganglion, cut in longitudinal section. 2. Transverse section of segment. 3. Plane of longitudinal section of the segment.

From the second rat of the pair the seventh cervical segment of the cord, without the nerve roots, was removed and fixed also in Bouin's fluid. The nerve roots and nerve fixed in osmic acid were washed for twelve hours, run through the alcohols, cleared in xylol, rapidly imbedded in paraffin and cut in sections 8μ thick. The piece of the spinal cord with the ganglion from the first rat and the piece of cord from the second rat, both of which had been fixed in Bouin's solution, were washed for five minutes in running water, then treated as above, cut in sections 12μ thick and stained with thionin.

Figure 1 shows the localities at which the six series of sections were made.

From the material as represented in figure 1, the following series of cross-sections of myelinated fibers fixed in osmic acid were obtained:

At A, in the seventh cervical nerve close to the ganglion.

At B, in the ventral root.

At C, in the dorsal root.

Also, the following sections of nerve-cell bodies from material fixed in Bouin's fluid:

At 1, a longitudinal section of the spinal ganglion.

At 2, a transverse section of the spinal cord.

At 3, a longitudinal frontal section of the spinal cord (in the plane of the rectangle—fig. 1).

In the sections from A, B and C, the fibers were cut as nearly as possible at right angles to their long axes, which made the cross-section of a myelinated fiber nearly circular in outline. In this case but a single measurement of the diameter of the entire fiber and of the axis, respectively, was made. For measurement a Zeiss ocular no. 6 and oil-immersion obj. 2 mm. were used with the micrometer eyepiece having each division equal to 2μ . Ten of the largest fibers in a single section were thus measured for each locality.

In the case of the nerve cells, more measurements were necessary because, in the first place, the outline of the cell bodies is not circular, and, in the second place, it was necessary to measure the nuclei also.

In the case of the spinal ganglion cells the two maximum diameters at right angles to each other were determined, while one diameter alone was taken for the nucleus.

In the case of the spinal cord cells the longitudinal diameter was the longer one, passing through the long axis of the cell and at right angles to the transverse or short diameter which was measured through the middle of the nucleus. This is similar to the method described by Hardesty ('02). Here again, but one diameter of the nucleus was measured. In each instance the largest cells in a given section were those measured. These series of measurements taken on the fibers at A, B, and C, and on the cells at 1, 2, and 3, furnish the data that are to be consid-

ered. In each instance, both for cells and for fibers, the values given in tables 2 to 6 are averages based on ten measurements.

In table 2 are given the values for the diameters of the largest nerve fibers found in the seventh spinal nerve and in the dorsal and ventral spinal roots, respectively, in twelve albino rats ranging from 18.7 to 316.3 grams in body weight. The measurements are not only for the entire fiber, but for the axis also. At the bottom of each column is given the ratio of the diameter at 18.7

TABLE 2

Giving in micra the mean diameters of the largest entire fibers in the seventh cervical nerve and in the ventral and dorsal roots, together with the diameters of their respective axes. The ratio between the first and the last measurement stands at the bottom of each column

BODY WEIGHT	VENTRAL ROOT DIAMETER		DORSAL ROOT DIAMETER		SEVENTH NERVE JUST DISTAL TO THE GANGLION DIAMETER	
	Entire fiber	Axis	Entire fiber	Axis	Entire fiber	Axis
<i>grams</i>						
18.7	8.8	5.5	8.6	5.4	8.9	5.6
25.0	11.5	7.2	11.8	7.5	11.4	7.2
43.3	11.9	7.7	12.0	7.8	11.9	7.5
59.2	12.1	7.7	12.3	7.9	12.2	7.7
81.0	12.8	7.6	13.2	7.8	13.0	8.0
115.1	13.2	9.0	13.6	9.8	13.6	9.8
120.3	14.3	9.8	14.5	10.0	14.3	9.6
149.3	14.6	9.8	14.8	9.6	15.0	9.8
178.0	17.6	12.7	17.8	12.2	18.1	12.6
233.1	16.7	12.4	17.1	12.4	16.9	12.0
243.1	17.6	11.6	17.6	13.4	17.6	13.2
316.3	20.2	14.0	20.3	14.3	19.8	14.2
Ratios.....	1:2.3	1:2.5	1:2.3	1:2.6	1:2.2	1:2.5

grams to that at 316.3 grams of body weight. For the entire fiber this ranges between 2.2 for the fibers from the nerve and 2.3 for both the ventral root and dorsal root fibers. The difference is so slight that we conclude that all three sets of fibers increase in diameter by the same amount. When the ratios for the axes are considered, it is seen that they also are nearly alike (i.e., from 2.5 to 2.6), but higher than those for the entire fiber, showing that the axis is growing in diameter somewhat more rapidly than

the myelin sheath which encloses it. To this point we shall return later.

Passing to the ganglion cells, the measurements obtained for groups of the ten largest cells in a single longitudinal section in each of twelve albino rats (the same rats that furnished the nerve fibers for table 2) are given in table 3.

The first column gives the long diameter, the second the short diameter, and the third column the 'computed diameter,' i.e.,

TABLE 3

Mean diameters in micra of the ten largest spinal ganglion cells in the seventh cervical ganglion. Long diameter, short diameter, and the 'computed diameter'—which is the square root of the product of the long and short diameters. Also the mean diameters of the respective nuclei. The ratio of the last to the first entry is given at the foot of each column

BODY WEIGHT	CELL BODY			NUCLEUS DIAMETER
	Long diameter	Short diameter	Computed diameter	
<i>grams</i>				
18.7	26.4	17.6	21.6	10.6
25.0	29.2	18.4	23.2	10.8
43.3	33.2	19.8	25.6	14.4
59.2	35.2	19.8	29.1	14.8
81.0	36.0	24.0	29.4	15.2
115.1	36.8	25.6	30.8	14.4
120.3	36.6	28.4	32.2	15.2
149.3	38.4	30.0	33.9	16.0
178.0	39.2	29.8	34.2	16.4
233.1	40.4	34.4	37.2	18.2
243.1	41.6	37.2	39.4	18.0
316.3	41.8	34.0	37.7	17.8
Ratios.....	1:1.6	1:1.9	1:1.8	1:1.7

the square root of their products. These last values approximate the mean diameters of the cells. Finally, the last column in the table gives the diameters of the nuclei.

Determining the ratios for the last two columns, it appears that the spinal ganglion cells have increased 1.8 times in diameter and the nuclei 1.7 times. This increase is considerable, but somewhat less than that of the dorsal root fibers or of the fibers just distal to the ganglion.

In table 4 are a series of measurements for the large cell bodies in the ventrolateral part of the ventral horn of the seventh cervical segment of the spinal cord as they appear in transverse section (at 2, fig. 1). The arrangement of the data is as given in table 3. The increase for the computed diameters is 1.3 for the cell bodies and 1.2 for the nuclei.

When the corresponding data for the longitudinal section of the spinal cord (at 3, in fig. 1) are tabulated, they appear as in table 5

TABLE 4

Mean diameters in micra of the ten largest spinal cord cells—from the ventrolateral area of the ventral horn as they appear in a transverse section. Long diameter, short diameter, and 'computed diameter,' which is the square root of the product of the long and short diameters. Also the mean diameters of the respective nuclei. The ratio of the last to the first entry is given at the foot of each column

BODY WEIGHT	CELLS			NUCLEI DIAMETER
	Long diameter	Short diameter	Computed diameter]	
<i>grams</i>				
18.7	29.4	18.0	23.0	12.8
25.0	30.8	18.0	23.5	13.0
43.3	34.6	18.4	25.2	13.4
59.2	35.4	18.8	25.8	14.4
81.0	34.0	22.0	27.4	14.8
115.0	37.6	21.6	28.6	14.8
120.3	36.0	22.0	28.2	16.0
149.3	38.4	22.4	29.4	15.2
178.0	37.0	22.6	28.9	15.2
233.1	36.6	22.0	28.4	15.2
243.1	36.4	22.4	28.6	15.2
316.3	36.8	24.4	29.9	15.4
Ratios.....	1:1.3-	1:1.3+	1:1.3	1:1.2

and show an increase of 1.2 in the diameter cell body and 1.2 in the nuclei.

The relations represented by the numbers in tables 2 to 5 are shown graphically in charts 1, 2, and 3.

In this connection it may be well to repeat the statement that necessarily two different specimens were used for the cells in the spinal cord so that the data in tables 4 and 5 are not only from sections made in different planes, but also from a different series

of rats. The object of making the sections and measurements in different planes was to determine whether the long axes of the cells were in a fixed relation to the long axis of the cord. There is a slight difference between the long axes in these two cases in favor of the longitudinal section, but the difference is too small to warrant placing any emphasis on it at present. This problem of orientation must be taken up later.

TABLE 5

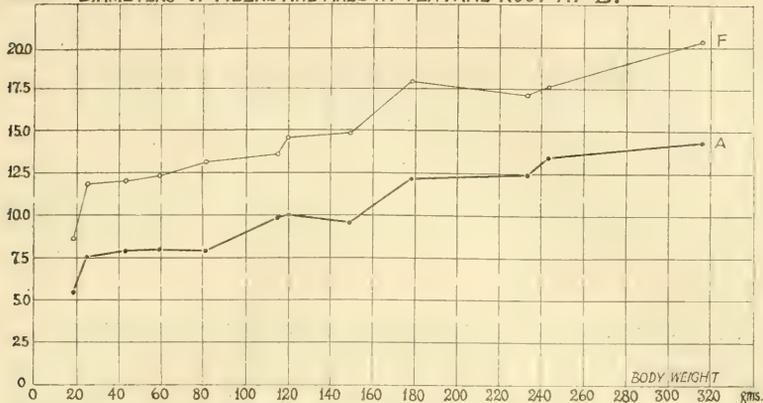
Mean diameters in micra of the ten largest spinal cord cells, from the ventrolateral area of the ventral horn as they appear in a longitudinal section. Long diameter, short diameter, and 'computed diameter,' which is the square root of the product of the long and short diameters. Also the mean diameters of the respective nuclei. The ratio of the last to the first entry is given at the foot of each column

BODY WEIGHT	CELLS			NUCLEI DIAMETER
	Long diameter	Short diameter	Computed diameter	
<i>grams</i>				
18.7	32.2	19.0	24.8	13.0
25.2	33.6	18.2	24.8	13.2
42.8	34.8	18.4	25.3	13.4
58.9	35.8	18.8	25.9	14.2
82.0	37.6	22.4	29.0	15.6
114.5	40.0	23.2	30.5	16.8
117.0	36.0	22.4	28.4	14.8
153.5	39.0	25.2	31.4	16.4
180.8	37.4	22.8	29.2	15.0
228.8	36.6	23.6	29.4	17.2
236.5	38.8	22.8	29.8	16.8
314.1	37.6	22.8	29.2	15.2
Ratios.....	1:1.2-	1:1.2	1:1.2	1:1.2-

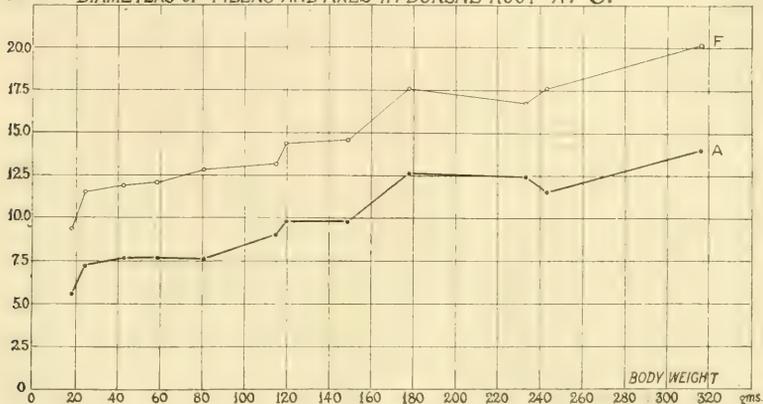
In the meantime we shall treat the data as though the position of the long axis of the cells in relation to that of the cord was indeterminate, and, for discussion, the two series of data may be combined. Table 6 contains the combined values for the two series, taken from tables 4 and 5.

In order to determine the relations of the values given in tables 2 to 5 it has seemed best to condense these tables by taking the means of the entries, in successive groups of three, as thus several relations among the data can be brought out more clearly.

micra. DIAMETERS OF FIBERS AND AXES IN VENTRAL ROOT AT B.



micra. DIAMETERS OF FIBERS AND AXES IN DORSAL ROOT AT C.



micra. DIAMETERS OF FIBERS AND AXES, SLIGHTLY DISTAL TO SPINAL GANGLION AT A.

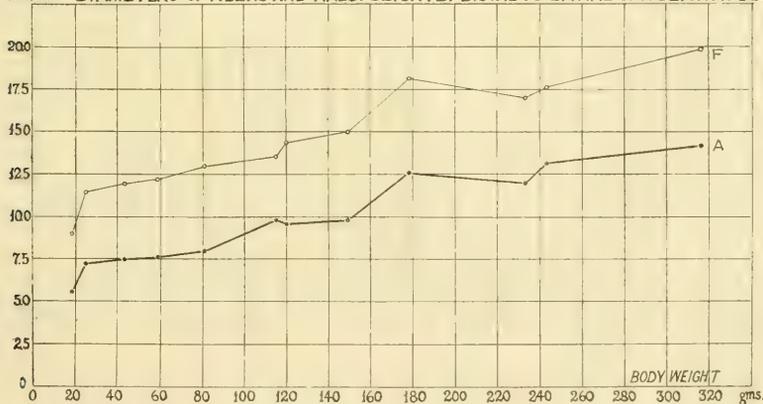


Chart 1 shows on body weight the graphs in micra for the diameters of the fibers and their axes in the ventral root at B, in the dorsal root at C, and in the nerve just distal to the spinal ganglion at A. F, entire fiber; A, axis.

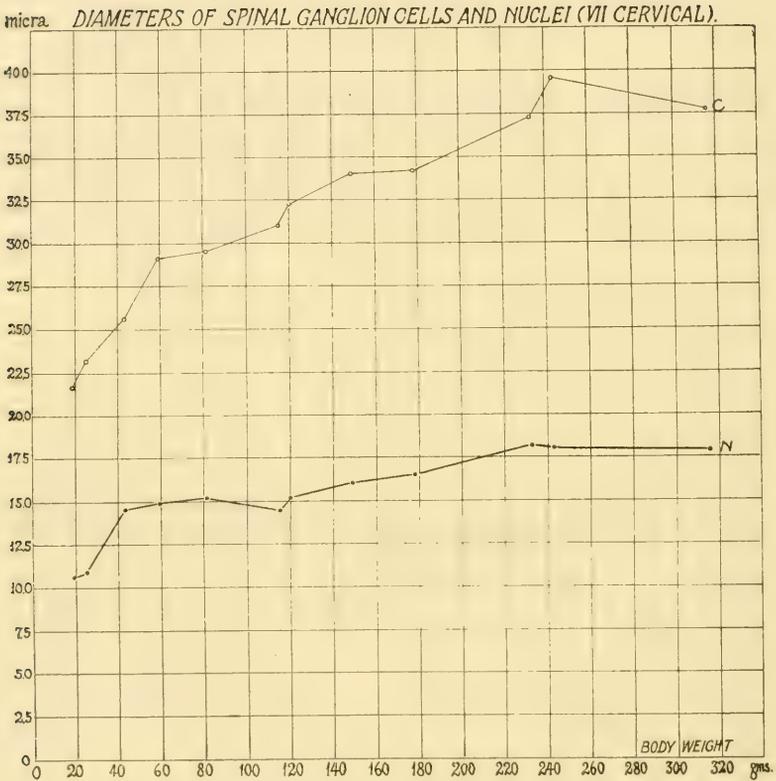


Chart 2 shows on body weight the graphs, in micra, for the spinal ganglion cells and their nuclei. *C*, cell body. *N*, nucleus.

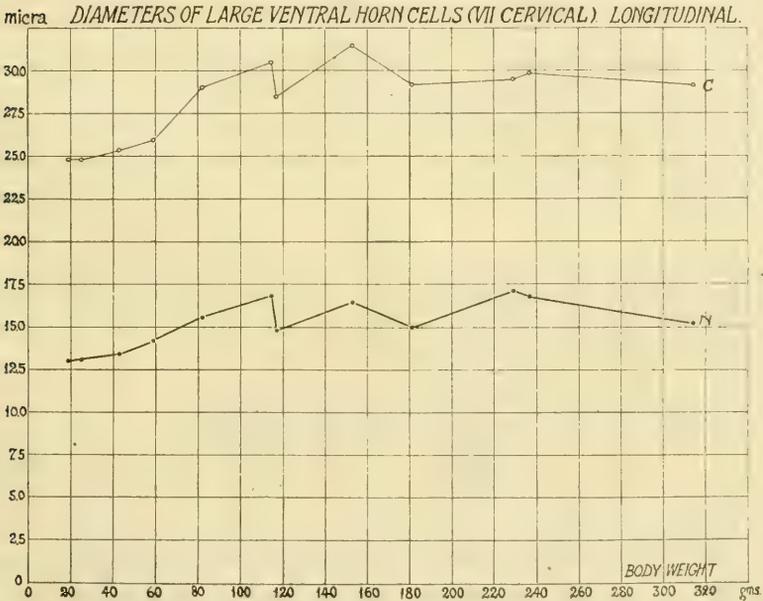
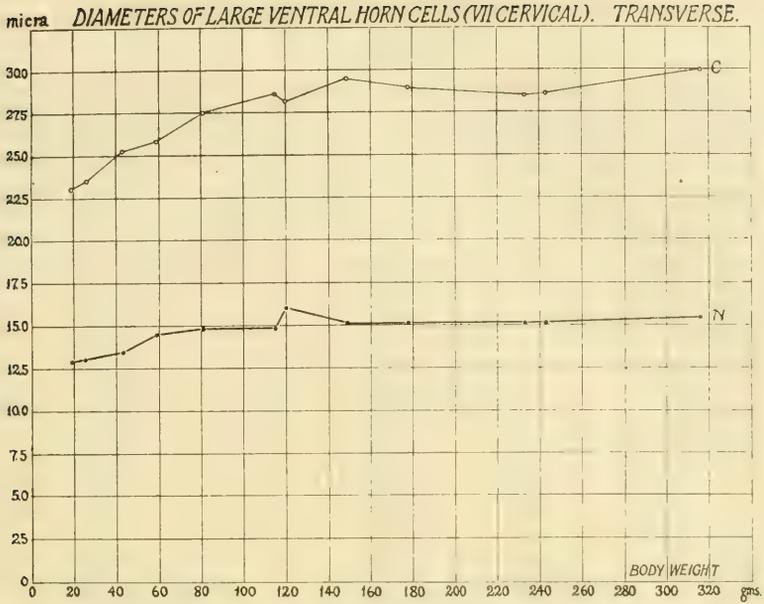


Chart 3 shows on body weight the graphs, in micra, for the ventral horn cells, above, as seen in transverse section, below, as seen in longitudinal section. C, cell body. N, nucleus.

TABLE 6

Giving in micra the mean values for the computed diameter of the cell body and of the nucleus of cells from the ventrolateral area of the ventral horn by combining the data as they appear in tables 4 and 5

MEAN BODY WEIGHT	CELL BODY MEAN 'COMPUTED DIAMETER'	NUCLEUS MEAN DIAMETER
<i>grams</i>		
18.7	23.9	12.9
25.1	24.2	13.1
42.9	25.3	13.4
59.1	25.9	14.3
81.5	28.2	15.2
114.8	29.6	15.8
118.7	28.3	15.4
151.4	30.4	15.8
179.4	29.5	15.1
231.0	28.9	16.2
249.8	29.2	16.0
315.2	29.6	15.3
Ratios.....	1:1.2+	1:1.2-

Table 7 enables us to compare the average diameters of the largest nerve cells in the spinal ganglion of the seventh spinal nerve with the corresponding average diameters of the largest myelinated fibers at C in the dorsal nerve root, and at A in the spinal nerve just distal to the ganglion. Looking at the column

TABLE 7

Comparing the diameters of the spinal ganglion cells in albino rats of different sizes with the diameters of the corresponding dorsal root fibers and of the fibers just distal to the ganglion. In the last two columns are given the respective ratios. Data condensed from tables 2 and 3

AVERAGE BODY WEIGHT	AVERAGE AGE	AVERAGE DIAMETERS OF NERVE CELLS IN SPINAL GANGLION	AVERAGE DIAMETERS OF DORSAL ROOT FIBERS AT (C)	AVERAGE DIAMETERS OF FIBERS DISTAL TO THE GANGLION AT (A)	RATIOS	
					C: Sp. G.	A: Sp. G.
<i>grams</i>	<i>days</i>	μ	μ	μ		
29.0	24	23.5	10.8	10.7	1:2.18	1:2.20
85.1	56	29.8	13.0	12.9	1:2.29	1:2.31
149.2	105	33.4	15.7	15.8	1:2.13	1:2.11
264.2	267	38.1	18.3	18.1	1:2.08	1:2.10
Ratios.....		1:1.6	1:1.7	1:1.7		

next to the last it appears that the ratio is a trifle smaller in the last than in the first group—2.08 compared with 2.18. Therefore the entire nerve fibers have grown in diameter a little more rapidly than the ganglion cells from which they arise. In the last column the fibers from the distal side of the ganglion are compared with the ganglion cells and these behave in nearly the same manner. As will be shown later the increase in the diameters of the axes is somewhat more rapid than that of the entire fiber and the relation of the axes to the cell bodies is given for the fibers distal to the ganglion in table 9 (B).

While there is a slight tendency for the ratios in table 7 to decrease as we pass from the first to the last groups, by far the

TABLE 8

Comparing the computed diameters of the spinal cord cells in albino rats of different sizes with the diameters of the corresponding ventral root fibers. In the last column are given the ratios. Data condensed from tables 2 and 6

AVERAGE BODY WEIGHT	AVERAGE AGE	AVERAGE DIAMETERS OF SPINAL CORD CELLS. MEAN FROM TRANSVERSE AND LONGITUDINAL SECTIONS	AVERAGE DIAMETER OF VENTRAL ROOT FIBERS AT (B)	RATIOS
				B: Sp. G. C.
<i>grams</i>	<i>days</i>			
29.0	24	24.5	10.7	1: 2.29
85.1	56	27.9	12.7	1: 2.20
149.5	105	29.4	15.5	1: 1.90
264.8	267	29.2	18.2	1: 1.60
Ratios.....		1: 1.2	1: 1.7	

most striking point is their similarity at all ages (=body weights), the increase in the diameters of the cells and fibers running nearly parallel.

Table 8 is based on tables 2 and 6, and gives the mean values for the diameters of the spinal cord cells (data from the longitudinal and transverse sections combined) and the diameters of the largest myelinated fibers in the ventral root. In the last column it is seen that the relative value for the nerve cells diminishes very rapidly because the growth of the cell bodies in diameter early (56 days, chart 3) becomes very slow, while the nerve fibers con-

tinue to increase rather rapidly in diameter with the increase in body size.

There appear therefore to be the following relations between the cells and fibers which have been chosen for study. All of the (largest) fibers, dorsal root fibers, the fibers just distal to the ganglion, and ventral root fibers increase at about the same rate and to about the same diameter (table 2, chart 1). The spinal ganglion cells increase in diameter at nearly the same rate (not quite so rapidly) as the fibers which come from them (table 7, chart 2). On the other hand, the spinal cord cells early reach nearly full size (tables 4, 5, and 6, chart 3), after which they grow very slowly. Therefore the ventral root fibers increase in diameter much more than do the cells from which they come. The difference in growth appears therefore to be between the two classes of cell bodies.

DISCUSSION

In the first place we note that the spinal ganglion cells are afferent neurons of the first order—and the spinal cord cells (here studied) are efferent neurons of the first order. In looking for other differences which might explain this lack of agreement, we recall that the distal process (nerve fiber) from the ganglion cell is physiologically a dendrite—that is, it carries impulses into the cell body—whereas the dorsal root fibers and the ventral root fibers both convey impulses from the cell body.

Growth of the axon process in diameter is not necessarily accompanied by a corresponding growth of the cell body, as is shown by the spinal cord cells. We should not, therefore, look for an explanation of the growth of the cell body of the spinal ganglion neuron as due to the enlargement of its central or axon process which forms a fiber in the dorsal root. If this argument is sound, then it is to the distal process which forms a fiber in the nerve trunk, but which has the function of a dendrite, that we must turn for an explanation. As the body surface (and the surface of other organs innervated by afferent fibers) increases, not only is the area innervated by the fiber increased, but sensory discrimination (the 'local sign') is in a measure maintained.

It is fair to assume that this maintenance of the sensory discrimination calls for an increase of histological complexity in the cell body, and with this we might associate the increase of size.

In this connection it is worth noting first that if we take the data from table 7 and assume, as is usually done, that the squares of the cube roots of the body weights stand in the same relation as the respective surfaces of the animals compared, then

TABLE 9

Giving (A) the ratios of the relative body areas (squares of the cube roots of the body weights) of the four groups of rats and the ratios of the corresponding relative volumes (cubes of the diameters) of the spinal ganglion cells; and (B), the ratios of the relative body areas compared with the relative areas of the axis cylinders in the corresponding dorsal root fibers—as given in table 10

(A)

RELATIVE AREAS OF BODY		RELATIVE VOLUME OF GANGLION CELLS	
Body weights, grams	Ratios	Ganglion cell diameters, μ	Ratios
$\sqrt[3]{29.0^2}$: $\sqrt[3]{264.2^2}$:: 1 : 4.37		23.5 ³ : 38.1 ³ :: 1 : 4.26	
$\sqrt[3]{85.1^2}$: $\sqrt[3]{264.2^2}$:: 1 : 2.13		29.8 ³ : 38.1 ³ :: 1 : 2.09	
$\sqrt[3]{149.2^2}$: $\sqrt[3]{264.2^2}$:: 1 : 1.46		33.4 ³ : 38.1 ³ :: 1 : 1.48	
$\sqrt[3]{264.2^2}$: $\sqrt[3]{264.2^2}$:: 1 : 1.00		38.1 ³ : 38.1 ³ :: 1 : 1.00	

(B)

RELATIVE AREAS OF BODY		RELATIVE AREAS OF AXIS CYLINDERS IN SQUARE MICRA	
		In root fibers distal to ganglion at (A)	
:: 1 : 4.37		36.3 : 134.7 :: 1 : 3.71	
:: 1 : 2.13		56.7 : 134.7 :: 1 : 2.37	
:: 1 : 1.46		89.9 : 134.7 :: 1 : 1.49	
:: 1 : 1.00		134.7 : 134.7 :: 1 : 1.00	

the first column in table 9, giving the squares of the cube roots of the body weights can be used to obtain a series of ratios. The relative area for the heaviest group is used as the standard, and the ratios between it and the values for the preceding groups determined.

If the first three areas are compared successively with the final or fourth area, there appear the ratios given in the last column

under 'relative areas of body' in table 9 (A). If, for comparison, we take the cubes of the mean diameters of the ganglion cells, which correspond to the relative volumes of these cells, and compare these in a similar manner, we obtain the series of ratios in the last column under the 'relative volumes of ganglion cells.' The volume ratios there given correspond very closely with the ratios for the increasing areas. From these relations it is fair to conclude that within the limits of this series the volume of the spinal ganglion cells increases at the same rate as the area of the body surface. This result accords with the conclusion reached by Levi ('08) and with the general results of the later work by Busacca ('16), although the explanation of the relation here presented is an extension of that given by those authors.

It is hardly necessary to repeat that the cell bodies in the ventral horn of the spinal cord do not enlarge in a like way, as can be seen by comparing the data for cell diameters in table 3 with the corresponding data in table 6.

In this connection another important relation appears, although for the discussion of it data which are not given until table 10 must be used.

Linking the ganglion cell body with the surface of the body, and other points of termination, is the peripheral fiber in which the axis represents the conducting tissue. It might be assumed that this axis would increase in its cross-section in a definite relation to the increase in the surface to which it is distributed.

The relations of the increasing area of the axis cylinder to the increasing surface of the body are shown in table 9 (B) where the values for the areas of the axis cylinder in the fibers just distal to the ganglion (at A, fig. 1) are treated in the same manner as are the computed areas of the body in the several groups. The table shows that the areas of the axis cylinder increase at about the same rate as the areas of the entire body. However, in the first instance, when the area of the axis in the smallest group is compared with that in the largest, the ratio, 3.71, is found to be less than that for the body surface, which is 4.37. It is just possible that the smaller increase in the areas of the axes is due to the splitting of the fibers in their course to the periphery, but

a discussion of this point must be reserved until the relation has been more carefully examined. The relations between the volume of the ganglion cell and the area of the axis cylinder of the fibers passing to the periphery were briefly noted by Donaldson ('00), and the results of the present study are in good agreement with the earlier observations.

Bringing these observations together, it may be said that in the afferent fibers just distal to the ganglion the increase in the area of the axis, as the rat increases in size, during the later phases of growth tends to be at the same rate as the increase in the surface of the body and as the volume of the ganglion cells from which the fibers arise.

CONSIDERATION OF INCIDENTAL RESULTS HERE OBTAINED

In order to bring the incidental observations made in the course of this study into relation with other observations previously recorded for the albino rat, it has seemed worth while to compare our data with those already published.

The relations between the diameters of ganglion cell bodies and the diameters of the entire fibers cannot be directly compared with the results obtained by Hatai ('02, '07) after osmic acid, on account of differences in the fixation methods and in the procedure of measurement.¹ The records most suitable for comparison are those by Dunn ('12) on the diameters of the ventral root fibers of the second cervical nerve of the albino rat of different sizes. For like body weights the ventral root fibers in the second cervical nerve run about 2μ less in diameter than the fibers in the seventh cervical, but the increase in diameter within

¹ A special set of preparations of spinal ganglion cells shows that the mean diameter of the nucleus is much less after osmic acid than after fixation in Bouin's fluid.

	DIAMETERS IN μ	
	Cells	Nuclei
Fixation in Bouin.....	35.2	14.4
Fixation in osmic acid.....	34.0	10.8

the range of body weight which we have used is similar in both nerves. In the second and seventh cervical nerves, therefore, the ventral root fibers grow in diameter at the same rate.

It will be noted that in table 2 the diameters of the ax's cylinders are given for each group of nerve fibers. In 1905 Donaldson and Hoke published a series of observations on the areas of the axis cylinder and of the myelin sheath as seen in cross-sections of the spinal nerves of vertebrates. Since that time several similar determinations have been made, and it was thought important to have a determination made in this study also, since it permitted the comparison of the fibers in the ventral and dorsal

TABLE 10

Giving the areas of nerve fibers and their axes in square micra—also the percentage of the total area occupied by the axis, based on groups of three, from table 2

AVERAGE BODY WEIGHT	AGE	VENTRAL ROOT FIBERS			DORSAL ROOT FIBERS			IN THE SEVENTH CER- VICAL DISTAL TO THE SPINAL GANGLION		
		Areas		Per cent area of axis	Areas		Per cent area of axis	Areas		Per cent area of axis
		Ent. F.	Axis		Ent. F.	Axis		Ent. F.	Axis	
<i>grams</i>	<i>days</i>									
29.0	24	89.9	36.3	40	91.6	37.4	41	89.9	36.3	40
85.1	56	126.6	51.5	41	132.7	56.7	43	130.6	56.7	43
149.2	105	188.6	91.6	48	193.5	88.3	46	196.0	89.9	46
264.2	267	260.0	126.6	49	262.9	141.0	53	257.2	134.7	52

roots and in the nerve trunk near the ganglion, in respect of this character. In table 2 are given the diameters of the axes of the three classes of nerve fibers, and it has already been pointed out that the axes increase in diameter slightly more rapidly than do the entire fibers.

Using the diameters just mentioned the areas of the entire fiber and of the axis (considered as circles) have been computed and entered in the condensed table 10.

The columns which show the percentage of the entire area of the fiber represented by the axis reveal several interesting relations. In the first place, the order of percentages is the same in the three classes of fibers and their absolute values at the same

body weight are also very close in all three classes. Between 105 days and 267 days the area of the axis approximates 50 per cent of the entire area; i.e., the area of the axis is equal to the area of the ring of myelin surrounding it. This 'one to one' relation was that found by Donaldson and Hoke in 1905 (table VI, p. 9). That paper shows that in general the small fibers from young albino rats had an axis somewhat less than half the area of the fiber, while in the fibers from older rats this area was a trifle more than half that of the entire fiber, but in the study of 1905 no attention was paid to age or to the absolute size of the fibers. In 1912 Dunn examined these relations in the second cervical nerve of albino rats from the standpoint of age, sex,

TABLE 11

Showing the percentage of the area of the entire fiber represented by the area of the axis in the ten largest fibers found in the ventral root of the second cervical nerve of the albino rat—Dunn ('12)—and in the ten largest fibers in the ventral root of the seventh cervical nerve of the albino rat, as shown in table 10

DATA FROM TABLE 10		DATA FROM DUNN ('12)	
Age	Area of axis	Area of axis	Age
<i>days</i>	<i>per cent</i>	<i>per cent</i>	<i>days</i>
24	40	40	36
56	41	44	75
105	48	44	132
267	49	50	270

and body weight. The relations are expressed by her (*loc. cit.*, table 2, p. 135) as ratios of the area of the axis taken as one, to the area of the entire fiber. When, however, her data are recast in the form which we have chosen, and age is made the basis of comparison, there appear the relations shown in table 11.

When the comparison is made, as in table 11, it appears that the axis-sheath relation is similar in the fibers forming the ventral roots of the second and the seventh cervical nerves, respectively, and that in both cases the 'one to one' relationship is attained in the oldest group. These nerves were all measured with the eyepiece micrometer.

There are still other observations on this point. Greenman ('13, table 9) reported at the proximal end of a bit of normal

peroneal nerve from the albino rat the value of the area of the axis as 53.7 per cent and at the distal end of the same nerve the value of 49.9 per cent. The mean body weight of the rats was 135 gms. In another series of studies, Greenman ('17) has found the area of the axis about 40 per cent in a series of thirty peroneal nerves from fifteen animals, all about 151 days of age. In both these series the fibers were projected, outlined, and then measured with a planimeter. In the cases where the sheath was wavy this method would give a somewhat greater area for the sheath than would be determined by direct micrometric measure-

TABLE 12

Giving the relations of the spinal ganglion cells and their nuclei. In the last column appears the ratio of the volume of the cytoplasm (the volume of the entire cell less the volume of the nucleus) to the volume of the nucleus. Data condensed from table 3

AVERAGE BODY WEIGHT	AVERAGE AGE	NERVE CELLS		NUCLEI		RATIO OF VOLUME OF CYTOPLASM TO VOLUME OF NUCLEUS
		Mean diameter	Ratio of enlargement	Mean diameter	Ratio of enlargement	
<i>grams</i>	<i>days</i>	μ		μ		
29.0	24	23.5	1.00	11.9	1.00	1:6.70
85.1	56	29.8	1.29	14.8	1.24	1:7.16
149.2	105	33.4	1.42	15.9	1.34	1:8.27
264.2	267	38.1	1.62	18.0	1.51	1:8.48

ment, and thus contribute to giving a low percentage for the area of the axis, as it appears in the last 1917 series.

We may conclude from Dunn's record and our own that there is a growth in the relative area of the axis up to about 250 to 300 days and that the axes in the fibers of the ventral nerve roots of the spinal nerves have 50 per cent of the area of the fiber at this age, when the measurements are made with the eyepiece micrometer.

ON THE NUCLEUS-PLASMA RELATIONS

In the spinal ganglion cells here measured the mean diameters of the cell bodies and of their nuclei are given in the condensed table 12, and the ratios of the volume of the nucleus to that of the cytoplasm (= cell volume less nucleus volume) have been

entered in the last column. This ratio rises with the increasing weight (age) of the rat, being as table 12 shows 6.70 for the smallest group and 8.48 for the largest, an increase which is definite and also regular. This shows that these cells are not only growing in volume, but maturing, as indicated by the increase in the ratio.

Contrasted with these results are the relations which appear in the case of the ventral horn cells, as shown in table 13. Here, as the last column shows, the nucleus-plasma relation is not progressive and is only slightly higher in the largest rats as compared with the smallest—5.68 for the largest as compared with 5.54 for the smallest.

TABLE 13

Giving the relations of the spinal cord cells and their nuclei. In the last column appears the ratio of the volume of the cytoplasm (volume of entire cell less the volume of the nucleus) to the volume of the nucleus. Data condensed from table 6

AVERAGE BODY WEIGHT	AVERAGE AGE	NERVE CELLS		NUCLEI		RATIO OF VOLUME OF CYTOPLASM TO VOLUME OF NUCLEUS
		Mean diameter	Ratio of enlargement	Mean diameter	Ratio of enlargement	
<i>grams</i>	<i>days</i>	μ		μ		
28.9	24	24.5	1.00	13.1	1.00	1:5.54
85.1	56	27.9	1.14	15.1	1.15	1:5.31
149.8	105	29.4	1.20	15.4	1.18	1:5.95
265.3	267	29.2	1.19	15.5	1.18	1:5.68

We infer from this that at twenty-four days the nucleus-plasma relation in the ventral horn cells has nearly reached equilibrium, although there is some slight increase in volume of the entire cell body, as shown in the previous tables 4, 5, and 6.

The two types of cells here examined have a different nucleus-plasma relation, therefore, and the plasma in the case of the ganglion cells is not only absolutely more abundant, but increases with the size (age) of the rat.

This seems to be an important difference. As the spinal cord cells do not show a change in the nucleus-plasma relation, despite the continued growth of the axon in diameter, we should not consider the change in the spinal ganglion cell as due to the growth

of its axon process, the process which runs in the dorsal spinal root. The change must therefore be associated with the distal process of the ganglion cell, which is to be considered physiologically as a dendrite, bringing impulses into the cell body and in some way stimulating not only its growth as a whole, but the progressive change in the nucleus-plasma relation, which appears to be an adaptation to maintain the discriminative sensibility despite the increase in the skin area over which a given fiber is necessarily distributed.

CONCLUSIONS

This study was made to determine whether in the albino rat the increase in the diameter of the cell body of a neuron and in the diameter of the fiber, or fibers, coming from it ceased at the same time. It was therefore a study of the later phases of the growth of the neuron.

The material was taken from the seventh cervical segment of the spinal cord with the accompanying nerves, and measurements were made on the largest fibers in the dorsal and ventral roots and in the nerve just distal to the ganglion cells (all fixed in osmic acid) and also on the spinal ganglion cells and on the ventrolateral group of large efferent cells in the ventral horn of the spinal cord (both fixed in Bouin's fluid).

Under these conditions of preparation, and as shown in tables 7 to 13—

1. All of the nerve fibers enlarge to the same extent, showing (tables 7 and 8) in the heaviest group, diameters 1.7 greater than in the lightest group of rats which weighed 29 grams and were twenty-four days old.

2. The axis-sheath relation in these fibers was such that the area of the axis in the youngest groups was about 40 per cent of the area of the entire fiber, but this area increases with the increasing age (and size) of the rat until it becomes about 50 per cent in the largest animals (Table 10). This is in agreement with the results of previous studies in which the same methods of measurement were used, and shows that the axis has grown in diameter a trifle more rapidly than the entire fiber.

3. The ganglion cells continue to increase in diameter with the growth of the rat, and in the largest group (as indicated in the condensed table 7) have a diameter about 1.6 times that found in the smallest group. The ratio between the diameters of the ganglion cells and those of the fibers arising from them decreases somewhat with increasing body size, showing that the fibers are increasing in diameter slightly more rapidly than is the cell body (table 7); but in general the cell is enlarging nearly in proportion to its entire fibers, but less rapidly than the corresponding axes. This enlargement of the ganglion cells is accompanied by a relative overgrowth of the cytoplasm as shown by the nucleus-plasma relation, and further a study of the volumes of the ganglion cells shows them to increase in volume in direct proportion to the enlargement of the area or skin surface of the rat (table 9). This enlargement of the cell is considered as an adaptation for maintaining the sensory discrimination despite the extension of the area supplied by a single neuron.

4. The areas of the axes of the afferent fibers also increase in proportion to the increase of the body surface. (Table 9,B.)

5. The growth of the large spinal cord cell bodies is comparatively slight. The diameter of the fibers increases much more rapidly than that of the cell body, as shown by the ratios in table 8, and in the cell body the nucleus-plasma relation is nearly constant within the limits of these observations (table 13). The enlargement of the axon to meet the requirements of the increased muscle mass to be innervated is therefore not accompanied by any notable increase in the size or internal arrangements of the cell.

These results reveal a marked difference, then, between the growth changes which take place in the afferent as contrasted with the efferent neurons of the first order, but it remains for future investigation to determine the corresponding growth changes in the case of the central neurons (i.e., neurons which lie entirely within the central system) as well as in those which constitute the peripheral ganglia.

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NERVE ENDINGS OF SENSORY TYPE IN THE MUSCULAR COAT OF THE STOMACH AND SMALL INTESTINE

PRELIMINARY NOTE

F. W. CARPENTER

Biological Laboratory of Trinity College, Hartford, Connecticut

FOUR FIGURES

A variety of visceral sensations are attributed by physiologists to impulses originating in the muscular coats of hollow organs. Such sensations of the alimentary canal as fullness and distension, emptiness and hunger, and especially pain, are believed to be due to the stimulation of sensory nerve endings lying, not in the mucous or submucous tunics, but in the coat of smooth muscle external to these. Much of the evidence for this view, based on physiological experimentation and clinical observations, is given by Hurst ('11) in his Goulstonian Lectures on "The Sensibility of the Alimentary Canal." The cause of visceral pain receives particular consideration from this author, who regards tension on the fibers of smooth muscle to be the adequate stimulus for the sensation. His general conclusion is, indeed, that "tension is the only cause of true visceral pain."

The recent detailed investigations of Carlson and his co-workers on the physiology of the stomach tend to confirm the view that the nerve endings concerned in sensory impulses from this organ are to be sought in its muscular coats, although the submucosa is also recognized as a possible site of such endings. Carlson ('13) concludes that the gastric sensory apparatus for hunger lies in the muscularis or in the adjacent connective tissue of the submucosa, but not in the mucosa. Carlson and Braafladt ('15) find the normal gastric mucosa devoid of pain and tactile sensibility, and agree that "the literature seems to show that the

gastric pain accompanying excessive inflation, gastric ulcers, and chronic obstruction is due to the mechanical stimulation of hypersensitive nerves or nerve endings in the muscularis or sub-mucosa by excessive distention or contraction."

Neurohistologists on the other hand, have been unable to verify by direct observation the presence of sensory nerve endings in the smooth muscle of the abdominal viscera. As far as the writer is aware, no figures or descriptions of such structures are to be found in the text-books of neurology or general histology. Barker ('01), in his 'Nervous System' refers to a variety of pain characteristic enough to be designated as 'smooth muscle pain,' but leaves it to further investigation to determine the afferent elements among the numerous fibrils supplying smooth muscle membranes. Herrick ('15) recognizes the presence of general visceral receptors in visceral muscles, but points out that their endings have not been differentiated histologically from the simple terminations of the effector fibers. In their recently published 'Text-book of Histology,' Jordan and Ferguson ('16) describe only motor nerve endings in smooth muscle, although they, too, agree that "many of the nerve fibers in smooth muscle are undoubtedly of sensory function." In their chapter on the histology of the digestive system they give a diagram (from Kuntz, '13) illustrating the probable relationship of sympathetic neurones in the myenteric and submucous plexuses. This scheme shows sensory fibers distributed, outside the plexuses, to the epithelium and tunica propria of the mucosa only; no afferent fibers are represented as ending in the muscular coat.

In searching the special literature of the subject one meets, as has been intimated, with exceedingly few references to nerve endings in smooth muscle that give evidence of being sensory. Practically all the endings described, such as the terminations in involuntary muscle figured by Huber and DeWitt ('98) are, by general agreement, regarded as motor in function. Schultz, in 1895, described multipolar nerve cells, which he believed to be sensory elements, in the muscularis of the frog's stomach. His observations, however, have not been confirmed, and Huber and DeWitt were doubtless right in regarding these as specialized

cells of connective-tissue origin falling in the same category as the so-called 'interstitial ganglion cells' of Ramon y Cajal. Ploshko ('97) found intermuscular 'Endbäumschen' in the wall of the trachea. These arborescent endings appear to be of sensory type. They will be referred to again in connection with the description of somewhat similar terminations present in the muscularis of the intestine.

ENDINGS IN THE LONGITUDINAL MUSCLE OF THE CARDIAC STOMACH OF THE CAT

In a series of sections of the cardiac stomach of the cat stained *intra-vitam* with methylene blue there appear in the longitudinal muscle layer numerous nervous structures, many of them terminal, which seem to be receptive rather than effective in type. They are wholly different in their structural details from the simple motor endings which have previously been described as terminating on the cells of involuntary muscle tissue. They have so far been found only in the longitudinal layer of the muscularis and in the thin serous coat external to it. In the latter tunic a few have been seen in the connective tissue subjacent to the peritoneal epithelium; but the great majority are confined to the region of the longitudinal muscle. Not one of these structures has as yet been seen in the circular muscle layer or elsewhere in the stomach wall.

The structures in question may be described as, (1) skeins and, (2) networks of very fine varicose fibrils. The fibrils arise from the division of nerve fibers of somewhat larger caliber, which also show varicosities, and which appear to be non-medullated as far as they have been traced. Their source has not been determined, but they have been followed in a central direction close to the region of the myenteric plexus.

The delicate fibrils composing a typical skein (fig. 1) lie for the most part roughly parallel to one another, and form a rather wide, loose bundle which is often spirally twisted. The skein may terminate a fiber, frequently branching to make a T-shaped ending, or it may occur midway in the course of a fairly compact strand of fibrils derived from a fiber by the splitting up of the latter.



Fig. 1 Terminal skin from the longitudinal muscle coat of the cardiac stomach of the cat.

Fig. 2 Terminal net from the longitudinal muscle coat of the cardiac stomach of the cat.

Both figures were drawn with the aid of a camera lucida under a no. 4 Leitz ocular and a 1/12 in. oil-immersion objective.

In the net-like terminal structures the component fibrils apparently anastomose to form a reticulum (fig. 2). The central region of this reticulum sometimes takes on a slight stain suggesting the presence of some homogeneous substance on or in which the net lies.

Not infrequently the strand of fibrils into which a main fiber divides continues for some distance without developing skeins or nets and interlaces with other fibrils to form a wide-meshed plexus running through the muscular tissue. From this plexus terminal skeins, and in some cases terminal networks, may be given off laterally. Loops from such an interlacement of fibrils have been traced into the serous coat, where they give rise to terminal nets.

ENDINGS IN THE LONGITUDINAL MUSCLE OF THE SMALL INTESTINE OF THE DOG

In the longitudinal muscle of the dog's small intestine methylene blue staining has revealed nerve terminals to which the name of end tufts may appropriately be given. Each occurs at the extremity of a fine, non-medullated, varicose fiber, which has been seen, in the limits of a single section, actually to emerge from the myenteric plexus (fig. 3). Such fibers are noticeably finer than certain others (such as the one marked '*m.f.*' in fig. 3) which run parallel to the muscle cells, and have been traced to simple motor endings on these cells.

The structure of the end tufts themselves is difficult to make out satisfactorily even with the highest powers of the microscope. Under oil immersion they appear to consist of exceedingly delicate fibrils liberally besprinkled with minute varicosities (fig. 4). The exact relation of the ultimate fibrils to one another has not been positively determined, but the impression gained has been that they spread out into a brush- or tuft-like structure without uniting into a network. Except for the extreme delicacy of its fibrillar constituents the ending under consideration bears a general resemblance to the intermuscular end arborizations ('Endbäumschen') described by Ploschko ('97) as terminating a rather large medullated nerve fiber in the wall of the trachea.



Fig. 3 End tuft from the longitudinal muscle coat of the small intestine of the dog. The nerve fiber with which the end tuft is connected emerges from the myenteric plexus. Drawn with the aid of a camera lucida under a no. 2 Leitz ocular and a 1/12 in. oil-immersion objective. *m.f.*, motor nerve fiber; *m.p.*, region of myenteric plexus.

Fig. 4 End tuft from the longitudinal muscle coat of the small intestine of the dog. Drawn with the aid of a camera lucida under a no. 4 Leitz ocular and a 1/12 in. oil-immersion objective.

As is also true of the skeins and end nets in the stomach of the cat, these intestinal endings of the dog are confined in all the preparations studied to the outer or longitudinal muscle coat and to the adjacent connective tissue of the serous coat. All three types of ending are thus so placed that they would doubtless be directly affected by the contractions or distentions of the smooth muscle tunic within which the majority of them lie. As has been pointed out above, stimuli arising in this manner are, in the opinion of the physiologists quoted, the source of most of the sensations, including pain, associated with the alimentary canal.

SUMMARY

1. Terminal structures in the form of, 1) skeins and, 2) nets, both composed of fine fibrils with numerous varicosities, occur in the longitudinal muscle coat of the cardiac stomach of the cat. A few are present in the serous coat. These endings are connected with unmyelinated, varicose nerve fibers, the source of which has not been determined.

2. Terminal structures in the form of tufts of exceedingly delicate fibrils exhibiting more plainly differentiated varicosities in great abundance occur in the longitudinal muscle coat of the small intestine of the dog, and also to some extent in the subperitoneal connective tissue. These end tufts terminate fine non-medullated nerve fibers which appear of smaller caliber than the motor fibers supplying the smooth muscle cells. They have been traced centrally into the myenteric plexus.

3. Structurally these endings conform to the sensory rather than to the motor type of nerve terminations. Their presence in the muscular coat, but not in the mucosa or submucosa, is consistent with the results of recent physiological experimentation on the sensibility of the alimentary canal.

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