

(apart from needing to get through it to reach year two)

Philip Wilson

Acknowledgements

- Christine Puckering
- Helen Minnis
- Justin Williams
- Daniel and Judy
- Mellow babies and their mothers
- The Chief Scientist Office

Why so interesting?

- General practice longitudinal and trans-generational work with families
- SNAP report
- Gene-environment interactions

Public Health Institute of Scotland



Needs Assessment Report on Child and Adolescent Mental Health Final report – May 2003



















Overview

To what extent do early life experiences shape our later social behaviour?

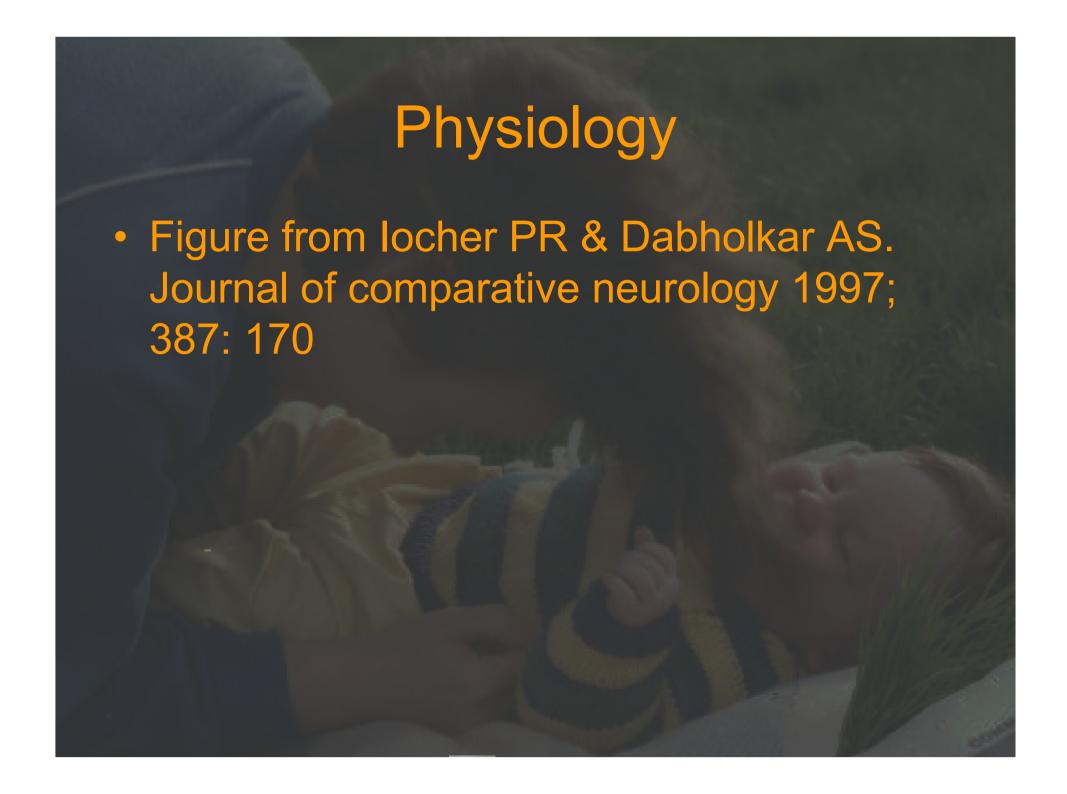
- Some developmental psychology
- Some physiology
- Some epidemiology
- Some experimental psychology
- Detecting problems early
- Early intervention
- Some thoughts about child development screening in the NHS

Social development – first year

- Language
 - "Babble", some spoken words, lots of words understood
- Separation anxiety and stranger anxiety
 - Patterns of attachment (Ainsworth "strange situation"
 - A: Insecure-Avoidant. No evident distress during separation and caregiver ignored on return
 - B: Secure: Infants actively seek proximity to caregivers on reunion. Communicate stress and distress openly and then readily return to play
 - C: Insecure-Resistant. Become distressed when caregiver departs but are ambivalent on return. Remain near but might rebuff the caregiver.
 - D: Disorganised (?)

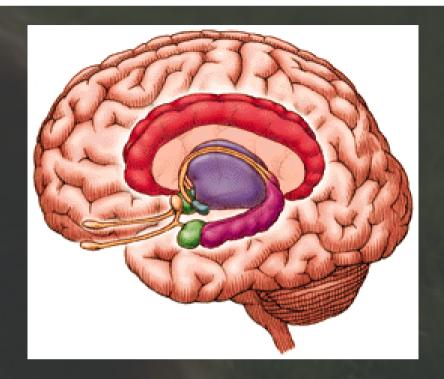
Physiology

- Plasticity and mammalian evolution
 - The more evolved the organism, the less 'hardwired' the CNS at birth
- Human brain growth
 - Cell migration ends by sixth month of gestation
 - Myelination
 - Sensory and motor regions myelinated at birth
 - Prefrontal cortex unmyelinated until adolescence
 - Synaptogenesis
 - Some regions form synapses before others (visual →auditory → prefrontal/frontal)
 - All regions overproduce synapses which are 'pruned' at different ages
 - Production and pruning depend on neuronal activity/experience
 - Adult numbers of synapses not reached in prefrontal regions until adolescence



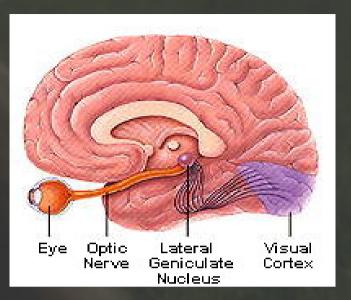
Physiology

- So basic structure fixed at birth, function and connections sorted later
- Different bits of brain become active at different ages
 - Eg hippocampus and amygdala active at birth but orbital-frontal cortex inactive until 6 months
- Plasticity in brain injury
 - Generally fewer specific deficits following injury in infancy than later. But sometimes early brain injury does produce specific deficits e.g. bilateral hippocampal lesions cause autism-like behaviours in adult monkeys only if produced in the neonatal period



Physiology

 'Critical periods' and the visual system



- Cataracts, hypermetropia and amblyopia
- Amblyopia represents the selective pruning of synapses in the lateral geniculate nucleus and visual cortex as a result of lack of 'through traffic'
- Even more specific pruning of orientation and colour receptors in visual cortex – Blakemore and others
- To all intents and purposes, the wiring of the visual system is fixed by about a year
- Is social development like visual development?

Epidemiology

Today's Vol.1, No.1 Epidemiologist

Confessions Of An Index Case Time, Place, and Person Revealed!

Don't Ask, Don't Tell Double Blinding In Military Studies

Boosting Your Confidence Intervals

Do You Have Survey Phobia? Take Our Quiz And Find Out....

Cross-Over Designs

Absent Sex Life? Lucky You! 38 Sexually Transmitted Diseases You Won't Get NEW DIET Lowers P Values

Do's & Don'ts of Epi-Quette

Adjusting For Sex In 10 Easy Lessons What The Kama Sutra Failed To Mention

Sensitivity Analysis
Are You Really
A New Man?



 Is there a relationship between exposure to a risk factor at one time point and behavioural problems years later?

Toxins: is mercury dangerous?



Two studies:

- In Seychelles, high mercury exposure is associated with higher IQ
 - mercury levels correlate with higher fish consumption and better diet means higher IQ.
- In Faeroes, high mercury exposure is associated with lower IQ.
 - mercury levels reflect whale meat consumption. Greater consumption in part of the town where child care is poor.

So relationships between exposure and level of later problems are not straightforward.

Toxins: tobacco

- Very difficult to disentangle antenatal and postnatal influences
- Eskenazi and Castorina (1999): review of 17 studies:
 - Poorer academic achievement
 - Increased ADHD
- Paternal smoking just as strongly related as maternal smoking to such outcomes.
- Sillberg et al (2003) and Maughan et al (2004): latent genetic conduct factor accounted for difference in twin studies



Toxins: tobacco

- Maughan et al 2004 'E-risk' study of 1100 high risk twins

Toxins: summary 1

- Some substances <u>may</u> have mechanism-specific effects, rather than just causing a general brain insult.
- The effects of toxins vary with age.
- A number of factors modulate the adverse effect of the toxin on neurodevelopment. For toxins such as PCB's and mercury, it appears that a nutritious diet including breast milk, confers neuro-protection.
- Parental IQ and the quality of care-giving environment confer resilience.



- A few specific findings are consistent:
 - Lead and PCB's have a general effect on brain development, no specific link to psychiatric disorder
 - The relation between parental smoking and later delinquency is largely mediated by genetically inherited factors.

- Babies are designed to communicate they can't do much else:
 - brains, limited cognitions, and weak bodies, are specifically motivated, beyond instinctive behaviours that attract parental care for rhythms of interest and feeling displayed by

- So, what happens if babies can't communicate with anyone?
- Controlled intervention studies considered ethically impossible in humans
- Animal studies can inform debate, but great caution needed in generalising to humans

Harlow's "The Nature of Love" (1958):

"a baby monkey raised on a bare wire-mesh cage floor survives with difficulty, if at all, during the first five days of life. If a wire-mesh cone is introduced, the baby does better; and, if the cone is covered with terry cloth, husky, healthy, happy babies evolve".

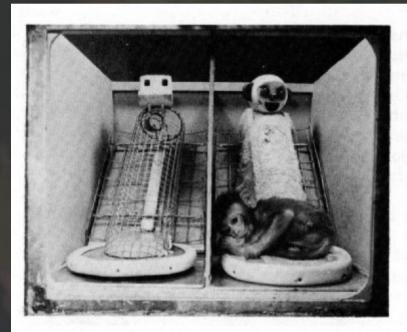


Figure 4. Wire and cloth mother surrogates

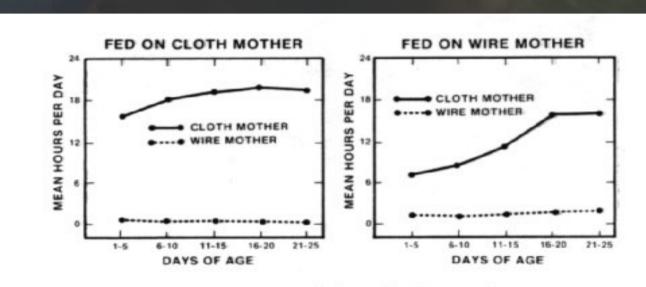


Figure 5. Time spent on cloth and wire mother surrogates.

"contact comfort is a variable of overwhelming importance in the development of affectional response, whereas lactation is a variable of negligible importance".

- 'Strange situation' open field test with cloth mother absent or present
- Little exploration when cloth mother absent
- After an interval, when cloth mother present, baby monkeys show much more exploratory behaviour, returning to her as a 'base of operations'
- In older monkeys, even the presence of cloth mother in a Perspex box enables exploration to take place

- Harlow et al 1965: described behaviour in monkeys exposed to social contact after total social deprivation
- In the group <u>isolated for first 3 months</u>, initial anorexia, autistic self-clutching and rocking. 2/6 refused to eat and one died.
 - Gradual recovery of most social functions over several months
- In the groups isolated for first 6 or 12 months, as in 3 month group, but little anorexia.
 - Very little recovery of social function. Only social behaviour was bursts of aggression towards other isolate animals
- In the group <u>isolated from 6-12 months</u>, rapid recovery of social interaction, but marked physical and sexual aggression towards adults and infants
- In <u>all groups</u> at least some abnormalities of social and sexual behaviour still seen after 18 months.
 - Maternally deprived monkeys always at the bottom of social hierarchy

- Long term outcomes in institutionalised
 Romanian orphans:
 - mild neuro-cognitive impairment
 - Impulsivity
 - Attention deficits
 - Social deficits
 - Abnormalities of hypothalamic-pituitary-adrenal function

- Barbara Tizard children raised in institutions discouraging 'too strong attachment' with multiple, and changing caregivers
 - Appeared attached to multiple adults at age 2-4
 - Did not 'care deeply for anyone'
 - Not shy towards strangers, attention seeking
 - 'Indiscriminately friendly'
 - Unwilling to share
 - Quarrelsome and competitive
- After adoption or return to own family at age 2+:
 - In the 'restored to own family' group, major problems persisted
 - In the adopted group, compared to controls, by age 16 most problems had resolved apart from unusually strong orientation towards adults, peer difficulties (including indiscriminate friendliness) and fewer close relationships than controls.

- Reasonable evidence for persistence of attachment patterns through life, and of association of insecure attachment with psychopathology.
- 'Reactive attachment disorder' now in ICD-10 and DSM-IV:
 - Possibly two types:
 - Disinhibited indiscriminate affection
 - Inhibited 'frozen watchfulness'
 - Recent evidence of a significant genetic component, particularly in boys

- Chugani et al (2001): 'Glass brain'
- 10 orphans (mean age 9, in orphanages from 5 weeks old for mean 3 years) and 24 controls
- PET using 2deoxy-2- ¹⁸F glucose

Figure from: Harry T. Chugani, Michael E. Behen, Otto Muzik, Csaba Juhasz, Ferenc Nagy, and Diane C. Chugani. Local Brain Functional Activity Following Early Deprivation: A Study of Postinstitutionalized Romanian Orphans. NeuroImage 14, 1290–1301 (2001)

Harsh parenting and conduct disorder

- Strong association between erratic, coercive or punitive parenting and conduct disorder and other forms of aggression
- The earlier the exposure, the greater the risk
- Much more common in boys
- Great variability between individuals in response to harsh parenting

Harsh parenting and conduct disorder

- Dunedin cohort study:
 - MAO A gene lower
 MAO A activity shown in animal studies to be linked to aggression
 - MAO A gene lies on X chromosome
 - Caspi et al (2002) looked at the link between MAO A genotypes and conduct disorder
 - High MAO A activity protects against the tendency of abuse to lead to violence

Figure from Caspi et al Science 2002; 297; 852

Sensitive and insensitive parenting

- De Wolff & van IJzendoorn 1997 meta-analysis:
 "is maternal sensitivity associated with attachment security?"
- 66 studies (n=4,176)
- Overall, corrected effect size was 0.24 moderately strong
- So sensitivity is an important but not exclusive condition for attachment security – other aspects of parenting (e.g. effective management) may be important, as may genetic factors

'Insensitive parenting' and postnatal depression

- Lynn Murray et al work on postnatal depression
- PND is probably biologically similar to other types of depression
- PND prioritised by NHS because babies are assumed to be vulnerable to its effects

 though the evidence is not robust
- PND is associated with lack of maternal responsiveness to the baby, but the association is not very strong

Postnatal depression

Video clip of mother with severe postnatal depression but interacting well with her baby - Note the synchronicity, mutuality, child-centred speech, turntaking, eye contact, many aspects of 'intersubjectivity'. Note also the happy baby!

Postnatal depression

Video clip of mother with severe postnatal depression with little or no interaction with her baby

Postnatal depression

Video clip of same mother as in last slide following mellow parenting course, interacting very well with her baby - synchrony, child centred speech, joint attention and laughter beautiful intersubjectivity!

Reciprocity

- Babies modify their parents! Babies are not 'passive receptacles'
- Epidemiologically, it is difficult to isolate the effects of particular types of 'parenting' because parenting is a mutual process
- Aim of therapies like Mellow Parenting is to help parents 'fall in love with their babies'

Efficacy of early intervention to promote sensitivity & attachment

- Bakermans-Kranenburg, van IJzendoorn & Juffer (2003):
 Meta-analysis of 70 controlled studies
- 88 intervention studies on sensitivity (n = 7,636) and/or attachment (n = 1,503).
- Interventions effective in changing insensitive parenting (d = 0.33) and infant attachment insecurity (d = 0.20).
- Most effective interventions used a moderate number of sessions and a clear-cut behavioural focus
- Interventions better at enhancing parental sensitivity also better at enhancing attachment security
 - supports notion of a causal role of sensitivity in shaping attachment.

Epidemiology - synthesis

- ADHD probably 70% genetic, 30% environmental
 - But the environment may be more influential in infancy than later (Minnesota High Risk Project)
- Conduct disorder genetic factors heavily dependent on environmental influences for expression
 - 2 types of conduct disorder: adolescent and enduring. The enduring type is early onset and persists into adulthood, generally as antisocial personality disorder.
- Autism probably 90% genetic, 10% environmental
- Paradoxically, genetics becomes <u>more important</u> the older the child

Epidemiology - synthesis

- Not really much epidemiological evidence of a 'critical period' in relation to social development in humans
- But physiological evidence suggests it is likely that learning about social relations is easier when we are young – and unlearning is harder the older we are
- Strong predictors of social dysfunction are present early in life

Epidemiology – the bottom line

- Financial costs of conduct disorder (Scott et al 2001):
- 142 ten year olds from inner London followed up to adulthood.
- 3 groups: no problems, conduct problems, and conduct disorder. Costs for services used over and above-basic universal provision.
- By age 28, costs for individuals with conduct disorder
 10.0 X higher than for those with no problems and
 3.5 X higher than for those with conduct problems

Epidemiology – the bottom line

- Mean individual total costs £70k for conduct disorder group, £24k for the conduct problem group, £7k for the no problem group.
- Costs in all groups: Crime > extra educational provision > foster and residential care > state benefits > health costs (£2k for conduct disorder group Vs £247 for the no problem group).
- Note that differential health costs will rise with age
- Costs to the individual: people with conduct disorder are more than 9 X more likely to die in adolescence or early adulthood.

Early intervention

- David Olds 3 RCTs in US with long-term follow-up
- 1998 15-year follow up of 400 high-risk children in New York
- Intervention was 9 antenatal and 23 postnatal nurse visits before age 2 Vs control – addressing:
 - General health promotion
 - Maternal personal development
 - "Competent care of their children"

Early intervention

- Compared with controls, adolescents born to women who received nurse visits during pregnancy and postnatally displayed fewer:
 - instances of running away (0.24 Vs 0.60; P=.003)
 - arrests (0.20 Vs 0.45; P =.03),
 - convictions and violations of probation (0.09 Vs 0.47; P<.001),
 - lifetime sex partners (0.92 Vs 2.48; P=.003),
 - cigarettes smoked per day (1.50 Vs 2.50; P=.10),
 - days having consumed alcohol in the last 6 months (1.09 Vs 2.49; P = .03).
 - reported behavioural problems related to use of alcohol and other drugs (0.15 Vs 0.34; P=.08).

Early intervention: important elements

- Other lessons from Olds' other RCTs:
 - Nurses more effective and acceptable than "paraprofessionals"
 - Interventions produce lasting effects on the mother's life course as well as the child's
 - Some lack of clarity about which elements of the intervention are important
- Note less positive results in UK (eg Starting Well, Sure Start) – but short term follow up, and we already have health visitors!

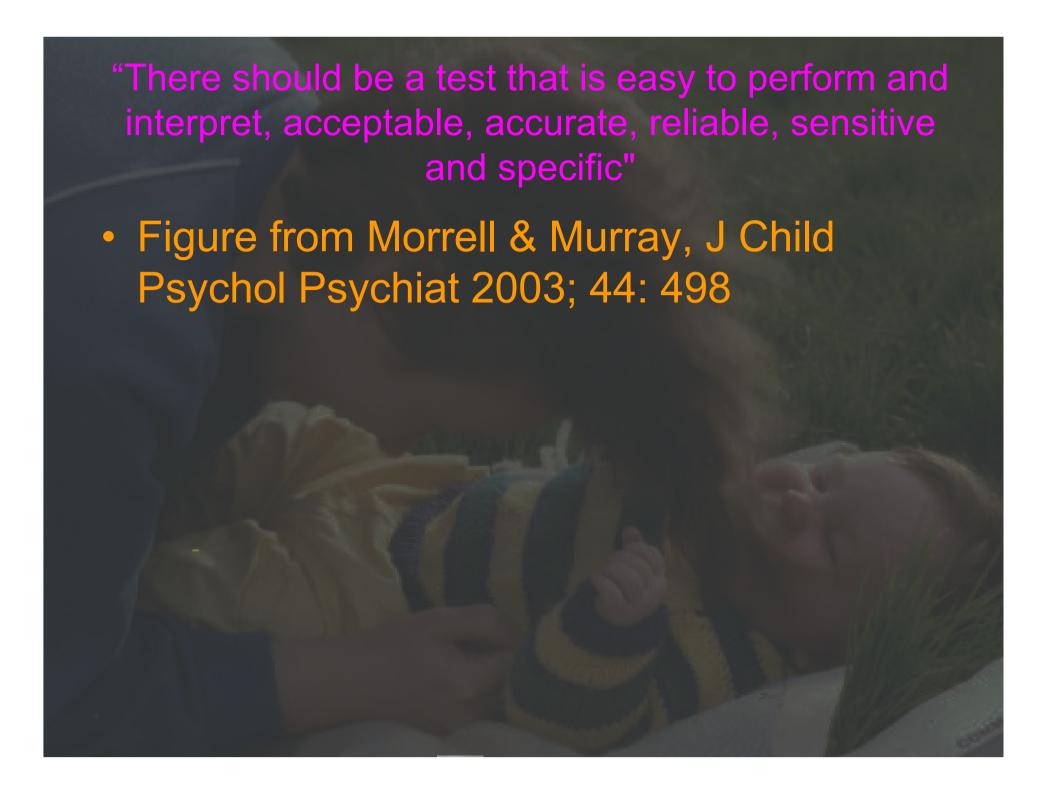
Detecting problems early

- Should we aspire to it? Wilson & Jungner's criteria for screening programmes:
 - The condition should be an important health problem
 - The natural history of the condition should be understood
 - There should be a recognisable latent or early symptomatic stage
 - There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific
 - There should be an accepted treatment recognised for the disease
 - Treatment should be more effective if started early
 - There should be a policy on who should be treated
 - Diagnosis and treatment should be cost-effective
 - Case-finding should be a continuous process

Detecting problems early

"There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific"

- Morrell & Murray 2003
 - Detailed observational data of mother-child interactions and assessment of prefrontal function (A not B task) in 59 babies
 - Symptoms of conduct disorder and hyperactivity at 5 & 8y
 - Emotional/behavioural dysregulation on the A not B task at 9 months predicted conduct disorder
 - delayed object reaching predicted hyperactive symptoms
 - These two developmental trajectories associated with distinct patterns of early parenting that were strongly influenced by infant gender



- "There should be a test that is easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific"
- We know a lot e.g. that low MAO A, hostile parenting, emotional dysregulation at 9 months predict conduct disorder
- More work needs to be done, ideally in a large birth cohort looking at:
 - multiple early measures
 - including direct observation of interactions
 - multiple psychiatric outcomes
- And there's still the question of whether some or all of us in primary care can already do part of it 'instinctively'!

Detecting problems early "Treatment should be more effective if started early"

- Little direct evidence, but Olds' et al results suggest early intervention is highly effective – probably more so with <u>better selection</u>
- Conduct disorder in 3-8 year olds effectively treated with Webster-Stratton parenting groups (effect size > 1 in Stott et al 2001)
- Plenty of evidence that treatment of antisocial personality disorder is extremely difficult and not very effective

Detecting problems early "There should be a policy on who should be treated"

- "PCOs should plan how to discharge their responsibility for the health care of all the children and young people living within their boundaries"
- "Screening, surveillance, parent support and health promotion activities should, where possible, be prioritized on the basis of evidence of effectiveness"

Picture of Hall 4 "Health for all Children" cover

Conclusions

- We are learning about human social development at a breathtaking rate
- We know more about the development of problems in social behaviour than most people think
- There are still pieces of the jigsaw to complete
- We may soon have the potential to use emerging evidence to help children and their families avoid disruption and misery