Developmental disorders

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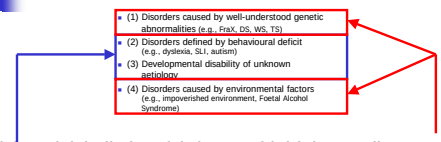
Outline

- Types of developmental disorder
- Explanatory frameworks
- Developmental language deficits
- The example of Williams syndrome
- The relation of genes to cognition

Types of developmental disorder

- (1) Disorders caused by well-understood genetic abnormalities
  - (e.g., Down syndrome, Williams syndrome, KE)
- (2) Disorders defined by behavioural deficit
  - (e.g., dyslexia, SLI, autism)
- (3) Developmental disability of unknown aetiology
- (4) Disorders caused by environmental factors
  - (e.g., impoverished environment, Foetal Alcohol syndrome)

Types of developmental disorder



- (1) and (4) distinguish locus of initial causality, nature/nurture distinction
- (2) and (3) relate to level of current understanding
  - e.g. dyslexia and autism have genetic component (heritability) but genes not yet identified

Genetic syndromes

- Alagille syndrome
- **Angelman syndrome**
- Apert syndrome
- Beckwith-Wiedemann syndrome
- Bloom syndrome
- Branchio-oto-renal syndrome
- **Cri du chat syndrome**
- Crouzon syndrome
- **Di George syndrome**
- **Down syndrome**
- Ehlers Danlos syndrome
- **Fragile-X syndrome**
- Jackson-Weiss syndrome
- Jervell Lange-Neilsen syndrome
- Kallman syndrome
- Kearns-Sayre syndrome
- Langer-Giedion syndrome
- Lesch-Nyhan syndrome
- Li-Fraumeni syndrome
- Marfan syndrome
- Miller-Diecker syndrome
- Nijmegen breakage syndrome
- Pfeiffer syndrome
- **Prader-Willi syndrome**
- Romano-Ward syndrome
- Rubinstein-Taybi syndrome
- Smith-Magenis syndrome
- Stickler syndrome
- Treacher Collins syndrome
- Tricho-rhino-phalangeal syndrome
- **Turner syndrome**
- Usher syndrome
- Waardenbrug syndrome
- WAGR syndrome
- **Williams syndrome**
- Wolf-Hirschhorn syndrome

(Strachan & Read, 1999)

Explanatory frameworks

- Static classical cognitive neuropsychology
  (e.g., Temple, 1997)
- Neuroconstructivism
  (e.g., Elman et al., 1996; Karmiloff-Smith, 1998)

Classical (static) cognitive neuropsychology

- For disorders with uneven cognitive profiles (e.g., in adulthood), use selective deficits to inform normal structure [general deficits less interesting…]
- Temple (1997):
  - "The objective of case studies in cognitive neuropsychology is not to produce a clinical taxonomy, but to propose selective deficits of a common modular architecture of a developmental system"
  - "It may be common for children to have problems with several components of the system, but the most informative child, in terms of revealing the structure of the system, will be the child who has selective difficulty with a particular element and therefore a dissociation of skills"

Classical (static) cognitive neuropsychology

- Temple (1997):
  - "Downstream effects do not mean that a developing system cannot have a modular organisation, but they may make the appearance of the classical double dissociations, which are the hallmark of cognitive neuropsychology, difficult to attain within developmental dis
  - "If the brain reorganised and generated n performance would not necessarily reflect a normal system minus those components that are disrupted, which is a basic assumption of cognitive neuropsychology (Saffran, 1982)"
  - "From the perspective of cognitive neuropsy erest in the issue of biological localisation, it is of language develops in the right or the left hemisphere, provided that the functional architecture of the language system is the same in both cases"

Interactions

Plasticity & Reorganisation

Relation to neural substrate

Reading

Developmental Phonological Dyslexia

Two approach

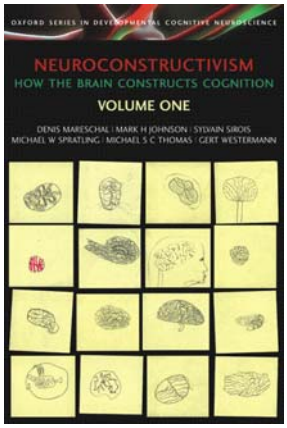
A horse can be described in terms of the parts of the MOT test that it passes and fails, but that doesn't mean it's a car...

Cognitive Neuropsychology

- Relate disorders to normal modular structure (age appropriate?) *dogma*
- Look for disorders with specific deficits => (genetic?) fractionatio
- Advantages
  - Most disorders can be described with reference to normal modular system
  - Good preliminary stage to describe disorder
- Disadvantages
  - No developmental process (origin of modular structure?)
  - Normal-looking behaviour may be produced by atypical process
  - Can't explain better performance (e.g., savant)

Neuroconstructivism

- Disorders result of development guided by atypical constraints
- Focus on developmental trajectories
- Sensitive measure of strengths and weaknesses – verify normality
- Advantages
  - Situates behavioural deficits within developmental theory – trace back to origins in infancy
  - Links to cognitive neuroscience (brain imaging, genetics)
- Disadvantages
  - Must whole brain be atypical? *dogma*
  - Little evidence for radically different modular structure
  - Hard to assess cognitive significance of biological atypicalities



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Developmental disorders of language

- Importance of plasticity illustrated by fact that children who experience same brain damage as adult aphasics end up with no symptoms of aphasia (Bates & Roe, 2001)
- Whatever is wrong in the developmentally disordered brain, plasticity cannot overcome it
- Doesn't imply plasticity isn't trying . . . plasticity itself may be atypical

Bates & Roe (2001) – no childhood aphasia

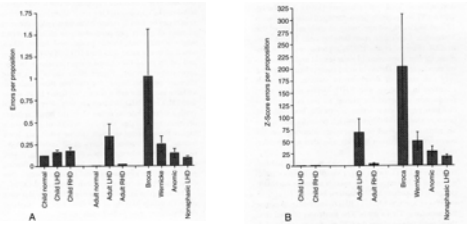
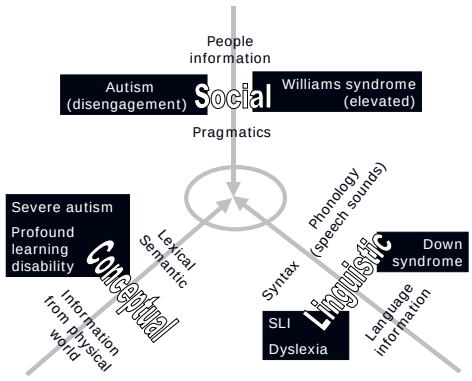


FIGURE 20.2 (A) The mean number of errors per proposition for normally developing children, adult controls, and children and adults with right or left hemisphere damage. LHD patients are further subdivided by aphasia type. (B) Z score error rates per proposition for children versus adults with right or left hemisphere damage. LHD patients are further subdivided by aphasia type.

Disorders of language

- Landau-Kleffner syndrome
  - Acquired Epileptic Aphasia
- Semantic disorders
- Grammatical disorders (SLI)
- Developmental dyslexia
- Pragmatic disorders
- Williams syndrome
- Down syndrome
- Autism
- Non-verbal learning disability



Developmental disorders of language

Landau-Kleffner syndrome (Acquired Epileptic Aphasia)

- profound receptive language impairment (may extend to total disappearance of auditory verbal comprehension)
- Onset 18 months - 13 years (peak incidence 4 years)
- 80% cases also seizure disorder with bilateral EEG abnormality
- disruption of processing of auditory input to Wernicke's area?
- no evidence of deafness - failure of words to be associated with meanings
- knock-on effects in development of syntax
- later the onset, better final language development (established knowledge)

Developmental disorders of language

- Semantic disorders
  - children with word finding difficulties
  - semantic but not phonological errors in naming
  - slow naming times
  - impoverished word definitions
- Grammatical disorders
  - SLI - esp. errors of morphology (differ across languages)
  - KE family (motor deficits too - FOXP2 gene)
  - grammatical SLI - restricted to difficulties with representational dependencies within syntactic constructions

Three current theories of SLI

(1) Deficits to rule-based language-specific structures (e.g., van der Lely)

- Impairment in specific structural relationships (agreement, specifier head-relations)
- Absent linguistic features
- Fixation in a period of development where tense marking is 'optional'
- Problems in more general language functions (implicit rule learning, representing relationships between structures)

Three current theories of SLI

(2) Non-linguistic processing deficit that particularly impact on language (e.g., Tallal)
- Reduced processing rate
- Capacity limitations on cognitive processing
- Deficit that particularly affects phonology
- Low-level perceptual or temporal processing deficit

(3) Procedural-Declarative theory (e.g., Ullman)
- Grammar relies on procedural memory (skill), vocabulary on declarative memory (knowledge)
- SLI = developmental deficit to procedural system

Developmental disorders of language

- Developmental dyslexia
  - Problems in forming phonological representations exist prior to literacy (e.g., revealed by phoneme discrimination, onset-rhyme knowledge)
  - Italian 'dyslexics' who have no problem with reading...
- Pragmatic disorders
  - language difficulties overlap with wider social communicative difficulties (autistic spectrum)

Other disorders

- Williams syndrome - language relative strength compared to visuospatial skills
- Downs syndrome - language development much delayed (esp. syntax), poor phonological working memory
- Autism - varying levels of language development, particular pragmatic impairment

Other disorders

- Non-Verbal Learning Disability (Rourke, 1987, 1989) - widespread brain damage causes recurring pattern:

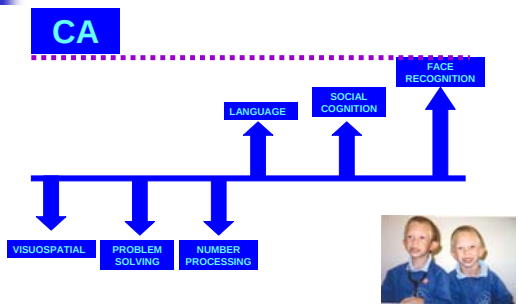
- <u>Relative weaknesses</u>
  - bilateral tactile-perceptual deficits, more marked on the left side of the body
  - impaired visual recognition and discrimination
  - impaired visuospatial organisation
  - bilateral psychomotor co-ordination problems, more marked on left
  - difficulties managing novel information
- <u>Relative strengths</u>
  - simple motor skills
  - auditory perception
  - rote learning
  - selective and sustained attention for auditory-verbal information
  - basic expressive and receptive language
  - word reading and spelling

The example of Williams syndrome

- Rare genetic disorder (1 in 20,000 live births) caused by a deletion of ~28 genes on the long arm of chromosome 7 at q.11,23
- Clinical features:
  - Heart abnormalities - typically SVAS
  - Facial dysmorphology
  - Small stature
  - Hernias
  - Hoarse voice
  - Premature ageing of skin
  - Constipation
  - Hyperacusis
  - Abnormal gait

- Cognitive features:
  - low IQ
  - a specific personality profile ('hypersociability', empathy, anxiety)
  - poor visuospatial constructive skills
  - particular difficulty with number processing
  - relatively good language abilities (though developmental delay)
  - relatively good face processing abilities

Williams syndrome



Brain anatomy in WS

- 80% of normal brain volume
- anterior regions and cerebrum:
  - small in proportion to other brain regions
- limbic and frontal regions:
  - small, but proportionally normal to other brain regions
- cerebellum:
  - large in proportion to other brain regions
- malformations in dorsal regions
- total grey matter reduced
- abnormal layering, orientation, density and size of neurons in several brain regions

Brain chemistry in WS

- Normal ratios in cerebellum:
  - Cho/Cre
- Abnormal ratios in cerebellum:
  - Cho/NAA
  - Cre/NAA
- Correlations with cognitive ability:
  - Increase in cognitive performance associated with increase in NAA for all cognitive tasks (particularly general speed of processing)

Structure-function relationships?

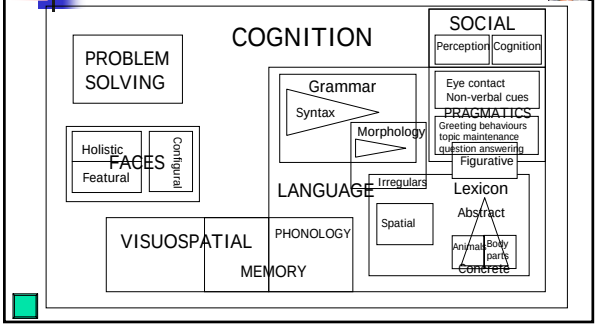
"Brain volume, brain anatomy, brain chemistry, hemispheric asymmetry, and the temporal patterns of brain activity are all atypical in people with WS. How could the resulting cognitive system be described in terms of a normal brain with parts intact and parts impaired, as the popular view holds? Rather, the brains of infants with WS develop differently from the outset, which has subtle, widespread repercussions at the cognitive level" (Karmiloff-Smith, 1998)

- Quote illustrates neuroconstructivist perspective on importance of substrate
- Possible response is to argue only some of atypicalities have functional importance (ungrounded)

Early views (static framework)

- Rossen et al. (1994): WS "presents a remarkable juxtaposition of impaired and intact mental capacities...[..]...linguistic functioning is preserved in Williams syndrome while problem solving ability and visuospatial cognition are impaired"
- "Although their IQ is measured at around 50, older children and adolescents with WS are described as hyperlinguistic with selective sparing of syntax, and grammatical abilities are close to normal in controlled testing. This is one of several kinds of dissociation in which language is preserved despite severe cognitive impairments, suggesting that the language system is autonomous of many other kinds of cognitive processing." (Pinker, 1994)
- Pinker (1999): WS and SLI represent 'genetic double dissociation' arguing for the developmental independence of language from cognition [innate modularity]

Fractionation in Williams syndrome?



WS language: More recent research

- Overall profile
  - Delayed language development (~ 2 years)
  - Usually MA / DS comparison groups - No independence from general cognition
- Precursors
  - Delayed pointing, impaired triadic interactions
  - Delay in using labels to aid categorisation
- Speech processing
  - Anomalous auditory ERPs
  - Lexical segmentation delayed
  - Phonological STM relative strength

More recent research suggests:

- Vocabulary acquisition
  - Vocabulary spurt doesn't coincide with usual semantic markers
  - Lexical constraints different? (whole object, taxonomic)
  - Difficulty in spatial, perhaps 'relational' vocabulary
- Semantics
  - Poorer / slower but not atypical in its underlying dynamics
  - Integration with syntax may be anomalous
  - Knowledge remains more perceptually-based and insufficiently abstract

More recent research suggests:

- Relation of grammar to vocabulary
  - Initially MLU predicts grammatical complexity
  - Complex structures apparently mastered
  - Grammar generally behind vocabulary (TROG vs. BPVS)
  - Exaggerated difficulty with complex structures
  - Atypical errors found in Italian, Spanish gender agreement, morphology, preposition use
- Pragmatics
  - Persistent deficits, e.g. in non-literal language (despite usage of this language), advance theory-of-mind reasoning (despite hypersocial personality profile)

Overall picture in WS

- Different lexical constraints
- Subtle grammatical impairments
- Atypical balance of semantics/phonology
- Language is relatively good but develops atypically
  - Notably good compared to individuals with Down syndrome matched for IQ – but maybe that tells us more about DS?
- However, some researchers still prefer static view
  - "the linguistic performance of [individuals with] WS can be explained in terms of selective deficits to an otherwise normal modular system" (Temple & Clahsen, 2003)
  - E.g., inflectional morphology debate

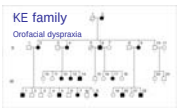
Brain imaging

- Genetic effects on brain development are widespread
  - Cognitive genetics
  - Evolutionary neurogenetics
- Developmental disorders are about interactivity, redundancy, compensation...
  - What's your developmental theory?

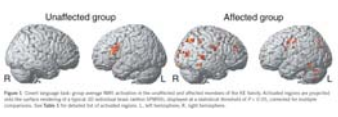
KE brain data

Chromosome 7 foxp2 mutation

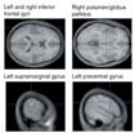
Foxp2 structure recent to humans?



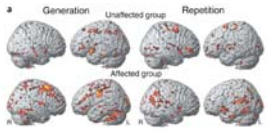
Covert naming



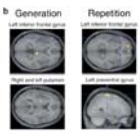
Under active regions in affected



Generation Repetition



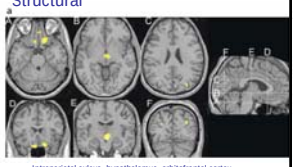
Under active regions in affected



Liegeois et al. (2003)

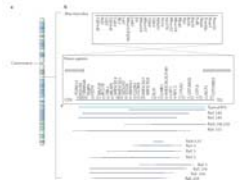
WS brain data

Structural



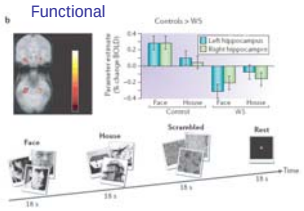
Intraparietal sulcus, hypothalamus, orbitofrontal cortex

Genetic



Deletion of ~28 genes from 1 copy of chromosome 7

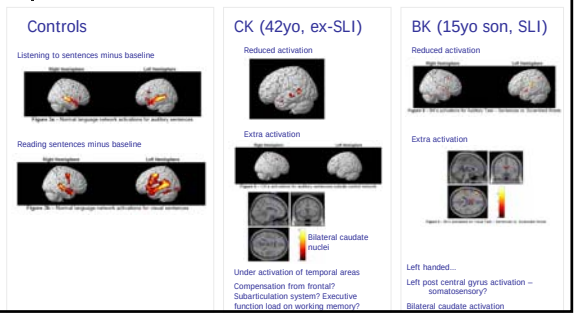
Functional



Hypoactivation of anterior hippocampal formation

Meyer-Lindenberg et al. (2006)

CK and BK brain data (in progress)



Comparison of disorders

- Comparison of developmental disorders may be informative about constraints acting on normal language development
  - e.g., importance of various information sources

Comparison of disorders

- McDonald (1997): routes to acquire linguistic structure
  - Prosodic and/or phonological information used to segment input into meaningful units
    - [Iscrambledtheeggs] = [I scrambled the eggs]
  - Analysis of distributional and co-occurrence patterns of linguistic elements

Comparison of disorders

- Two types of information from patterns:
  - Function words - mark syntactic structure; fast automatic use associated with emergent left lateralisation of language (ERP marker)
  - Morphological analysis of words into component parts
    - [I scrambled the eggs] = [I scramble + ed the egg + s]

	Phonology	Function words	Morphological decomposition	Other
Successful				
Disrupted Input	OK	Not developed	OK	More structure than in input
Williams syndrome	OK	OK	Some problems	Delay, some problems in pragmatics
Autism (high functioning)	OK	?	?	Problems in pragmatics
Unsuccessful				
Late L1 learners	Problems	?	Problems	Persistent problems; slow decoding => high working memory load
Late L2 learners	Problems	Do not show native ERP patterns	Some persistent problems (e.g., gender agreement)	Sign: Late L2 better than Late L1 (larger STM for signs?)
Down's syndrome	Problems	Short MLU	?	
Specific Language Impairment	Problems	Do not show normal left anterior temporal ERP specialisation (no automisation?)	Problems with morphology and agreement	

Good input: Necessary but not sufficient?

Conclusions

- Developmental deficits in language not due to brain damage analogous to adult case
- Genetic developmental disorders can show auditory, semantic, grammatical, and pragmatic deficits
- Competing explanations in terms of
  - (1) selective modular damage
  - (2) atypical neurocomputational constraints on developmental process

Conclusions

- Detailed testing required establish normal/delayed/atypical
- Computational modelling may be required to reveal role of developmental process
- Importance of input?
- Use of non-developmental models still widespread
  - can play role in early theory building