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SELECTIVE DEVELOPMENTAL NEUROPSYCHOLOGICAL DISORDERS

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The study of developmental disorders garners special respect from neuropsychologists. First, it is difficult enough to try to understand the mature brain and the effects that damage to it might have, but to try to appreciate how a brain works that develops in a qualitatively different manner because of early injury is daunting (e.g., Bishop, 1997; Frith, 2001a). Second, in specific cases very selective developmental disorders have been observed, and these observations have been interpreted as additional evidence for cognitive modularity (e.g., Baron-Cohen, 1998; Pinker, 1999). Third, there is evidence suggesting that the immature brain possesses more and perhaps different forms of plasticity than those that may be observed in the adult brain (e.g., Vicari et al., 2000). Fourth, developmental neuropsychology provides the basis for an interface with an important discipline within the neurosciences, namely, neurogenetics. Finally, neuropsychological disorders of development constitute a clinically important area, because the deficits often represent a life-sentence for large numbers of affected individuals.

There are a number of different phenomena that fall under the general term “developmental neuropsychology”. Sometimes the term is used interchangeably with child neuropsychology, while others use the term to include studies with adult subjects who have suffered all their lives from a specific cognitive impairment in the absence of neurological disease or birth complications. There are subdisciplines that focus on the major developmental psychiatric (e.g., autism or attention deficit-hyperactivity disorder – ADHD), genetic (e.g., fragile X or Down’s syndrome) or neurological (e.g., Gilles de la Tourette syndrome) conditions, although these categories are not sharply defined (e.g., Cornish et al., 1999). In contrast, researchers with a more cognitive neuropsychological background often study children with selective symptoms that mirror the deficits that are encountered in adults with acquired brain damage. We are convinced that these approaches are all valid and in this special issue we have included examples of all of these methodologies. The different contributions of this special issue are ordered from studies reporting on more diffuse cognitive disorders (e.g., Williams syndrome, ADHD, autism) to more selective developmental impairments in patients without evidence for a specific neurological disorder (prosopagnosia, colour agnosia). This is followed by investigations looking at specific disorders resulting from early brain damage (e.g., executive dysfunction).

Impairments of attention are highly common in a wide array of developmental disorders, and in many conditions, virtually define the syndrome (e.g., attention deficit disorder). Cornish et

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al. (2007, this issue) bring a new and powerful investigational approach to the domain of attention, by comparing and contrasting three developmental conditions that have traditionally been hallmarked by primary defects in attention: Fragile X syndrome, Down syndrome, and Williams syndrome. The investigators demonstrate that when the construct of attention is broken down into different subparts (e.g., inhibitory control, orienting, selective attention), and then investigated across development (from infants and toddlers to middle and late childhood), it becomes clear that there are important syndrome-specific differences in attentional component processes and in the developmental trajectory of these processes. For example, in some of the conditions the authors studied, certain aspects of attention tended to improve with development, while other aspects tended to worsen; moreover, this pattern varied depending on the disorder. This fine-grained approach to exploring the developmental trajectory of various subcomponents of attention has much to offer, not only in the understanding of the developmental conditions themselves, but also in the application of effective treatments, whether pharmacological or behavioural.

Another important clinical condition is autism. These children are characterized by impairments in social interaction, communication, and behaviour. Research has provided evidence for selective cognitive deficits in autism, and this has led to the hypothesis that these children suffer from impairments in perceptual and higher-order abilities necessary for understanding intentions of others (e.g., Frith, 2001b). The suggestion that there might be a specific neuroanatomical signature associated with autism is investigated in the work by Salmond et al. (2007, this issue). They explore the hypothesis that the variability in findings between different studies concerning the brain abnormalities observed in autistic subjects might be due to differences in general abilities. Low functioning autistic children might suffer from substantial comorbidity, and as a result, from more widespread brain abnormalities. The investigators studied two groups of autistic children, one with average or above average IQ and one with low IQ. Voxel-based morphometry analyses of structural magnetic resonance imaging (MRI) data showed bilateral abnormalities in the cerebellum, fusiform gyrus and frontal cortex in both groups. Differences between the two autistic groups concerned increased (high functioning group) *versus* decreased (low functioning group) grey matter density in the cerebellum, and additional bilateral abnormalities in the post-central gyrus and areas within the dorsolateral prefrontal cortex in the low functioning group. Event-related potential (ERP) analyses showed no differences between a normal comparison group and the high functioning autistic children, while the low functioning autistic children demonstrated delayed P3 components. This study underscores the fact that neuroimaging (functional and structural) investigations of developmental neuropsychological disorders require an approach that takes account of possible subtypes and co-morbidity.

Children with ADHD frequently manifest impairments in writing. A novel approach to studying this association is taken by Adi-Japha et al. (2007, this issue), who focus on the specific writing components of handwriting and spelling. The investigators demonstrate that ADHD children manifest errors in handwriting and spelling (e.g., excessive pen pressure, letter omissions) that can be largely explained as impairments in the attentional processes necessary for motor planning. This is an intriguing finding, suggesting that the writing defects in these children are mainly motor-related, rather than being linguistic in nature (the children had normal reading skills). This is a provocative claim that challenges current approaches to treatment, pointing especially to the potential of remediation through education and the use of word processors, and not just psychostimulant medication.

ADHD (DSM-IV – American Psychiatric Association, 1994), although one of the most commonly diagnosed developmental disorders, suffers (like many of the other DSM categories) from a relatively imprecise definition. Central for the diagnosis is the presence of the symptoms *inattention* and/or *hyperactivity* before the age of seven years. However, there

is very little information on the prevalence of these types of behaviour in normal preschool children. This imposes severe restrictions on the use of these symptoms in the diagnostic process. In a large survey of 652 parents of children between the ages of 3 and 6 years, Smidts and Oosterlaan (2007, this issue) ascertained the relative frequency of inattention and hyperactivity in children attending a regular preschool or primary school. Their overall finding was that ADHD symptoms are, in fact, very frequent in this age group. Moreover, hyperactive-impulsive symptoms are much more common in this age range than inattentive behaviour. This suggests that the latter might be a more reliable index for identifying young children who are at risk for developing ADHD.

The investigation of developmental conditions that tend to mirror the nature of conditions manifested in adult patients with acquired brain damage has been highly fruitful in neuropsychology, even if the developmental versions often have no detectable lesion correlate (e.g., Temple, 1997). Some notable examples are developmental prosopagnosia and developmental sociopathy, both of which - along with their adult acquired counterparts - have sparked intense scientific scrutiny (e.g., Jones and Tranel, 2001; Koenigs and Tranel, 2006). Since the original report by McConachie (1976), there have been several reports describing developmental recognition impairments for familiar faces (e.g., de Haan and Campbell, 1992; Jones and Tranel, 2001), or what is termed developmental prosopagnosia. These reports have hinted at the possibility that there are different types of this recognition impairment, perhaps comparable to the distinction put forward by De Renzi et al. (1991) of a perceptual ('apperceptive') and a mnemonic ('associative') prosopagnosia. The study of Dobel et al. (2007, this issue) reports a series of six subjects with developmental prosopagnosia. Following a detailed literature review, the authors proceed to carefully describe the subjects on the basis of an extensive test battery. The subjects were all of above average intelligence and none of them displayed general visual deficits or social dysfunction. Associated face processing abilities, such as perception of emotional expressions or memory for unfamiliar faces, were, on the whole, relatively mildly impaired, although some subjects manifested more severe difficulties. The available structural MRI data did not indicate any macroscopic neuroanatomical abnormalities.

In an earlier study of a healthy family with two parents and four children, de Haan (1999) reported evidence for a familial factor in the development of face recognition difficulties. The suggestion of a genetic basis was investigated further in a large study with seven families in which 38 cases of suspected hereditary prosopagnosia were observed (Grueter et al., 2007, this issue). Their analyses show that men and women are regularly affected and the disorder is often transmitted from one generation to the next. Segregation is best explained by a simple autosomal dominant mode of inheritance. This suggests to us that the search for the "face recognition gene" has now begun. This line of work is very exciting, as it could help shed light on the types of genetic and environmental influences that combine to yield high or low aptitude in face learning and recognition, arguably one of the most important skills that persons have to master in modern society.

Apart from familiar faces, the recognition of other types of visual stimuli may be affected from birth onwards; such stimuli include objects (e.g., Eriksson et al., 2003) and words (e.g., Samuelsson et al., 2000). In the first such case of its kind to appear in the literature, van Zandvoort et al. (2007, this issue) report a patient with developmental colour agnosia. Specifically, the patient was unable to recognize colours, despite intact colour perception and normal ability to name colours from memory. In an elegant series of experiments, the investigators demonstrated that the patient could not imagine the colours of familiar objects (e.g., what colour is your car?), discriminate veridical coloured objects from incorrectly coloured objects, or categorize colours. These findings are used to argue that the patient has an impaired internal colour space. By all reports, the patient had experienced this defect his

entire life, and he did not have any acquired damage to the neural structures normally associated with colour processing; hence, these facts provide a strong basis for the authors' argument that the patient has a developmental form of colour agnosia. Now that this case description is in the literature, and the syndrome of developmental colour agnosia has been highlighted as a legitimate condition, it will be interesting to see whether additional cases are identified by other investigators (as has been the case for developmental prosopagnosia).

A cognitive skill that has recently moved into the scientific spotlight in neuropsychology and cognitive neuroscience is number processing or what has been termed "numerical cognition" (e.g., Butterworth, 2005). Developmental impairments of numerical cognition are common, but very little is known about the neurobiological correlates of such defects, or about their developmental trajectory. The study by Ansari et al. (2007, this issue) contributes important new information on one aspect of numerical cognition. The investigators studied visual estimation, and more specifically, the ability to rapidly form a sense of the numerosity of an array of visual items (an ability that is considered a low-level aspect of numerical cognition, and that probably provides an important developmental foundation for higher-level number processing). It was found that children with Williams syndrome, who typically have impaired nonverbal cognitive abilities in the context of relatively normal language skills, were very impaired in visual estimation; moreover, Williams syndrome cohorts showed little improvement in visual estimation skills across development, unlike the case in typically developing children. These results are especially intriguing in light of the general finding that the sense of numerosity is often impaired by acquired damage to language-related cortices in left hemisphere in adults (especially lower posterior parietal and posterior superior temporal regions; e.g., Dehaene et al., 1999; Denburg and Tranel, 2003), and the data prompt new ways of conceptualizing the neural underpinnings of the development of numerical cognition.

The condition of specific language impairment (SLI), defined as a selective failure to develop language at a normal rate in the absence of frank neurological and psychiatric disease and adequate educational opportunity, has drawn increasing interest from neuropsychology researchers in recent years. Casalini et al. (2007, this issue) investigated several interesting questions in a cohort of participants with SLI, aimed at fleshing out the status of phonological working memory and long term verbal knowledge as indexed by reading morphologically complex non-words (e.g., 'womanist'). The investigators were also interested in whether different subtypes of SLI children would manifest different types of impairments on phonological working memory and long-term verbal knowledge tasks. There was clear support for the conclusion that SLI children utilized long-term verbal memory to perform the non-word reading tasks, suggesting that the defective phonological working memory in these children cannot be attributed to deficient long term verbal knowledge. This finding not only expands our understanding of the nature of verbal processing impairments in SLI, but it also has very intriguing ties with a variety of recent advances from functional neuroimaging and lesion studies regarding the neural correlates of verbal working memory (e.g., Ravizza et al., 2004; Wagner and Smith, 2003).

The hypothetical morphological brain differences between healthy children and those with developmental dyslexia have been the subject of considerable scientific debate (e.g., Galaburda et al., 1985; Rumsey et al., 1997). The study by Phinney et al. (2007, this issue) attempts to shed further light on this issue by looking at different subtypes of poor reading). Structural MRI data were correlated to performances on tests that are sensitive to specific components of the reading process, specifically, phonemic ability, orthographic ability, and rapid naming ability. Apart from a number of more specific relationships between certain brain areas (e.g., angular gyrus) and one of the three reading components (e.g., orthographic ability), the main finding was that phonemic ability predicted overall brain size in normal readers while there was no such relationship in the poor readers. This pattern of results was not apparent for the

other two measures of reading ability. These results suggest that developmental dyslexics may not just be the people in the bottom 5% of the normal reading distribution but are, perhaps, neurologically different from good readers, resulting in a pronounced problem in phonemic ability. This raises also the possibility that developmental dyslexia due to a phonetic impairment is a separate condition.

The final two papers in this special issue are concerned with early lesions to the prefrontal lobes. This is an intriguing field for many reasons (e.g., Stuss and Anderson, 2004). The frontal lobes subserve various higher-order cognitive abilities that allow us to regulate our behaviour, and frontal brain structures are the slowest to develop with neurophysiological changes progressing well into young adulthood. This suggests that the time of onset of damage is crucial for the ensuing clinical picture. This is exactly what Jacobs et al. (2007, this issue) investigated in their study involving 40 children with early lesions to the prefrontal cortex. Their findings suggest a non-linear relationship between age at injury and outcome, with critical periods during development when the frontal lobes are particularly vulnerable to damage. Children with prenatal lesions are at the greatest risk for developing neuropsychological deficits, while children who incurred their lesion in the range of 7 to 9 years were relatively spared. Children who suffered brain damage at a later age were again worse off. This suggests that, insofar as the frontal lobes and their associated functions are concerned, the period around 8 years offers relative protection against brain injury, possibly as a result of pronounced prefrontal activity during this phase, including synaptogenesis.

The immediate impact of very early brain damage is forcefully demonstrated in a single case study by Anderson et al. (2007, this issue), who studied a 14-month-old boy who was operated on for the removal of a vascular malformation in the right dorsolateral prefrontal cortex at the age of 3 days. In a number of elegantly devised observational studies they showed that this young boy suffered from subtle but significant impairments in the regulation of emotions and the engagement of attention. Although it is difficult to predict his cognitive and emotional development from hereon, it is clear from this study that early brain damage not only results in an alteration of behavior that resembles what happens in adult-onset brain injury, but also affects the route to getting there.

Overall, this special issue provides an up-to-date overview of developmental neuropsychology. The papers exemplify different topics that are currently under intense scientific scrutiny, and they also depict the types of methodologies – ranging from laboratory observations of toddlers to different neuroimaging techniques – that have been devised, and the complexity of investigating a developing system. If, as some would claim, understanding the human brain is the final scientific frontier, then surely we still would need to explain how it develops.

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