DEVELOPMENTAL NEUROPSYCHOLOGY

A CLINICAL APPROACH

SECOND EDITION

Vicki Anderson, Elisabeth Northam,
Jacquie Wrennall

ROUTLEDGE

Developmental Neuropsychology

This fully updated edition of *Developmental Neuropsychology: A Clinical Approach* addresses key issues in child neuropsychology but with a unique emphasis on evidence-informed clinical practice rather than research issues. Although research findings are presented, they are described with emphasis on what is relevant for the assessment, treatment and management of paediatric conditions. The authors focus on a number of areas. First, the text examines the natural history of childhood central nervous system (CNS) insult, highlighting studies where children have been followed over time to determine the impact of injury on ongoing development. Second, processes of normal and abnormal cerebral and cognitive development are outlined and the concepts of brain plasticity and the impact of early CNS insult discussed. Third, using a number of common childhood CNS disorders as examples, the authors develop a model that describes the complex interaction among biological, psychosocial and cognitive factors in the brain-injured child. Finally, principles of evidence-based assessment, diagnosis and intervention are discussed.

The text will be of use on advanced undergraduate courses in developmental neuropsychology, postgraduate clinical training programmes and for professionals working with children in clinical psychology, clinical neuropsychology and educational and rehabilitation contexts. The text is also an important reference for those working in paediatric research.

Vicki Anderson is a paediatric neuropsychologist at The Royal Children's Hospital and the Murdoch Children's Research Institute in Melbourne with 35 years of clinical experience.

Elisabeth Northam has been a clinical neuropsychologist at The Royal Children's Hospital, Melbourne, and a senior research fellow at the Murdoch Children's Research Institute for over 30 years.

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Routledge
Taylor & Francis Group
LONDON AND NEW YORK

Second edition published 2019
by Routledge
2 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN

and by Routledge
711 Third Avenue, New York, NY 10017

Routledge is an imprint of the Taylor & Francis Group, an informa business

First edition published by Psychology Press 2002

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British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging in Publication Data
Names: Anderson, Vicki, 1958– author. | Northam, Elisabeth, author. | Wrennall, Jacquie, author.
Title: Developmental neuropsychology / Vicki Anderson, Elisabeth Northam, Jacquie Wrennall.
Description: Second edition. | Milton Park, Abingdon, Oxon ; New York, NY : Routledge, 2018. | Revision of: Developmental neuropsychology / Vicki Anderson [and others].
Identifiers: LCCN 2017029285 (print) | LCCN 2017029585 (ebook) | ISBN 9780203799123 (Master e-book) | ISBN 9781848722033 (hardback) | ISBN 9781848722026 (paperback)
Subjects: LCSH: Pediatric neuropsychology. | Developmental disabilities. | Brain–Diseases.
Classification: LCC RJ486.5 (ebook) | LCC RJ486.5 .D48 2018 (print) | DDC 618.92/8–dc23
LC record available at https://lccn.loc.gov/2017029285

ISBN: 978-1-84872-203-3 (hbk)
ISBN: 978-1-84872-202-6 (pbk)
ISBN: 978-0-20379-912-3 (ebk)

Typeset in Times New Roman
by Out of House Publishing

Contents

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Acknowledgements

The second edition of *Developmental Neuropsychology: A Clinical Approach* endeavours to reflect advances in evidence-based practice in child neuropsychology. Our model of child neuropsychology relies on close links with the neurosciences, developmental principles and mental health, and the role of the child's family, all essential in the paediatric context. The influence of these perspectives is emphasised in our approach to understanding and treating children with developmental and acquired conditions impacting brain function. It was the vision of Dr Patricia Leaper in the 1980s that recognised the need for specialised child neuropsychology services within a tertiary child health environment, and her enlightened support facilitated the establishment and ongoing expansion and development of the discipline, both within our centre and in the wider community.

A large team of clinicians, researchers and students have contributed to our endeavours over the past 15 years, assessing and caring for children and families, conducting research programmes, contributing ideas and discussion, liaising with hospital and community workers and increasing the profile and recognition of child neuropsychology. We would like to note our appreciation for the ongoing contributions of The Royal Children's Hospital neuropsychology team and the research staff and students of the Australian Centre for Child Neuropsychology Studies and their collaborators. A special acknowledgement to Kate Anderson for her comprehensive review and editing of the text.

For the opportunity to develop and conduct research to help us better understand the needs of children with brain disorders, we recognise the generous support of the Melbourne Children's campus, which has supported the clinical work and the research we will describe in the coming pages.

Central to the development and formulation of our ideas and philosophy of child neuropsychology are the children and families who have contributed to our understanding of the impact of brain disease on child development. We appreciate their optimism and persistence and acknowledge the burden that such illness places on child and family.

Finally, we acknowledge the support, generosity and patience of our own families, who have 'endured' this project with us, and provided ongoing encouragement and distraction!

Part 1

Defining the neurodevelopmental dimension

1 Child neuropsychology
Theory and practice

Child neuropsychology, or paediatric neuropsychology, refers to the study of brain–behaviour relationships within the context of an immature but rapidly developing brain and the implementation of the knowledge gained into clinical practice. Child neuropsychology informs our understanding of typical child development by providing a framework within which to explore and map parallels between brain maturation and cognitive and socio-emotional development. For example, research has demonstrated that improvements in skills such as processing speed are closely associated with increases in myelination during infancy and childhood. Similarly, adolescent risk-taking behaviours have been linked to critical periods in frontal lobe development and connectivity. To date, the primary focus for the field of child neuropsychology has been the generation of a developmentally informed knowledge base that facilitates optimal understanding of the impact of early brain injury, insult or disruption on subsequent brain development and child function, guiding the design of evidence-based interventions to minimise disability.

Child neuropsychology takes its foundations from adult neuropsychological models, utilising pre-existing understandings of cerebral localisation and integrated brain systems to develop an appreciation of the functioning of the young brain. While adult models originally formed the basis of our knowledge of brain disorders in children, it quickly became evident that adult neuropsychology relates to a more 'static', tightly organised system, which is unable to easily accommodate the dynamic impact of brain pathology resulting from either brain insult or environmental disadvantage in early childhood (Anderson, Spencer-Smith, Leventer, Coleman et al., 2009; Anderson, Spencer-Smith, & Woods, 2011; Dennis, 1989; Dennis, Spiegler, Jaranek, Bigler, & Fletcher, 2013; Dennis, Spiegler, Simic, Sinopoli et al., 2014).

In an attempt to adapt adult-based models to be relevant for implementation with infants, children and adolescents, child neuropsychologists initially drew from a range of associated fields to establish a knowledge base from which to understand the unique consequences of early brain disruption. Developmental, cognitive and social psychology specialities and the neurosciences have been crucial elements for mapping the expected changes

that occur within the brain throughout infancy and childhood, until the brain reaches relative stability and maturity in early adulthood. Of specific relevance are research findings that support parallels between spurts within the brain and increments in cognitive and socio-emotional abilities (Anderson, Northam, Hendy, & Wrennall, 2001; Beauchamp & Anderson, 2010; Gogtay, Giedd, Lusk, Hayashi et al., 2004; Hudspeth & Pribram, 1990; 1992; Luciana, 2003). While not surprising, these convergent findings support the close relationship between brain and behaviour. Knowledge of typical development is especially important in child neuropsychology, as it provides a template for measuring deviations relating to early damage and subsequent interruption to normal growth processes across a range of functional domains – neurologic, cognitive, socio-emotional – not just at the time of insult, but also in the longer term. The likelihood that ongoing development may be influenced by an early cerebral insult or disruption in childhood is not novel or unreasonable. The challenge for the child neuropsychologist is to grapple with the interactions between biologic, cognitive, social and developmental factors to reach an understanding of how these factors affect the child and lead to observed outcomes.

This chapter aims to explore the domain of child neuropsychology, taking a developmental, biopsychosocial approach to describe a field where comprehensive assessment and diagnosis of brain dysfunction are central to clinical practice. Clinical experience tells us that there is no definitive formulae that can predict outcome from early brain insult: some children with severe injuries do well, while others with comparatively minor insults experience lifetime disability. It is our premise that, to fully understand the long-term consequences of brain dysfunction during childhood, it is essential to address the 'totality' of the child – the medical, cognitive and psychosocial experiences that interact to influence recovery and development. Further, the importance of viewing children as more than simply 'little adults' will be canvassed, with emphasis on the dynamic path of maturation and development and the potential for disruption to this process.

Child neuropsychology: historical perspectives

Plasticity, vulnerability and critical periods

The earliest theoretical contributions to child neuropsychology can be traced to descriptions of plasticity and recovery of function following childhood brain damage. Researchers such as Kennard (1936; 1940) and Teuber (1974) are well known for their seminal works describing relative sparing of function following early brain insult, with the Kennard Principle, interpreted by Teuber, suggesting that: *if you're going to have brain damage, have it early*. These early theorists documented relatively good recovery following early brain insult. For example, studies following recovery trajectories for aphasia note that, where injury severity is equivalent, there is greater improvement in

children than in adults (Alajouanine & Lhermitte, 1965; Lenneberg, 1967). Such results are interpreted according to a theory of recovery of function where the young child's brain is seen to be less differentiated than that of the mature adult and more capable of transferring functions from damaged cerebral tissue to healthy tissue. While there continues to be considerable debate regarding the conclusions drawn from this early research, the resultant theories represent an important contribution to the field of child neuropsychology, not least because they acknowledge the unique processes that may be acting in the developing brain following cerebral insult.

Notions of critical periods of development, while not constituting specific neuropsychological theory, have also added breadth to our understanding of the mechanisms at play following early brain insult. Mogford and Bishop (1993) define a critical period as "the time window during which external influences have a significant effect" (p. 252). Consistent with this view, others have argued that early brain insult will have different consequences at different times throughout development and, in some instances, may be more detrimental than later injury, because some aspects of cognitive development are critically dependent on the integrity of particular cerebral structures at certain stages of development (Dennis, Spiegler et al., 2013; Dennis et al., 2014). Thus, if a cerebral region is damaged or dysfunctional at a critical stage of cognitive development, it may be that the cognitive skill subsumed by that region is irreversibly impaired. Further, research suggests that, while there may be some functional plasticity early in life, the time frame may be quite restricted, and not necessarily related to age in a linear manner. For example, children with prenatal lesions, or those sustaining insults during the first few years of life, appear to exhibit particularly severe impairment (Anderson, Spencer-Smith et al., 2009; Anderson, Spencer-Smith, & Wood, 2011; Crowe, Catroppa, Babl, & Anderson, 2012; Dennis, Spiegler et al., 2013).

A perusal of the field of child neuropsychology since it has emerged as a distinct entity yields only a handful of attempts to formulate brain–behaviour paradigms of a truly developmental nature. To date, no theoretical framework has succeeded in integrating biological, psychological and environmental dimensions in a clinically meaningful way. However, two seminal models from the late 1980s, Byron Rourke's *non-verbal learning disability* (1989) and Maureen Dennis' *multidimensional age at insult* approach (1989) have both had, and continue to have, a major influence on the field. In fact, it may be argued that there has been little theoretical progress outside these two models over several decades.

Non-verbal learning disability (NVLD)

In the 1980s, Rourke (1988; 1989; 1995) described his clinically driven notion of NVLD to account for a consistent pattern of neurobehavioural deficits observed in children with a history of early, generalised cerebral dysfunction resulting from brain insult occurring during the perinatal period or in infancy.

The hallmark characteristics of NVLD include: (i) bilateral tactile–perceptual deficits, more marked on the left side of the body; (ii) impaired visual recognition and discrimination and visuospatial organisational deficiencies; (iii) bilateral psychomotor coordination problems, more marked on the left side of the body; and (iv) difficulties managing novel information. Children with NVLD may also demonstrate a range of intact skills, primarily within the auditory/verbal domain. Rourke lists these as: (i) simple motor skills; (ii) auditory perception; (iii) rote learning; (iv) selective and sustained attention for auditory–verbal information; (v) basic expressive and receptive language; and (vi) word reading and spelling.

Rourke's model is particularly noteworthy from a developmental perspective as it incorporates knowledge of the changing brain, the *neuro* dimension, with the development of a specific cognitive profile, the *psych* dimension, in a truly brain–behaviour model. Rourke (1988) continued to build on this model for almost 20 years, providing further descriptions of social and cognitive characteristics of NVLD and their relevance across disorders, arguing that the timing of the insult is of primary importance. NVLD theory explains the spectrum of children's neurobehavioural abilities and disabilities, as well as the development trajectories of the three principle axes of relevance in brain–behaviour relationships: left–right; up–down; and anterior–posterior. Further elements for incorporation in such models might include explanations of interactions among biologic, cognitive and psychosocial factors from a dynamic, developmental framework.

One of the greatest contributions of the NVLD model is linking cognitive characteristics to an underlying neurologic explanation: the 'white matter hypothesis'. Rourke's model is based on the assumption that normal development of white matter is essential for intact child development. NVLD occurs when there is disruption to white matter development during critical stages of early childhood. In support of the NVLD hypothesis, there is evidence of white matter pathology in many of the disorder groups that present with symptoms of NVLD, including traumatic brain injury, hydrocephalus, prematurity and cranial irradiation (Rourke, 1989). However, early brain insult does not always lead to symptoms consistent with NVLD, with some early insults, such as cerebral infection, presenting with language problems or executive dysfunction, but intact non-verbal skills (e.g., Anderson, Bond, Catroppa, Grimwood et al., 1997; Dennis, Simic, Taylor, Bigler et al., 2012; Dennis, Wilkinson, Koski, & Humphreys, 1995; Ewing-Cobbs & Barnes, 2002; Ewing-Cobbs, Prasad, Landry, Kramer, & DeLeon, 2004) or global cognitive impairments (e.g., Anderson, Spencer-Smith et al., 2009).

Developmental stage at insult and cognitive outcome

The second influential theory for the child neuropsychology field has been proposed by Maureen Dennis (1989), based on her extensive research into child brain disorders, including traumatic brain injury and spina bifida.

Dennis' 'heuristic' does not propose a specific neurological mechanism for her theory, although other researchers have offered possible biological explanations. Rather, it focuses primarily on age/developmental stage at time of insult and progression in cognitive skills with time since insult. Her heuristic describes the impact of brain damage on language development. She divides skill development into several levels: (i) *emerging*, where an ability is in the early stages of acquisition, but not yet functional; (ii) *developing*, where a capacity is partially acquired but not fully functional; and (iii) *established*, where abilities are fully matured.

Dennis integrates these developmental skill levels with three crucial age-related variables – age at time of lesion, age at testing and time since insult. Age at lesion, she argues, determines the nature of the cognitive dysfunction. For example, early lesions disrupt the onset and rate of language development, while later lesions are associated with a specific symptom pattern, such as high-level language dysfunction (e.g., impaired pragmatic skills). Time since injury refers to differing performance patterns identified at different stages of recovery, with increases in some cognitive skills, but failure to develop others. Age at testing is also important, as even healthy children vary in their ability to perform cognitive tasks at different developmental stages. In this context, Dennis highlights that, while early brain insults appear to cause relatively few problems early post-injury, with ongoing development, children may 'grow into' deficits as they fail to acquire age-expected skills. Dennis' model does not propose a specific neurological mechanism, but rather implies that the full impact of childhood brain injury is not clear until brain maturation is achieved in early adulthood. There is a range of research that supports the general thrust of Dennis' model. Many studies note the greater impact of younger age at insult (e.g., Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005a; 2009; Crowe et al., 2012), and others describe a pattern of increasing functional impairment with time since injury (e.g., Ewing-Cobbs, Fletcher, Levin, Francis et al., 1997; Ewing-Cobbs, Prasad, Landry et al., 2004).

Current multi-dimensional theoretical approaches

Advances in the neurosciences, particularly neuroimaging and neurogenetics, have led to theories that propose a complex relationship between risk factors, which interact and vary over time to determine functional outcomes after early brain insult.

The cognitive reserve model (Dennis, Yeates, Taylor, & Fletcher, 2007)

In an extension of their earlier work (Dennis, 1989; Fletcher & Taylor, 1984; Taylor & Alden, 1997), these authors postulate a model framed around the concept of individual differences in a child's 'reserve capacity', both *brain reserve capacity* (BRC) and *cognitive reserve capacity* (CRC) (Figure 1.1). BRC

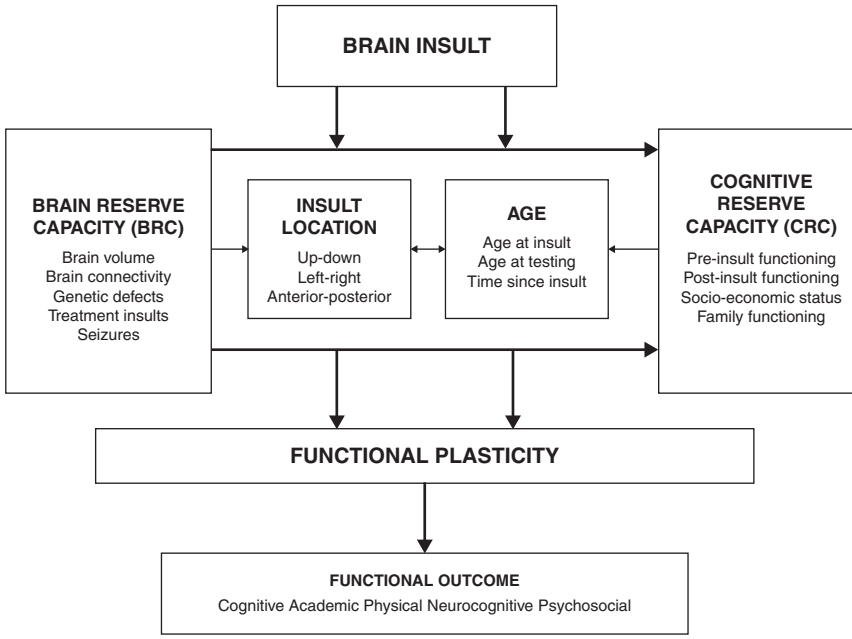


Figure 1.1 The cognitive reserve model
Source: Modified from Dennis et al. (2007)

is measured directly by quantifying variables such as insult severity, brain volume or structural connectivity, as well as neurological sequelae such as epilepsy. When BRC is depleted below threshold levels, functional deficits emerge, which might include physical, cognitive, and socio-emotional symptoms. CRC refers to factors both intrinsic (pre-injury cognition and behaviour and post-injury cognition) and extrinsic to the child (socio-economic status [SES] and family functioning), which impede or facilitate various functional outcomes.

In addition to the mediating role of reserve capacity, moderating factors for functional outcome are proposed, further explaining why a specific brain insult will not result in the same outcome for all individuals. *Age and time variables*, including age at the time of brain insult, time elapsed since brain insult and the child's age at evaluation, are relevant to understanding outcomes following early brain insult and highlight that early brain insult diminishes reserve to a greater extent than later insult, restricting the capacity to support subsequent recovery and development. *Lesion location and functional network involvement* have been shown to be important for determining functional outcome in a range of brain conditions, with varying degrees of functional plasticity and outcome associated with involvement of different brain structures and networks. A key concept of the model is that the influence of these moderating factors is not constant over time. This has been

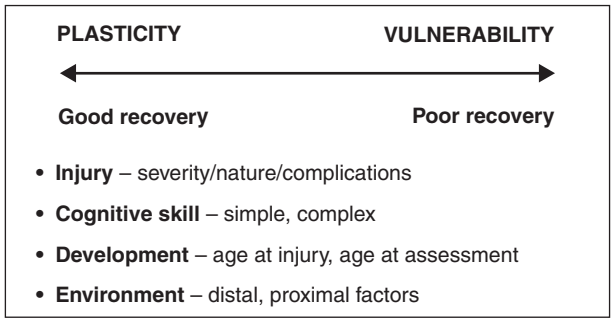


Figure 1.2 Plasticity versus vulnerability: a recovery continuum model

demonstrated in children with traumatic brain injury; the greater the time elapsed since injury, the less the effect of brain insult characteristics and the greater the effect of environmental variables on cognitive functioning.

Recovery continuum model (Anderson, Spencer-Smith, & Wood, 2011)

Using similar concepts, Anderson and colleagues argue that neither early plasticity nor early vulnerability theories in isolation are sufficient to explain the myriad of outcomes that occur following early brain insult. Rather, they propose that recovery is best understood by employing a 'continuum approach', whereby a number of potential risk and resilience factors interact to determine long-term outcome (Figure 1.2). As with Dennis and colleagues (2007), they suggest that this model necessarily incorporates factors already established as important for outcome post-child insult, including: (i) nature (global, diffuse) and severity (mild/severe, presence of complications) of insult; (ii) developmental stage of child (infant, child, adolescent) and timing of assessment; (iii) pre-injury child characteristics; and (iv) environmental context (distal and proximal factors) and access to interventions and social supports. They argue further that the impact of these factors may not be linear. For example, larger lesions do not always result in poorer outcomes, particularly if they result in hemispheric transfer. Similarly, earlier injury is not always more toxic than later injury, with critical developmental periods needing to be considered. These factors are also likely to interact, whether additively or synergistically, with research demonstrating that younger age at injury and more severe insult leading to very poor recovery, while severe insult and environmental disadvantage also incur higher risk of poor outcome than either factor alone.

Dimensions of child neuropsychology: a biopsychosocial model

Research has established the unique resilience and vulnerability of early childhood for healthy development. Threats to healthy development are

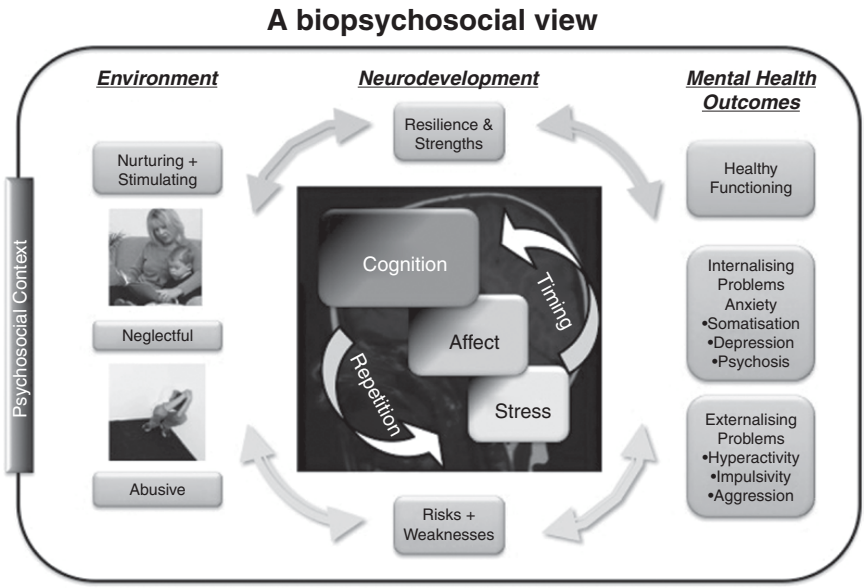


Figure 1.3 A biopsychosocial framework for understanding child development (courtesy of J. Delio)

Source: J. Delio, personal communication

numerous and span multiple domains from health and environment to cognitive development, mental health and quality of life. To date, these threats have been explored largely within disciplines (e.g., neuroscience, psychology or sociology). With recent advances in neuroimaging and genetics, we now have tools that can more comprehensively explore the interacting influences of biology and environment. The challenge is to integrate this knowledge with evidence from the related fields of child development, education and mental health, using frameworks such as that illustrated in Figure 1.3. In order to achieve this, we need to build robust cross-discipline collaborations, which will lead to combined knowledge, which can then be translated into 'best' practice in the field to enhance optimal outcomes for individual children and for the benefit of the community.

Brain: the 'bio' dimension

The brain can be identified quite early in gestation, with rapid development ongoing through infancy and childhood. In the prenatal period, development is largely concerned with structural formation, establishing the basic 'hardware' of the brain. Interruptions to brain development during this period have been shown to result primarily in structural abnormalities (e.g., dysplasia, neural tube defects, agenesis of the corpus callosum). In contrast, postnatal

development is largely directed towards elaboration of the brain, establishing the connectivity vital for the system to function effectively. This process of elaboration continues into early adolescence, with the primary processes including dendritisation, synaptogenesis and myelination. It is generally thought that development occurs in a hierarchical manner, with anterior regions the last to reach maturity, in late puberty. While some controversy remains, there is support for a step-wise model of brain development, rather than a gradual or linear progression, with convergent evidence from both animal and human research that growth spurts occur in early infancy, again around 7–10 years of age, with a final spurt during early adolescence (Gogtay et al., 2004; Paus, 2005; Thompson, Giedd, Woods, MacDonald et al., 2000; Toga, Thompson, & Sowell, 2006). A number of influences can impact on these developmental processes, including direct brain injury or insult, infection, or a variety of environmental factors such as malnutrition, trauma (e.g., neglect, abuse) or environmental toxins (e.g., lead, radiation).

Early disruption to central nervous system (CNS) development may have irreversible consequences. As is true for adults, the nature and severity of cerebral insult are of primary importance, with more severe and widespread disruption leading to poorest outcomes. Paediatric research consistently supports the dose–response relationships documented in adult populations, with more severe cerebral pathology generally leading to greater physical and cognitive impairment. However, in contrast to the more localised cerebral pathologies of adulthood (e.g., stroke, tumour), childhood brain disorders are more commonly diffuse, impacting on the brain as a whole (e.g., traumatic brain injury, hydrocephalus, cerebral infection, metabolic disorder). In contrast, focal disorders, such as tumour and stroke, are relatively rare. As a result, specific impairments, such as aphasias or modality-specific memory disorders, are less common in children, while generalised disturbances of information processing (attention, memory, psychomotor skills), executive function and social cognition are more frequently observed (Dennis et al., 2012; Eslinger, Biddle, Pennington, & Page, 1999; Ewing-Cobbs, Prasad, Landry et al., 2004; Muscara, Catroppa, & Anderson et al., 2008a; 2008b).

Discrepancies between adult and child insults are also found for recovery trajectories. Acute recovery appears to be similar irrespective of age; however, long-term recovery patterns differ in favour of the more mature brain (Anderson & Moore, 1995; Ewing-Cobbs et al., 1997), and prognosis is more difficult to predict following childhood injury. Plasticity theorists have argued that damage to the immature brain yields less significant disability than equivalent insults in adults. However, recent longitudinal research indicates that such interpretations may be overly optimistic, and that children with early insults may 'grow into' their difficulties as demands increase through late childhood into adolescence. Certainly, current conceptualisations of neural recovery suggest little advantage for the immature brain (Anderson et al., 2011; Anderson, Catroppa et al., 2009; Dennis, Spiegler et al., 2013; 2014; Duchowny, Jayakar, Harvey, Altman et al., 1996; Kolb & Gibb, 2001).

In particular, the traditional notion of transfer of function, where cognitive functions subsumed by damaged brain tissue are said to be transferred to healthy tissue with minimal functional implications, is now under debate. At best, the mechanisms associated with such transfer of function are likely to be far more complex than initially thought, varying with respect to both timing (i.e., pre-, post-natal) and nature (i.e., focal, diffuse) of insult (Anderson, Harvey, Saling, Anderson et al., 2006; Dennis, Spiegler et al., 2013; Duchowny et al., 1996). Recent research, employing structural and functional imaging techniques, indicates that prenatal brain injury may not result in functional transfer, but that skills may be maintained ineffectually in damaged tissue, leading to developmental delays (Anderson, Harvey et al., 2006; Anderson, Spencer-Smith et al., 2009; Leventer, Phelan, Coleman, Kean et al., 1999). Even post-natally, where transfer or recruitment of healthy brain regions has been shown to occur, this may result in 'crowding' of skills and generalised depression of function (Mogford & Bishop, 1993).

Within the child context, a number of important interactions or synergies have been described. Following early brain insult, age at insult (as a proxy for developmental stage) and nature of insult appear to have a complex relationship, with earlier insults and more diffuse or complicated insults leading to slow recovery and very poor outcomes. For example, in children sustaining severe traumatic brain injury, serial brain scans have detected increasing cerebral atrophy with time (e.g., Anderson, Northam et al., 2001), while behavioural studies have reported widening gaps in development between injured children and age-matched peers (Kolb & Gibb, 2001; Taylor & Alden, 1997). Children contracting meningitis or suffering from febrile convulsions have been noted to develop hippocampal sclerosis leading to epilepsy (Gonzalez, Anderson, Wood, Mitchell, & Harvey, 2007). Similarly, studies of children treated with cranial irradiation for cerebral tumour or leukaemia document development of delayed cerebral pathology, specifically cerebral calcifications and evolving white matter pathology (Paako, Vainionpaa, Lanning, Laitnen et al., 1992), with parallel disruption of attention and information processing skills (Catroppa, Anderson, & Stargatt, 1999). Such findings suggest that recovery following early brain insult is not static, but is likely to reflect ongoing disruption to maturation of functional neural networks and to have a major negative impact on long-term outcome.

Early neurologic and neuropsychologic theories of child neurodevelopment reflect electrophysiologic techniques available at the time. Electroencephalograms (EEGs) and event-related potentials (ERPs) have also been employed to measure temporal aspects of cerebral function via electrical activity. EEGs are traditionally used in the diagnosis of epileptic disorders and sleep disturbance, while ERPs focus on dysfunction within sensory or information processing systems. Each of these measures provides useful temporal information both clinically and for the endeavour of correlating more accurately the brain–behaviour relationships seen following early brain insult. Further, such methods have been found to be helpful in mapping age-related

changes through childhood. Thatcher's (1992; 1997) EEG coherence studies have suggested cyclical growth spurts within the CNS, which begin at about 12–18 months of age, last for about 2–4 years, and involve an expansion from the posterior to anterior cerebral regions, as well as a lateralised sequence.

More recently, advances in structural and functional neuroimaging have provided invaluable insights into developmental processes within the brain. Sophisticated image analysis has demonstrated both the rate and localisation of developmental neural processes, such as myelination and differentiation, through childhood (Giedd, Blumenthal, Jeffries, Castellanos et al., 1999; Klinberg, Vaidya, Gabrieli, Moseley, & Hedehus, 1999; Sowell, Trauner, Gamst, & Jernigan, 2002). Functional imaging methods, such as cerebral blood flow studies, single photon emission computed tomography (SPECT) or positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), enable researchers to map cerebral activation in quite young children, thus directly describing the neural correlates of specific behaviours. Possible functional reorganisation can be investigated using non-invasive measures, such as fMRI or tractography, as opposed to the more invasive procedures used in the past, such as sodium amytal ablation and cortical mapping.

Environment: the 'social' dimension

In addition to a well-functioning, normally developing brain, an enriching early environment is critically important for optimal child development. The child exists within a tight social system, the family unit, with that system responsible for the quality of the environment, access to resources and provision of an appropriate context for learning. It is well established that the development of a child's cognitive and socio-emotional skills is dependent, to a large extent, on the quality of the home environment and the role models provided by parents (Root, Hastings, & Maxwell, 2012). In infancy, social interactions are supported and structured within the family unit. The child acquires language and cognitive skills and social behaviours and rules within this context. As he/she begins to move into the outside world, to preschool and further, there is a need for the child to develop independence and a capacity to function in extrafamilial contexts. With the advent of adolescence, independence is paramount, and the need to develop an identity, via peer groups and broader social contexts, becomes vitally important. Most children pass through childhood without crisis; however, where some disruption or impairment is present, each transition may be more problematic. Theorists stress the importance of the biological characteristics of the individual, the immediate home environment and the broader social context as playing crucial roles in child development. The child adapts to the features and demands of the environment, which, in turn, are modified by the characteristics of the child. This results in a dynamic interplay in which both the child and the environment influence each other. Adaptive and positive interactions promote healthy, social development. Alternatively, when problems exist (e.g., family

trauma), they may lead to a disruption in both the child and the environment. The importance of this intuitive relationship is firmly established in clinical practice, where clinicians must integrate information regarding a child's early environment and learning opportunities with medical history in order to generate their case formulations. In contrast, child neuropsychology research has explored the role of environmental factors in development to only a limited extent until recently. The primary emphasis has been on 'distal' environmental factors (e.g., SES, parent education and income). The role of 'proximal' environment factors, such as parent mental health, family function and exposure to trauma (e.g., abuse, neglect, illness), on brain, cognitive and socio-emotional development has received relatively less attention until recently.

Environment, neglect, trauma and abuse

The cognitive and socio-emotional consequences of child neglect and abuse are well established and include reduced intellectual ability, attention, working memory and self-regulatory deficits, lower levels of academic achievement and self-confidence, as well as mental health problems (Rutter, Moffitt, & Caspi, 2006). There is also evidence for changes in structure and function in the developing brain, which are thought to be underpinned by a range of physiological and neurochemical processes. Studies have demonstrated reduced brain volume, impacting both grey and white matter, as well as deficits in structural connectivity and atypical brain activation in survivors of early trauma. Specific brain regions most susceptible to the impact of neglect and abuse include fronto-limbic networks, impacting the medial prefrontal cortex, orbital prefrontal cortex, hippocampus, amygdala and corpus callosum (Teicher, Anderson, Polcari, Anderson et al., 2003; Teicher, Samson, Polcari, & McGreenery, 2006).

Environment, chronic illness and brain insult

Research addressing the role of the environment in outcomes for children with chronic illness and disability provides convincing evidence of the impact of disability, and consequent atypical experience, on parental, family and child adjustment and quality of life (Kassam-Adams, Fleisher, & Winston, 2009; Kazak, Kassam-Adams, Schneider, Zelikovsky et al., 2006; Muscara, McCarthy, Woolf, Hearps et al., 2015). More recently, the impact of environment, and particularly more proximal influences, on outcomes following early-acquired brain insult has also been explored. Such investigations consistently identify a combination of environmental factors – low SES, presence of multiple family stresses, previous psychological disturbance and low levels of maternal education – as predictive of poorer long-term outcome. Further, research has shown that children from previously dysfunctional or low SES families show more problems, and where parents are depressed or distressed, the cognitive and social development of the child is

reported to be poorer (Muscara et al., 2015; Woolf, Anderson, McCarthy, & Muscara, 2015). Conversely, better outcomes are found where there is family cohesion and supportive social networks (Kazak et al., 2006). These findings are consistent with the 'double-hazard hypothesis' (Breslau, 1990; Taylor & Alden, 1997), which postulates that brain insults may have greater consequences in children from socially disadvantaged backgrounds.

In the early-acquired brain insult literature, environmental risks have been most comprehensively examined in childhood stroke and traumatic brain injury, with important negative influences identified for family function and parent mental health, as well as child outcome. These factors have also been linked to increasing child mental health and social problems as time post-insult increases (Anderson, Gomes, Greenham, Hearps et al., 2014). The relationship between these proximal environmental influences and child outcomes is likely to be bidirectional (Gerring, Slomine, Vasa, Grados et al., 2002). While intact parent function is important for optimal child outcomes, the physical, cognitive and socio-emotional challenges of the child recovering from brain insult will also have consequences at the family level. Further, and of particular importance, the identification of key environment predictors for outcome after early child insult signifies a potential 'modifiable risk factor', whereby improving parent and family function may have follow-on benefits for child outcome. In fact, a handful of recent studies have explored this possibility, with pleasing outcomes, suggesting that a focus on parenting and parent mental health interventions can result in improved child outcomes, particularly in the domains of social and behavioural function (Wade, 2010; Wade, Taylor, Yeates, Drotar et al., 2006b; Woods, Catroppa, Godfrey, & Anderson, 2014; Woods, Catroppa, Godfrey, Giallo et al., 2014a).

Child cognitive and socio-emotional function: the 'psych' dimension

Cognitive development

Cognitive development is rapid during childhood. Early conceptual models of cognitive development (e.g., Piaget, 1963) have emphasised a hierarchical or stage-like process, with children needing to pass through a pre-set series of developmental stages, not unlike the pre-set genetic code underpinning cerebral development (Rourke, 1988). While individual variation occurs with respect to the timing of these stages, the need to pass through each stage in order is argued to be invariant (Piaget, 1963).

An analysis of the content of these cognitive stages suggests that quality and level of thinking are the key characteristics to change and progress. For example, classical Piagetian models, as well as those of more contemporary developmental psychologists, describe a number of stages of development, each characterised by increasing symbolic thought and the ability to deal with increasingly complex and abstract information (Flavell, 1999). The first of these stages (from birth to two years of age) is usually defined

primarily in terms of simple motor and sensory activities with little evidence of any abstract thought, with a gradual emergence of object permanence that has been argued to provide the earliest indicator of working memory. Early attention skills, such as joint attention, also come online during this period and are critical for socio-emotional development, particularly attachment (Rueda, Posner, & Rothbart, 2005). The development of symbolic thought at around two years of age is evidenced by the emergence of early language, communication and mental imagery, with rudimentary theory of mind and empathy becoming apparent later during this developmental stage (Zelaso, Craik, & Booth, 2004). However, higher-level skills remain limited, and the child is restricted to 'uni-dimensional' approaches to problem-solving and egocentric responses. The transition to rudimentary levels of 'operational' thought at approximately seven years of age is roughly consistent with school entry in most cultures, and heralds increased reasoning and problem-solving ability, as well as the capacity to integrate information across multiple dimensions and to perform mental transformations. This stage heralds the emergence of executive skills, including both 'cold' (reasoning, problem-solving, organisation and mental flexibility) and 'hot' (social cognition) abilities. These executive functions, which represent more mature cognitive processes, are said to become fully established during the formal operational stage, which is thought to progress through adolescence.

While there is some controversy regarding the exact ages at which these transitions occur, most agree that children undergo extensive cognitive growth from birth to adulthood, with maturation occurring through a series of stages, not unlike that described for brain development. Indeed, the timing of growth spurts in myelination, and metabolic and electrical activity, are roughly consistent with cognitive progressions (Flavell, 1999; Luciana, 2003; Paus, 2005; Stiles, Moses, Passarotti, Dick, & Buxton, 2003).

Traditionally, cognitive theories focus on particular skills or modules. In contrast, cognitive-developmental theories are not specific to isolated cognitive domains, but argue for a generalised progression of cognitive abilities through childhood (Flavell, 1999), suggesting a 'domain-general' developmental model, more in keeping with the characteristics of the functional neural networks underpinning such skills. In support of this position, recent evidence suggests that, as well as individual variations in the timing of transitions between developmental stages, there may also be different rates and progressions within specific cognitive domains, and it is likely that the development of individual cognitive modalities is not an independent process. Rather, it appears that domain-specific development occurs in cooperation with similar maturation occurring within other brain systems. The developing memory system provides an illustration of this concept: children's capacity to store and retain information increases progressively through childhood, with this improved 'memory' capacity likely explained by more efficient information processing and an increasing ability to develop and implement strategies for recall (e.g., rehearsal, chunking). This suggests that a multidimensional

relationship between memory, processing speed and executive functions is likely to be responsible for age-related progress. Similarly for executive functions, research has shown that developmental increases in speed of information processing may enhance executive skills (Anderson, 2002; Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Smidts, Jacobs, & Anderson, 2004). Once again, this pattern of hierarchical functioning and interaction across skill areas is consistent with our knowledge of maturational processes within the CNS.

What is the relevance of such developmental theories to neuropsychology? First and foremost, such theories require that the presence of neuropsychological impairment in children is measured against age-appropriate expectations. Age-standardised assessment tools provide a valid and reliable benchmark for such comparisons. Using these tools, the child neuropsychologist is able to identify significant deviations from expected patterns of development and formulate a diagnosis and treatment plan based on this information. A further consideration for the child neuropsychologist is the use of assessment tools derived from adult models for the evaluation of developing cognitive skills. Fletcher and Taylor (1984) note the unfounded assumption that tests designed for adults measure the same skills in children. To fully appreciate this statement, it is useful to consider the multidimensional nature of most neuropsychological measures, where test performances are dependent on the relative contributions of various skill domains. Children may achieve similar endpoint scores by utilising a range of cognitive skills, or alternatively, they may perform poorly due to a range of cognitive deficits. For example, a commonly administered clinical test, such as the Rey Complex Figure (Rey, 1941), is frequently employed in adult neuropsychology as a measure of higher-order cognitive skills, including organisation and planning. However, such an interpretation of test performance is problematic in children, where poor performance may equally reflect impairment of lower-order skills such as visual perception, motor control and visuo-motor coordination.

A corollary of this 'development' is a need to acknowledge the limitations of evaluating immature skills when seeking evidence of deficits. We know from cognitive-developmental theory that while executive skills develop from infancy, they may not be comprehensively measured until late childhood. Thus, the identification of executive dysfunction cannot reliably occur until a stage at which these skills are present and accessible in the child. For example, when assessing a five-year-old child with a frontal lobe tumour, executive dysfunction may not be elicited in the child's neuropsychological profile because normal test expectations for young children do not necessitate mature executive abilities. By age 12, however, the same child may demonstrate hallmark symptoms of executive dysfunction, such as poor planning, mental inflexibility, impulsivity and reduced empathy, as the developmental expectations for the child extend to include functional independence and a capacity to plan, problem-solve and think flexibly.

In early work in the field, Banich, Levine, Kim, and Huttenlocher (1990) illustrate this principle by comparing a sample of children with congenital cerebral injuries to age-matched controls using the Vocabulary and Block Design subtests of the Wechsler Intelligence Scale for Children. When children were aged six years, there were no differences across the groups on these measures, but as the children progressed through childhood, significant discrepancies emerged. By late childhood, children who had sustained congenital cerebral injuries were failing to exhibit expected developmental progress, with this pattern of impairment continuing into adolescence. In terms of test results, the child may appear to 'grow into' his/her cognitive deficits as the brain matures. This picture of progressively emerging deficits does not necessarily reflect deterioration in cognitive skills or an underlying progressive neurologic condition. Rather, it may be interpreted as a feature of early cerebral insult, suggestive of inefficient skill acquisition and associated slowing of cognitive development. In our lab, we have reported a similar pattern of slowed development in a follow-up study of children with hydrocephalus. When seen between one and two years of age, these children recorded high average abilities (group mean = 60th centile). By four to five years, performance had reduced to the 40th centile, and by 11 years, group mean results were at the 25th centile (Figure 1.4), in keeping with a picture of gradually global cognitive deficits emerging as new skills failed to come online through childhood (Jacobs, Northam, & Anderson, 2001).

Socio-emotional development

Children with an early brain insult may have problems acquiring social and emotional skills and knowledge and comprehending social rules due

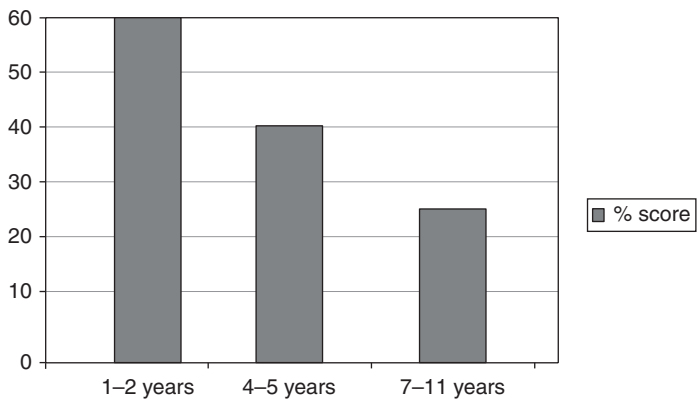


Figure 1.4 Reducing IQ percentiles with age for children with hydrocephalus
Source: Jacobs et al. (2001)

to intellectual impairments, reduced self-regulation, functional disability, social stigma and limited interaction with the environment (Beauchamp & Anderson, 2010). As the child grows, and less support is available, child behaviours and social interactions may become more problematic, eventually resulting in mental health problems and social withdrawal. On reaching adolescence, the young person often has a greater awareness of the severity of their residual deficits and their functional implications. Physical disabilities, such as motor or speech impairments, are often present, and may restrict the young person's capacity to participate in a full range of normal activities and emphasise the cognitive limitations that may be causing extra pressure in coping with academic and social expectations. Such a developmental pattern of increasing social problems has been identified in association with many neurodevelopmental and acquired brain disorders, such as NVLD (Rourke, 1989) and traumatic brain injury (Yeates, Bigler, Dennis, Gerhardt et al., 2007).

With increased emphasis on child well-being and quality of life, recent research has described high levels of socio-emotional impairment in children following early insult. Left untreated or unacknowledged, up to 50% of survivors of early brain insult will experience significant mental health problems, with attention deficit hyperactivity disorder, anxiety, depression and post-traumatic stress symptoms being among the most common diagnoses (Max, Levin, Landis, Schachar et al., 2005a; Max, Schachar, Levin, Ewing-Cobbs et al., 2005b). There is also some suggestion that socio-emotional problems may increase with time since insult (Yeates et al., 2007), suggesting a multidimensional basis for these problems, including both the direct effects of brain injury and secondary psychosocial factors. These mechanisms may interact to produce the increased socio-emotional disturbance that emerges over time in early brain-injured individuals.

NEUROLOGIC CORRELATES

The notion that socio-emotional changes post-insult are specifically related to brain dysfunction was initially addressed by Rutter and colleagues (Rutter, Chadwick, & Shaffer, 1983). They found that psychiatric disorders occurred five times more frequently in brain-damaged children than in children with physical disorders not involving the CNS, with presence of epilepsy an additional risk factor. These findings have been supported in a number of subsequent studies using larger samples and including comparison groups of children with chronic physical illness (Anderson et al., 2014; Max, Levin et al., 2005a; Max, Schachar et al., 2005b), suggesting a direct contribution of brain dysfunction to behaviour and psychosocial functioning. Depending on the nature and localisation of cerebral pathology, children may present as impulsive, hyperactive, aggressive, lacking in insight, depressed and anxious, and may demonstrate reduced empathy, theory of mind and moral reasoning skills (Beauchamp & Anderson, 2010; Dennis, Simic et al., 2012).

Recent advances in the social neurosciences have facilitated better understanding of the biological bases of these behaviours and social skills. In particular, the seminal work of Adolphs (2003a; 2009; Burnett, Sebastian, Kadosh, & Blakemore, 2011; Choudry & Blakemore, 2006) in documenting the 'social brain network' has provided a blueprint (albeit based primarily on adult data) describing the primary brain regions and functional neural network involved in socio-emotional processing. The social brain network includes the superior temporal sulcus (STS), fusiform gyrus (FG), temporal pole (TP), medial prefrontal cortex (mPFC), frontal pole (FP), orbitofrontal cortex (OFC), amygdala, insula, temporoparietal junction (TPG) and cingulate. Socio-affective skills subsumed by this network are vulnerable to disruption from early brain injury and are shown to elevate risk for later maladaptive behaviour (Beauchamp & Anderson, 2010; Robinson, Fountain-Zaragoza, Dennis, Taylor et al., 2014; Ryan, Anderson, Godfrey, Beauchamp et al., 2014; Ryan, Catroppa, Cooper, Beare et al., 2015; Ryan, Hughes, Godfrey, Rosema et al., 2015b; Yeates et al., 2007).

PSYCHOSOCIAL CORRELATES

There is little doubt that social factors, both internal (e.g., child temperament, disability) and external (e.g., school, home), influence the behavioural development of children with brain disorders. Following brain insult, children must deal with a range of difficulties related to acceptance of, and adjustment to, illness and possible disability, as well as specific behavioural deficits directly associated with the nature and severity of brain insult, and psychological trauma related to the precipitating event. As is the case with children with medical and physical disabilities not involving the brain, they will experience anxiety and uncertainty relating to their situation. They may miss substantial time at school, leading to reduced experience and confidence both socially and cognitively. Residual impairments (e.g., motor and speech impairments) may restrict their ability to interact normally with peers and lead to social stigma. For the family, similar changes may occur: anxiety associated with illness/injury, separation within the family due to hospitalisation and difficulties coping with the new and different demands of the child. If the condition is life threatening, a plethora of other 'trauma'-related factors come into play.

Recent research has also found that the relative importance of risk factors may change with time since onset of the disorder. Recent results from a number of prospective, longitudinal studies of children with an early brain insult show that while early child outcome is best predicted by insult severity, long-term status is more closely linked to psychosocial factors (Treyvaud, Anderson, Lee, Woodward et al., 2010; Yeates et al., 2007). Such findings suggest that it may be too simplistic to treat biological and social issues in a linear manner. Rather, evaluation of the relative impact of these factors may

be best conducted using a multidimensional approach, where a series of likely predictors of outcome can be assessed simultaneously and at different time intervals.

Findings from studies of cognitive and socio-emotional outcomes following child brain insult argue for the dynamic and changing nature of impairments and the importance of longitudinal research to fully understand the consequences of such early insult. Insult occurs in an ever-changing context with respect to development and may restrict the ongoing acquisition of appropriate skills, perhaps with a cumulative effect. While group-based studies suggest increasing behavioural disturbance over time following cerebral insult, at an individual level, recovery patterns vary widely, with no one factor able to predict outcome reliably. One way of conceptualising such variations may be to see the child in terms of relative vulnerability, on the basis of a number of possible risk factors, including pre-morbid characteristics of child and family, severity of insult and related impairment, age/developmental stage at insult, and socioeconomic factors, as well as other influences not usually investigated in child brain injury (e.g., blood biomarkers, genetic factors).

Following is a case study illustrating some of these complexities and tracking the interactions that occur between injury, social, developmental and pre-morbid factors for the child post-cerebral insult. This case describes a child with a severe cerebral insult, with reported normal development prior to her injury. Similarly, the family unit appeared to be previously well functioning and resourceful. Despite these various advantages, long-term follow-up shows continuing deterioration in neurologic, cognitive and behavioural function for the child and ongoing stress and social difficulties for the family.

Case illustration: Hannah

Hannah was originally referred for neuropsychological evaluation and follow-up during her admission to a tertiary metropolitan, paediatric hospital where she had presented to the Emergency Medicine Service following a motor vehicle accident in which she was a pedestrian hit by a car. Hannah and her family were reviewed on several occasions over a ten-year period, usually in response to novel functional difficulties emerging at key developmental transitions (e.g., school entry, adolescence). This opportunity to monitor recovery and development from acute hospitalisation through rehabilitation and education provides important insights into the ever-changing challenges faced by the child with serious brain insult and their supporting family network.

Background

Hannah was aged four years at the time of her injury. Her early history was uneventful, with age-appropriate acquisition of developmental milestones, no medical illnesses and no reported social or behavioural problems. Hannah

had an older and a younger sibling, both healthy. There were no significant family, social or marital difficulties prior to Hannah's accident, and the family had a wide social network.

On the day of her injury, Hannah was playing in her front garden with her father and older brother when she chased a ball onto the street and was hit by an oncoming car travelling at high speed. Hannah was unconscious at the scene of the accident and was taken to the local hospital by ambulance.

Early recovery

'NEURO' DIMENSION

On admission to hospital, Hannah was deeply unconscious and diagnosed as suffering from a severe traumatic brain injury. Acute brain imaging (magnetic resonance imaging [MRI]) detected bilateral frontal lobe pathology and haemorrhage, necessitating surgical intervention. Repeat scan one week post-injury noted focal frontal contusions and generalised cortical and subcortical damage.

Hannah was initially nursed in the intensive care unit for two weeks, during which time her conscious state lightened and she began to respond to her environment. On regaining consciousness, the neuropsychologist monitored Hannah's post-traumatic amnesia daily, until resolution at day 20 post-injury. At that stage, she was noted to have significant speech, mobility and coordination impairments and was transferred to the rehabilitation service for intensive physical, occupational and speech therapy. Process notes indicated that major attentional problems impacted Hannah's capacity to benefit optimally from rehabilitation input.

On discharge at six weeks post-injury, Hannah had progressed but continued to display limited functional communication, with both expressive and receptive skills reduced and persisting severe attentional problems. Hannah also displayed a severe truncal ataxia and motor incoordination.

'SOCIAL' DIMENSION

During Hannah's hospitalisation, her mother remained at the hospital, sleeping by her bed. Hannah's younger sister was cared for by grandparents during the week, while her older brother remained at home with her father, who needed to maintain the family business and income. On weekends, the family spent much of their time with Hannah at the hospital. Such family disruption and fragmentation is not uncommon following an acute illness and can result in an inability of the family to communicate adequately at a time of severe stress and to support each other and deal with acute responses to trauma. Each family member may have a different experience of the acute illness period. In Hannah's case, her mother was consumed with the day-to-day survival and intense rehabilitation of her child, while her father was more

involved with regular day-to-day domestic and childcare routines and with the financial pressures caused by the accident. Not surprisingly, Hannah's older brother, who witnessed the accident, experienced significant trauma symptoms (nightmares, reliving), with associated behavioural symptoms, which added to the family challenges. During Hannah's admission, her parents received support from the hospital social worker to assist them with childcare and financial issues. They also met with the team's neuropsychologist, who provided psycho-education regarding traumatic brain injury and its consequences.

'PSYCH' DIMENSION

Neuropsychological evaluation was first attempted just prior to discharge, approximately five weeks post-injury. At that time, Hannah was unable to cooperate fully with testing due to reduced attention, limited motor coordination (i.e., unable to pick up large wooden blocks to complete jigsaw puzzles) and little expressive speech. Hannah's parents noted that, at this point in recovery, she was totally dependent for daily living skills (e.g., eating, toileting and dressing), despite these being well-established skills pre-injury. Her behaviour had also changed, with frequent episodes of frustration and poor impulse control described. Hannah's parents found these episodes distressing and difficult to manage, noting that she had been an easy-going child prior to her injury.

Transition: hospital to home and school

'NEURO' DIMENSION

Hannah was discharged six weeks post-injury, after a trial weekend at home. At this time she was medically stable, but required ongoing outpatient rehabilitation to ensure optimal development. Hannah attended the hospital two mornings per week, where she continued to receive physical, speech and occupational therapy.

'SOCIAL' DIMENSION

The transition from hospital to home is a time of significant family stress. Parents must take over responsibility for their child's care, a process that highlights the extent of disability and requires parents to accept the ongoing needs of their injured child. Hannah's parents and siblings must also re-establish family routines and connections, while adjusting to the added burden of caring for her and managing her significant disability. A key task for her parents was setting up community resources, which in Hannah's case included early intervention services and support for return to preschool. As these tasks are unfamiliar to most parents, assistance from

Hannah's rehabilitation team was critical and included kindergarten meetings and provision of written reports and referral to the local child rehabilitation team.

'PSYCH' DIMENSION

For Hannah, discharge home was associated with a major change in routine, less support for daily living activities and adjusting to the busy home environment. Early challenges included excessive fatigue, often seen in the early stages of recovery, as well as continuing attentional problems.

Chronic recovery and ongoing development

The long-term repercussions of acute, serious brain injury, subsequent family separation and ongoing stresses are significant, and often alter family dynamics irreversibly.

'NEURO' DIMENSION

Hannah continued to receive outpatient rehabilitation through early intervention services prior to school entry, with specific emphasis on speech and motor coordination. Post-injury, Hannah has experienced multiple secondary medical complications, including post-traumatic epilepsy and precocious puberty. Communication problems have persisted, and her speech remains slow and laboured, restricting her capacity for normal communication. Mobility and coordination difficulties also remain, and Hannah struggles to participate in many age-appropriate leisure and sporting activities. A recent MRI scan shows evidence of the previous pathology, with abnormalities in frontal, cerebellar and brainstem regions. Additionally, she exhibits significant cerebral atrophy, particularly in anterior areas, perhaps indicating a lack of expected development of these areas through childhood.

'SOCIAL' DIMENSION

The long-term psychosocial repercussions for Hannah and her family are substantial. Hannah's family tended to follow a pattern commonly observed after unexpected childhood brain insult, where their recovery from the trauma of her injury evolved gradually over the first year following Hannah's injury (Kazak et al., 2006; Muscara et al., 2015). Pre-injury family resilience and solid family support assisted the family to adapt to their new family unit, develop new skills and work through their grief.

Hannah's mother took on the primary role for managing Hannah's medical and educational requirements, spending large amounts of time travelling

to multiple therapy sessions, and then following up on rehabilitation activities at home, organising appropriate community/educational resources and taking care of Hannah's daily needs. Not surprisingly, this left little time for her husband, her other children or for herself. Hannah's father, having been supervising her at the time of the accident, experienced ongoing feelings of guilt, which impacted on his relationship with his partner and compromised his ability to accept Hannah's residual impairments. Hannah's brother was also impacted, experiencing nightmares and flashbacks from the accident for many months, consistent with post-traumatic stress. Only her younger sister remained relatively unscathed. Eventually, the family was able to accept Hannah's disabilities and set about providing appropriate resources for her. Once Hannah's initial recovery slowed, her parents accepted support, by way of group-based, video-delivered psychosocial intervention, to address their personal psychological issues. However, they describe the continuing burden of needing to access resources for Hannah, manage her physical, intellectual and behavioural difficulties and accept them, while maintaining a well-functioning family environment.

'PSYCH' DIMENSION

Hannah was first comprehensively assessed at ten months post-injury, prior to school commencement, and then on a number of subsequent occasions until the age of 16. On each occasion, qualitative features of presentation included high levels of distractibility and impulsivity. These behavioural characteristics often impeded her test performance. Hannah exhibited age-expected progress in the two years post-injury, probably reflecting some early recovery of function and/or slightly slowed developmental progress. After this, her progress slowed, with little improvement evident in the following years. By age 16, Hannah's best results on neuropsychological test measures were at the level expected for a seven-year-old child.

Hannah's poor progress is consistent with her school history and reflects her inability to cope in the face of increasingly complex life demands. She commenced school at age five, attending a mainstream setting, with integration aide support and a modified educational curriculum. After several years, Hannah's reduced abilities, impaired attention and impulsive behaviours became difficult to manage within a busy classroom, and she moved to a special school environment for children with intellectual impairment. Hannah continued to experience difficulties, both social and academic. In a recent review aimed at looking at future vocational options, it was evident that Hannah is unlikely to live independently, attain employment or manage her financial affairs. While she is now able to manage basic daily living skills including bathing, washing, dressing and feeding, she is unable to perform more complex activities, such as cooking or shopping, without supervision.

Following Hannah from the time of her injury into adolescence highlights the complex interaction among neurologic, cognitive and social influences. Several crises have occurred over the years, reflecting the severity of Hannah's injury, the importance of the ongoing developmental process and the relevance of the family unit. Hannah's family have become socially isolated, maintaining few old friendships and with little capacity or motivation to establish new networks. Hannah herself initially displayed limited insight regarding her problems. She progressed through her early school years quite happily despite significant academic and social challenges necessitating transfer to a special school context. As she moves through adolescence, Hannah has developed some degree of insight and is able to express some of her feelings of sadness and anger about being different from her peers. One of the major problems for Hannah, and for many other children who suffer brain insults, is that her physical appearance is largely normal, leading to unrealistic expectations and resultant disappointments for teachers, peers and family.

At the outset, Hannah may have been predicted to have a good prognosis, despite the severity of her injury. Her injury was at a young age, suggesting the possibility of functional brain reorganisation. She had normal pre-injury development and her family unit was cohesive and well functioning. She had access to appropriate early treatment, later rehabilitation and adequate academic support. The observation of significant and increasing difficulties over time, for both Hannah and her family, emphasise the persisting stresses associated with early brain injury and the ongoing needs of such children and their families.

Conclusions

The dimensions of knowledge important to child neuropsychology – neurologic, cognitive, socio-emotional, environmental – must each be incorporated into future theory in the child neuropsychology field. Current theoretical perspectives represent a significant progression over the past 20 years, when understandings were based primarily on adult models of brain lesions. Today, developmental perspectives extend our breadth of knowledge, but continue to fall short in explaining the complexities of interruption to a system in a rapid state of development. There continues to be an unacceptably high degree of unexplained variation in outcome following early childhood brain insult. The challenge is to improve prediction of outcome by measuring the interacting influences of neural, cognitive and psychosocial parameters and their ever-changing matrix through childhood.

2 The developing brain

The healthy adult brain is highly specialised in both structure and function, and this was originally thought to reflect a *modular organisation*. This approach attributes the processing of particular behavioural functions to distinct cortical regions, connected via specific functional neural networks or circuits (Johnson, 2001; Paus, 2005). In keeping with this view, neuroimaging lesion studies demonstrate that specific brain regions support particular cognitive processes. For example, more than 150 years ago, Paul Broca (1861) described expressive language impairment due to pathology in the prefrontal cortex identified at post-mortem. Advances in neuroimaging have enabled more timely detection of such brain–behaviour relationships, for example the importance of the medial prefrontal region for attentional control processes such as focused attention (Bench, Frith, Grasby, Friston et al., 1993) and self-regulation (Marsh, Zhu, Schultz, Quackenbush et al., 2006). Recent evidence, mainly from sophisticated neuroimaging studies, challenges traditional 'localisationist' approaches, proposing that many behaviours and skills are mediated by complex neural networks, incorporating both frontal and extra-frontal systems (Fair, Dosenbach, Church, Cohen et al., 2007; Smith, Giampietro, Brammer, Taylor et al., 2011; Stevens, Kiehl, Pearlson, & Calhoun, 2007). Such connectionist views have received growing support, with increasing evidence that functional neural networks underpin a range of more complex skills, including attention, working memory, executive function and social cognition. Thus, it appears that, even in the mature, adult brain, integrity of the whole brain may be necessary for efficient executive function (EF) (Della Sala, Gray, Spinnler, & Trivelli, 1998; Stuss, 1992; Welsh & Pennington, 1988). In the developing brain, both structures and connectivity are rapidly developing, and evidence suggests that functional organisation is also incomplete (Ezekiel, Bosma, & Morton, 2013).

The 'how and when' of brain specialisation is still only partially understood, but is particularly relevant to understanding the neurobehavioural consequences of early brain lesions. Early researchers, such as Lenneberg (1967), argued that the infant's brain was '*equipotential*', with all brain regions equally able to take responsibility for any function. Functional specialisation was thought to emerge gradually through early childhood and that, in the

event of early brain insult, 'healthy brain regions' could be recruited to take up the normal functions of damaged brain regions. In contrast, the '*innate specialisation*' model argues that key skills such as language are localised at birth, an argument that is supported by findings that the language-dominant cerebral hemisphere is larger in the new-born (Witelson & Paille, 1973).

More contemporary research examining human functional brain development highlights the importance of also accounting for the influence of genetics and experience on the developing organisation of the brain, reflecting an '*interactive specialisation approach*'. Employing this framework, M. Johnson (2007) acknowledges these influences and identifies three separate, but not necessarily incompatible, approaches to understanding progression of cognitive abilities in infants: (a) *maturation*; (b) *interactive specialisation*; and (c) *skill learning*.

The *maturational view* proposes there is a genetically predetermined, developmental sequence of specific neuroanatomical regions, which provides the foundation for the hierarchical emergence of sensory, motor and cognitive processes. For example, the infant is largely dependent on lower-order, sensory functions (e.g., oral, motor), but by the second year of life, the rapidly developing prefrontal cortex supports successful performance on the object retrieval task, designed to assess working memory and inhibitory control in children (Diamond & Goldman-Rakic, 1989). While successful performance on this task involves activation of several brain regions, the particularly protracted development of the dorsolateral prefrontal cortex is thought to be primarily responsible for change in behaviour, limiting the child's efficiency until these brain regions are mature.

The *interactive specialisation* view suggests that emergence of a new skill reflects refinement of connectivity between brain regions, not just activity in one or more region. For example, Anderson and colleagues (Anderson, Harvey, Saling, Anderson et al., 2002) reported differential language activation over time in eight-year-old identical twins discordant for a left frontal tumour and seizures commencing at age five. The affected twin initially demonstrated typical left-sided brain activation on a language paradigm. Over time, activation became bilateral, thought to be associated with growth in the tumour. However, with emerging and increasing right hemisphere activation over time, deterioration in expressive language skills was documented in the affected twin, but not the unaffected twin. The authors suggest that the emerging right activation might reflect pathophysiologic effects of the tumour in the prototypical language cortex, rather than language transfer. Or, increasing right hemisphere activation might represent an unsuccessful attempt to reorganise language to the non-dominant hemisphere. In this case, disruption of left hemisphere language by the epileptogenic, progressive tumour might have limited or prevented its functional reintegration, instead provoking further recruitment of right hemisphere homologues. Alternatively, the right hemisphere activation might reflect the loss of active inhibition from the homologous left frontal region or loss of some other form of reciprocal interaction between frontal homologues.

Skill learning is based on the observation that patterns of brain activation change during skill acquisition. For example, recent functional neuroimaging studies demonstrate more diffuse activation within prefrontal and extra-frontal regions in children performing executive tasks compared with adults, likely reflecting that the immature brain needs to recruit more brain regions to successfully complete an activity than does the healthy adult brain. In support of this hypotheses, increasingly focal brain activation has been observed with age (Marsh et al., 2006; Tamm, Menon, & Reiss, 2002), reflecting an association between performance and emerging patterns of interactions between different regions.

Developmental progression of brain development

Cerebral development is ongoing, beginning early in gestation and continuing into childhood through to early adulthood. The fastest rate of brain growth occurs prenatally, when it is estimated that every minute 250,000 brain cells are formed through continuous rapid cell division (Papalia & Olds, 1992). Although the structural morphology of the brain is mature by birth, growth continues during the post-natal period (Figure 2.1). Between birth and adulthood, the human brain quadruples in size, increasing from around 400 grams at birth to 1500 grams at maturity in early adulthood, peaking between 18 and 30 years and then commencing a gradual decline (Caeser,

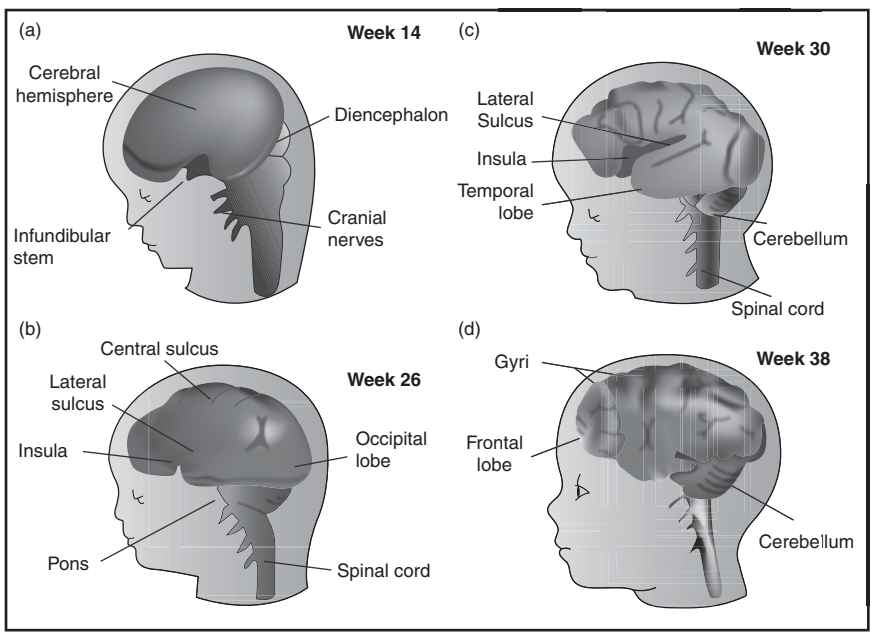


Figure 2.1 Graphic representation of early brain development through the prenatal period to birth

1993; Dekaban & Sadowsky, 1978). The post-natal increase in brain weight is largely due to differentiation, growth and maturation of existing neurons, including elaboration of dendrites and synapses, and ongoing myelination.

Brain development can be separated into two qualitatively distinct stages, with birth providing a rough marker for the transition. Prenatal development is primarily concerned with the structural formation of the CNS and is thought to be largely genetically determined. Interruptions to development during this period via genetic mechanisms or interuterine trauma or infection are likely to have a dramatic impact on cerebral structure, so that the brain's morphology appears abnormal even at a macroscopic level. In contrast, post-natal development is mostly characterised by elaboration of the brain, in particular dendritic arborisation, myelination and synaptogenesis. While still largely genetically regulated, these processes are thought to be more susceptible to the impact of neuronal activity and thus to environmental and experiential influences (Ables, Breuning, Eisch, & Rakic, 2011; Nowakowski, 1999; Orzhekhovskaya, 1981; Paolicelli, Bolasco, Pagani, Maggi et al., 2011; Yakovlev, 1962). Brain damage sustained postnatally may have less impact on gross brain morphology, but is likely to interfere with ongoing CNS elaboration and interrupt the development of interconnections and functional neural networks.

The CNS begins to develop early in gestation, around day 40 of embryonic life, commencing a process of lifelong change. The brain is recognisable in its mature form from around 100 days of gestation, as illustrated in Figure 2.2, but continues to mature, albeit at a less rapid pace, until early adulthood. Such a protracted developmental time frame is unique to the human species. During this prolonged period of maturation, a range of developmental mechanisms are interacting, reflecting the complexity of the process. Cerebral development is not a simple, linear, progression throughout the brain; rather, there is

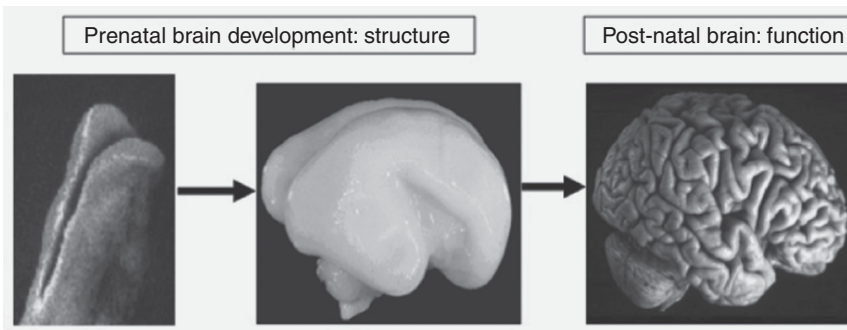


Figure 2.2 Structural progression of the brain from gestation to early childhood. A colour version of this figure can be found at: www.routledge.com/9781848722026

Source: R. Leventer, personal communication

a range of developmental processes, many occurring concurrently, reflecting differential developmental timing for various brain regions and varying developmental models for specific elements of the cerebral system. These developmental processes include: (i) hierarchical progression; (ii) regressive and additive processes; and (iii) growth spurts in neurological processes. A basic understanding of these maturational processes is central to a discussion of CNS development.

Hierarchical progression

In general, there is a hierarchical progression in brain development, with the brainstem and cerebellar regions developing first, followed by posterior areas, and anterior regions reaching maturity last (Fuster, 1993; Gogtay et al., 2004; Hudspeth & Pribram, 1990; 1992; Staudt, Schropp, Staudt, Obletter et al., 1993; Toga, Thompson, & Sowell, 2006). Synaptogenesis appears to be simultaneous in multiple areas and layers of the cortex (Rakic, Bourgeois, Eckenhoff, Zecevic, & Goldman-Rakic, 1986), with neurotransmitter receptors throughout the brain reported to mature at the same time (Lidow & Goldman-Rakic, 1991). Such findings suggest concurrent rather than hierarchical development, with posterior and anterior structures developing along approximately the same timeline. Not all research supports this view of simultaneous maturation even for neurochemical markers, with some arguing that this pattern, while present in non-human species, may not hold for humans (Gibson, 1991). This pattern of posterior to anterior maturation has been observed using many methodologies, including whole-brain volume and white matter volume (Giedd et al., 1999), electroencephalography (EEG) (Hudspeth & Pribram, 1990) and metabolic activity (Chugani, Phelps, & Mazziota, 1987). For example, increases in white matter volume (reflecting myelination progression) have been observed to occur in stages from primary and sensory areas, to association areas, and finally frontal regions (Giedd et al., 1999). Not all brain regions follow this pattern of development. For example, myelination of anterior regions of the corpus callosum is complete prior to posterior regions, which do not mature until adolescence (Giedd et al., 1999; Thompson et al., 2000).

Additive and regressive events

Additive development refers to the ongoing accumulation of growth processes. Several neural processes progress in this way. Myelination is one such process, as it progresses in a stage-like manner throughout the brain during childhood and early adulthood (Giedd et al., 1999; Huttenlocher & Dabholkar, 1997), as illustrated in Figure 2.3, which shows increasing connectivity of myelinated white matter from birth to 18 years. Similarly, there is a continuous increase in the formation and elaboration of dendritic connections throughout the brain.

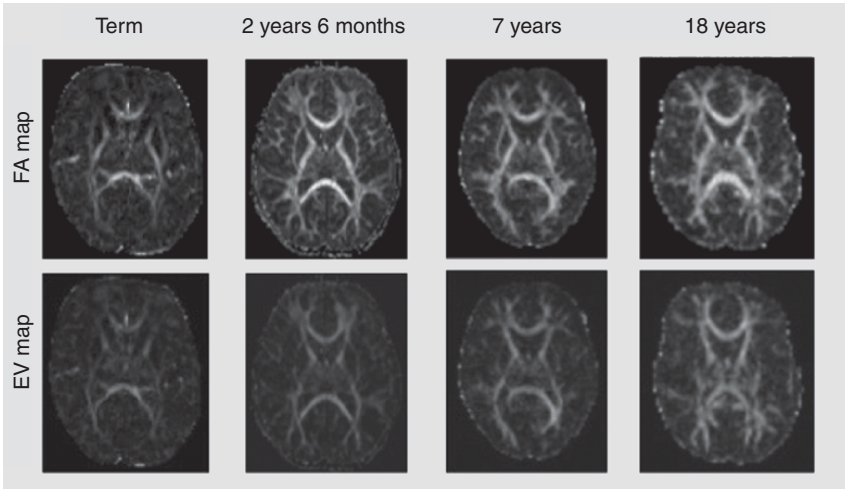


Figure 2.3 Brain connectivity through childhood. The child brain is characterised by ongoing white matter myelination, which continues through childhood and into early adulthood (courtesy of J. Yang). EV = eigenvalue; FA = fractional anisotropy. A colour version of this figure can be found at: www.routledge.com/9781848722026

Other neuronal processes demonstrate an inverse association or regression over time, characterised by an initial overproduction and then selective elimination of redundant elements. For example, excess synapses are formed in infancy and, through experience, those that do not form functional neural networks become obsolete connections and are pruned (Huttenlocher, 1979). There is also an initial overproduction of dendrites followed by pruning, to leave only the most functional branches (de Graaf-Peters & Hadders-Algra, 2006; Kolb, Forgie, Gibb, Gorny, & Rowntree, 1998; Webb, Monk, & Nelson, 2001). This is well illustrated in the work of O'Donnell and colleagues (2005), who demonstrated a linear decrease in cortical thickness between 8 and 20 years of age in the fronto-polar region and dorsolateral prefrontal cortex. This finding is consistent with volumetric studies showing increases in frontal grey matter during pre-adolescence followed by a decrease during adolescence (Gogtay et al., 2004; Sowell, Thompson, Holmes, Batth, et al., 1999; Sowell, Thompson, Tessner, & Toga, 2001; Sowell, Trauner, Gamst, & Jernigan, 2002).

The prenatal period

The pre-natal period is characterised by dynamic activity and is primarily concerned with gross structural formation (Casey, Giedd, & Thompson, 2000; Orzhekhiovskaya, 1981). A series of intricate processes – neurolation, proliferation, migration, dendritic development, synaptogenesis, differentiation

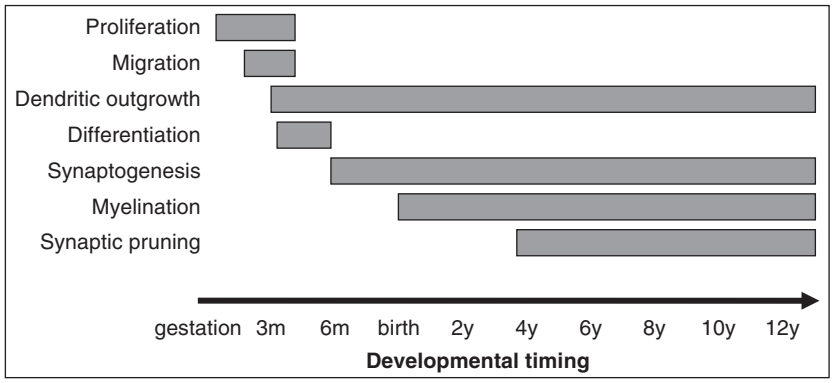


Figure 2.4 Timing and sequence of developmental processes of the central nervous system

Source: Adapted from Spencer-Smith and Anderson (2009)

and apoptosis – underpin the transformation of the primitive neural tube into a series of complex neural networks comprising the CNS. Interruptions to development during this period (e.g., genetic aberrations, intrauterine compromise, infection) will have a significant impact on cerebral development, so that brain morphology appears abnormal even at a macroscopic level. Figure 2.4 illustrates the onset and conclusion of these key neurological processes, represented by the horizontal bars.

Cellular basis of development

The process of neurolation progresses via the rapid generation of cells within the system and includes two main classes of cells: neurons and glial cells, produced by division of neuroblasts and glioblasts. The neuron is the basic functional unit of the CNS and is responsible for neural transmission within the brain. The neuron is made up of four primary components: (i) the cell body, important for the neuron's metabolic functions, holds RNA and DNA; (ii) the axon, projecting from the cell body, conducts neural impulses away from the cell body and is progressively sheathed with myelin throughout childhood; (iii) dendrites branch off the cell body and receive impulses from other neurons, conducting them towards the cell body – dendritic spines are the locus of the synapse, where information is transmitted from one neuron to another; and (iv) the presynaptic terminals, where neurotransmitters are stored and released, cross the synaptic cleft and activate the neurons at the post-synapse.

Glial cells, in contrast, play a supportive and nutrient role within the CNS, enabling regeneration of damaged neurons, producing scar tissue to occupy damage sites and transporting nutrients from nerve cells. Types of glial cells

include: (i) astrocytes, which form the blood–brain barrier, support the brain's cellular structure, contribute to the migration of neurons and clean up and plug injury sites; (ii) oligodendrocytes, which are responsible for speeding up the transmission of neural impulses throughout the nervous system by coating axons with myelin; and (iii) microglia, which clean up injury sites, primarily in the grey matter. Glial cells are relatively immature in the early stages of development and continue to generate with the increased maturity of the CNS.

Following fertilisation, rapid cell division occurs, leading to clusters of proliferating cells, which then differentiate in a matter of days into a three-layered structure known as the embryonic disk. Each of the three layers of this disk is destined to form a major organ system. The inner layer (endoderm) will form the internal organs, including the digestive and respiratory systems, while the skeletal and muscular structures will develop from the middle layer, or mesoderm. The outer layer, or ectoderm, eventually forms the nervous system and the skin surface (Johnson, 1997).

The early CNS is initially represented by a neural plate, which folds in on itself to form the neural tube, within which *neurolation* occurs in gestational months 1 through 5 (Figure 2.5) (Altman & Bayer, 1993; Rakic, 1995; Spencer-Smith & Anderson, 2009). This process is precisely regulated so that appropriate numbers of cells are formed at predetermined times and in well-defined regions. Interruption to this tightly timed sequence may cause neural tube defects and associated major structural abnormalities, such as spina bifida or anencephaly (Verity, Frith, & French-Constant, 2003) (Table 2.1).

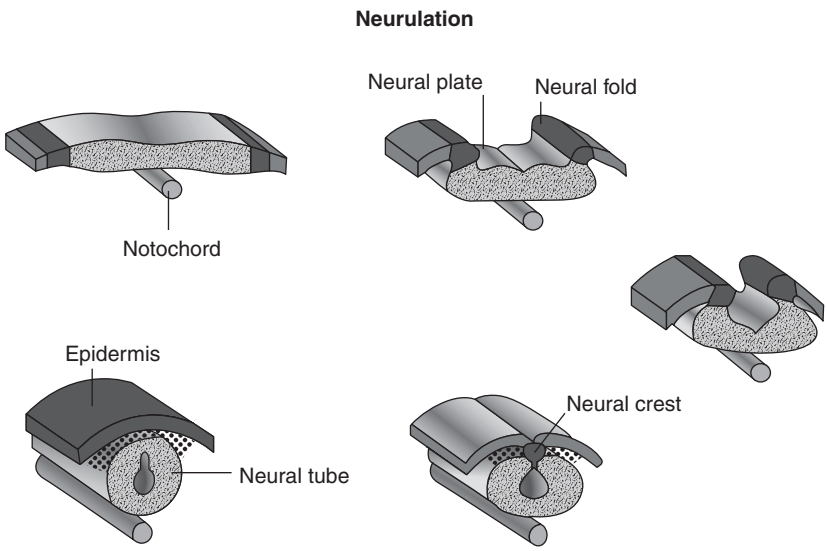


Figure 2.5 Development of the neural tube during weeks 3 and 4 of gestation. A colour version of this figure can be found at: www.routledge.com/9781848722026

Table 2.1 Impact of prenatal brain dysfunction

Timing of insults	*Description*	*Aetiology*	*Clinical manifestations*
Dorsal induction (weeks 3–4)			
Myelomeningocele/ spina bifida	Failure of closure of spinal cord	Genetic or nutritional factors	Motor, perceptual deficits
Anencephaly	Failure of neural tube to close, creating an absent vault of skull	Severe trauma, day 18 to week 4	Incompatible with life
Ventral induction (weeks 5–6)			
Holoprosencephaly	Defective division of forebrain, failure to form two hemispheres	Often genetic (e.g., anomalies in chromosomes 13 or 18)	Generally incompatible with life
Proliferation (2–5 months)			
Microencephaly	Early cessation of cell division, causing abnormally small head	Genetic or trauma factors (e.g., infection, foetal alcohol syndrome)	Low intellectual abilities
Megalencephaly	Overproduction/ poor elimination of neurons, abnormally large brain	Familial/genetic	No typical picture
Hydranencephaly	Cystic sacs containing cerebrospinal fluid replacing cerebral hemispheres	Possibly vascular aetiology, umbilical cord strangulation	Incompatible with life
Migration (2–5 months)			
Lissencephaly (agyria)	Smooth cortex, absence of sulci and gyri, but normal cortical thickness, neurons in abnormal locations	Disorder of migration, 11–13 weeks	Severe mental retardation, seizures, neuromotor disorders
Schizencephaly	Agenesis of part of cerebral wall, cortical layers not evident	Disorder of migration, 8 weeks	Mental retardation, seizures, neuromotor disorders

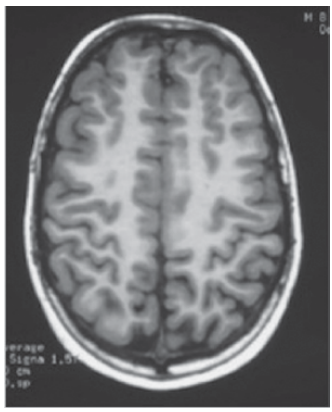
(*continued*)

Table 2.1 (Cont.)

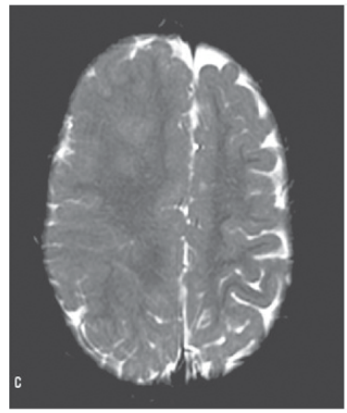
Timing of insults	*Description*	*Aetiology*	*Clinical manifestations*
Polymicrogyria	Multiple small, shallow convolutions on brain surface, neurons in abnormal locations	Migrational disorder, 16–20 weeks. Genetic/ infectious mechanisms	May be asymptomatic or associated with epilepsy, learning and behaviour problems
Agenesis of the corpus callosum	Absence or malformation of fibres crossing between the cerebral hemispheres	Genetic, weeks 12–22 of gestation	May be asymptomatic, but has been associated with other disorders (e.g., spina bifida)
Focal dysplasias (heterotopias)	Abnormalities of laminar structure or abnormally positioned cells	Migrational disorder, multiple origins	Epilepsy, learning disability, schizophrenia
Double cortex	Diffuse cortical dysplasia with a band of heterotropic matter between cortex and ventricles. Cerebral surface may look normal	Migrational disorder, late in migration, once some waves of migration are complete	Often asymptomatic Epilepsy sometimes detected
<u>Differentiation</u>			
Porencephaly	Presence of large cystic lesions, usually bilaterally	5–7 months of gestation, traumatic cause/ vascular/ infection	Sometimes asymptomatic, but also with retardation and epilepsy

Proliferation is the developmental stage during which neurons intended to form the cerebral cortex are generated, and it occurs from gestational weeks 6 to 18. During this time period, specific cell populations emerge in unique locations within the neural tube and will later develop into specific cerebral structures (Johnson, 1997; Rourke, 1989). Disruptions to brain development during this period may lead to overproduction of neurons, as seen in megalencephaly or polymicrogyria (Verity et al., 2003) (Figure 2.6). Between gestational months 5 and 7, neuroblasts (from which neurons are later derived) *migrate* to their permanent locations (Evrard, Miladi, Bonnier, & Gressens,

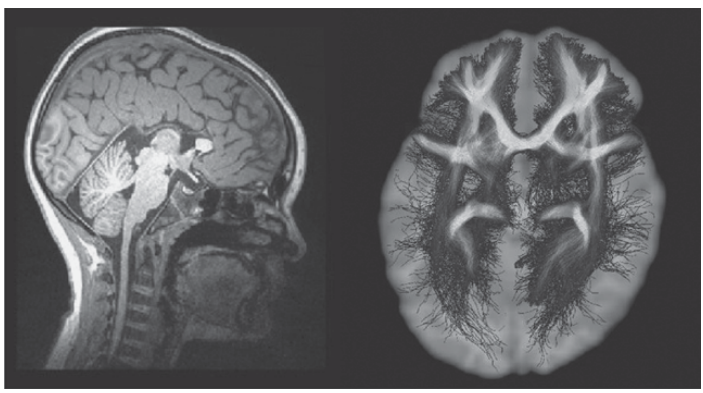
(a) Polymicrogyria



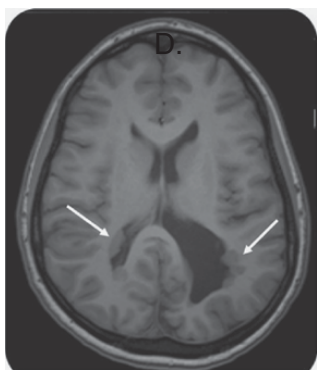
(b) Hemimegalencephaly



(c) Agenesis of the corpus callosum – i) structural and ii) functional images



(d) Subependymal heterotopia



(e) Cortical dysplasia

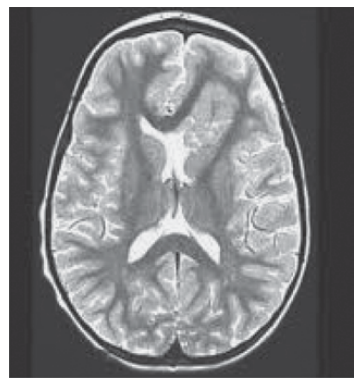


Figure 2.6 Examples of developmental brain malformations. (A) Polymicrogyria, (B) hemimegalencephaly, (C) agenesis of the corpus callosum, (D) subependymal heterotopia and (E) cortical dysplasia. A colour version of this figure can be found at: www.routledge.com/9781848722026

1992; Gupta, Hasan, Trivedi, Pradhan et al., 2005), mostly in a *radial pattern* (Johnson, 1997; Nadarajah & Parnavelas, 2002; Rakic, 1972; 1978), travelling along radial glial fibres via previously generated neurons. Arrest of neuronal migration may result in focal cortical or subcortical dysplasias (Spencer-Smith, Leventer, Jacobs, De Luca, & Anderson, 2009; Verity et al., 2003).

Dendritic development and synaptogenesis are critical for the establishment of cerebral connections. As axons extend and dendrites arborise, the developing brain becomes densely packed and the brain surface begins to fold (sulci and gyri) to accommodate this increased cortical mass (Kostovic & Jovanov-Milosevic, 2006; Kostovic & Rakic, 1990; Monk, Webb, & Nelson, 2001; Mrzljak, Uylings, Kostovic, & Van Eden, 1988; Mrzljak, Uylings, Van Eden, & Judas, 1990). Once neurons have migrated, *differentiation* begins, with cells becoming committed to specialised systems, relevant connections being established and functional activity commencing. Cells not associated with these functional systems may be eliminated (Uylings, 2006). *Apoptosis*, a form of programmed cell death that eliminates cells with poor or unnecessary synaptic connections (Henderson, 1996), results in degeneration of nearly half of all neurons during development. While necessary for healthy development, excessive rates of apoptosis have been linked to conditions such as Down syndrome (Busciglio & Yanker, 1995), while depressed or slowed rates of apoptosis have recently been linked to autism (Anagnostou & Taylor, 2011; Pardo & Eberhart, 2007).

Implications for the development of brain connectivity

Prenatal and perinatal development are characterised by expanding cortical connectivity, linked to increases in the number and size of cortical regions (Rakic, 1988). The increase in cortico-cortical connections leads to the formation of distributed neural networks (Seleman & Goldman-Rakic, 1988), which underpin the complexity of human behaviour. A critical component for the development of this connectivity is the transient subplate zone (Kostovic & Molliver, 1974; Kostovic & Rakic, 1990), which growing afferent fibres use as a waiting zone while they grow over months before they gradually invade target cortical areas that have developed (Isaacs, Christie, Vargha-Khadem, & Mishkin, 1996; Palmer, Gajjar, Reddick, Glass et al., 2003; Stiles, Stern, Applebaum, Nass et al., 2008). Many neurons in the transient subplate zone are transformed into the gyral white matter, and others disappear (Palmer et al., 2003). The general pattern of pathway growth is through axonal strata (fibrilar compartments that provide connectivity within frontal and posterior occipital and temporal lobes) of the intermediate zone and gradual ingrowth of the subplate zone. Rapid synaptic development within the cortical plate is enhanced by relocation of the thalamo-cortical afferents from subplate to cortical plate (Chapman, Waber, Bernstein, Pomeroy et al., 1995; Strauss, Hunter, & Wada, 1995; Vargha-Khadem, Isaacs, & Muter, 1994; Vargha-Khadem, Isaacs, van der Werf, Robb, & Wilson, 1992).

The late foetal period is characterised by growth of the cortico-cortical connections: long associative bundles begin to appear in the human cerebrum and are in position by birth. The transient subplate zone is present in the new-born cortex, but is gradually replaced by the permanent circuitry of the cortical plate. The change from diffuse circuitry to focused networks is characteristic of the developing networks and occurs mainly in primary somatosensory networks during this time. In contrast, early post-natal development is characterised by growth of short cortico-cortical connections and development of local circuitry (Eyre, 2005; Eyre, Miller, & Clowry, 2002).

Rates at which different pathways are established vary. Corticospinal axons reach the lower spinal cord by 24 weeks of gestation, after which they progressively innervate grey matter and, prior to birth, there is extensive innervation of spinal neurons, including motor neurons (Eyre, 2005; Eyre et al., 2002; Eyre, Miller, Clowry, Conway, & Watts, 2000). By 40 weeks, corticospinal axons begin to express neurofilaments and to undergo myelination (Eyre et al., 2002). Consistent with this early anatomical maturation of corticospinal axons and their innervation of the spinal cord, functional monosynaptic corticospinal projections to motoneurons and spinal interneurons are established during the final trimester of pregnancy (e.g., Eyre, 2005; Eyre et al., 2000). In the new-born, significant bilateral innervation from each motor cortex has been observed and rapid differential development of both ipsilateral and contralateral projections occurs by two years of age, consistent with a withdrawal of ipsilateral cortico-motoneuronal projections. In contrast, cortical pathways and networks associated with higher-order skills (e.g., executive functions) are established later, and continue to mature through childhood and adolescence, as described above. These more protracted developmental trajectories are likely to be associated with different outcomes from those observed for motor circuits, with an extended period of vulnerability while networks and their associated neurobehavioural functions emerge and mature.

The post-natal period

Post-natal development is primarily associated with brain elaboration, with differentiation and maturation progressing into adolescence and early adulthood. As with prenatal processes, post-natal development appears to follow a set sequence, with early development characterised by growth of short cortico-cortical connections, rapid synaptogenesis and dendritic development, myelination and development of local circuitry. These various processes progress in a largely hierarchical manner, with anterior regions the last to reach maturity (Gogtay et al., 2004; Klinberg et al., 1999). Rapid dendritic growth and synaptogenesis occur from around eight months to two years, culminating in levels higher than those seen in adulthood, and followed by selective elimination. This process of selective pruning provides an opportunity for CNS structures to be influenced by environment and experience (Luciana, 2003; Uylings, 2006).

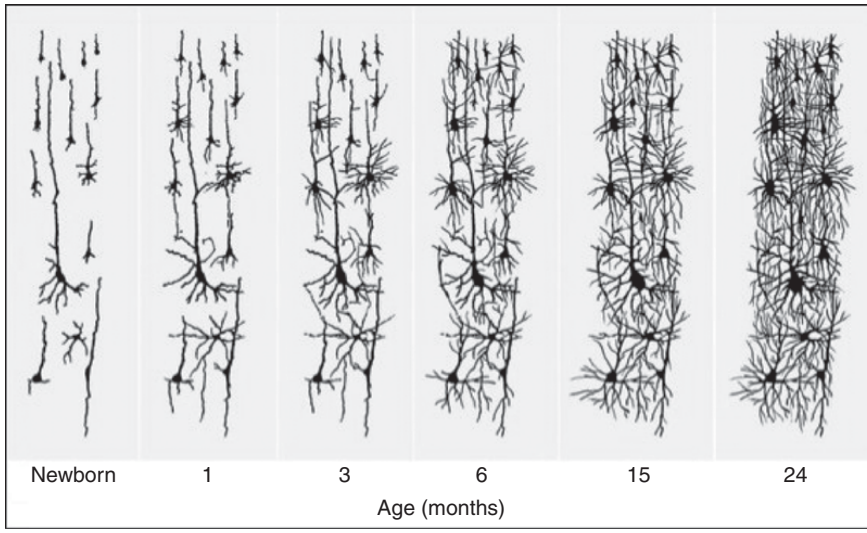


Figure 2.7 Cellular structure and development from birth to adulthood. A colour version of this figure can be found at: www.routledge.com/9781848722026

From 16 months to 2.5 years, *dendrites* display growth spurts resulting in full maturity. An initial overproduction of dendrites is followed by pruning, to leave only the most functional branches (Kolb & Gibb, 2002; Webb et al., 2001). Accelerated dendritic growth is seen in the first year of life (Eyre et al., 2000), and continues at a reduced rate to five years, followed by a stable period up to at least age 27 (Koenderink & Uylings, 1995; Koenderink, Uylings, & Mrzljak, 1994) (Figure 2.7). The pattern of dendritic development largely parallels patterns in grey matter volume changes. The age-related changes in grey matter volume may also be dependent on other maturational processes including neuronal pruning and cell death (Matsuzawa, Matsui, Kinoshih, Noguchi et al., 2001), synaptic reorganisation (Bourgeois, Goldman-Rakic, & Rakic, 1994; Huttenlocher, 1979) and gain in white matter (myelination) (Gogtay et al., 2004; Paus, 2005). Early brain lesions and neurodevelopmental conditions have been associated with interruption to dendritic development; for example, dendrites may be thinner, have smaller numbers of spines or shorter branches (Kelleher & Bear, 2008; Purpura, 1975; 1982; Webb et al., 2001).

Synaptogenesis roughly parallels dendritic development (Goldman-Rakic, 1987). Research suggests maximum synaptic density between 15 months (Huttenlocher & Dabholkar, 1997) and two to three years (Mrzljak et al., 1988), followed by a decline over the next 16 years (Blakemore & Choudry, 2006; Bourgeois et al., 1994; Huttenlocher, 1979; Zecevic & Rakic, 1991). Initial overproduction of synapses may provide scope for recovery and adaptation after a prenatal or post-natal brain lesion (Bertenthal & Campos, 1987; Huttenlocher, 1984; Kolb, Gibb, & Gorny, 2000) and may underpin critical

periods in development associated with better capacity for recovery. Further, Bertenthal and Campos (1987) suggest that, through the overproduction of synapses, there is potential to select and refine active synapses, resulting in reorganisation for greater efficiency (Rakic et al., 1986). In contrast, Rakic and colleagues (1986) argue that a reduction in synapse number and density may equally reflect reorganisation for greater efficiency, supported by the observation of progress of cognitive and behavioural processes.

Myelination is the process of neuronal insulation that ensures rapid transmission of electrical signals (Johnson, 1997; Yaklovlev & Lecours, 1967) and transmission of information within and between neural circuits (Paus, 2005). It is of particular interest as it is considered to reflect interregional communication in the developing brain underpinned by a continuous increase in white matter volume, both global and local, from early childhood through to late adolescence (Barnea-Goraly, Menon, Eckert, Tamm et al., 2005; Giedd et al., 1999; Jernigan, Trauner, Hesselink, & Tallal, 1991; Klinberg et al., 1999) (also see Figure 2.3). Myelination processes begin at about gestation month 4 and peaks in myelination have been documented around 2 years, 7–9 years and 11–12 years (Thatcher, 1991; 1997), with some further changes during adolescence and beyond (Giedd et al., 1999; Paus, Zijdenbos, Worsley, Collins et al., 1999). Disruption to myelination has been reported in association with toxicities, inflammation and cranial irritation, resulting in decreased conduction velocity, increased refractory periods after synaptic firing and more frequent conduction failures (Konner, 1991).

In a longitudinal magnetic resonance imaging (MRI) study, Giedd and colleagues (1999) demonstrated that white matter volume increased in a linear fashion in the frontal cortex throughout the studied age range of 4–20 years. However, precisely when mature levels of myelination in the frontal regions are achieved remains controversial. Some studies report that myelination is completed around late adolescence (Giedd et al., 1999: Huppi et al., 1998; Klinberg et al., 1999; Yakovlev & Lecous, 1967), while others suggest it is not completed until around 25 years (Paus et al., 1999). More recent volumetric imaging studies indicate that it takes at least four decades before the myelination process ceases, with intra-cortical connections being amongst the last to become myelinated (Paus et al., 1999; Sowell et al., 2001).

Infant studies suggest a relationship between delays in myelination and neurodevelopmental lag (Van der Knaap, Valk, de Neeling, & Nauta, 1991) or global developmental delay (Huttenlocher & Dabholkar, 1997; Jan & Jan, 2010; Parrish, Kim, Jan, & Jan, 2006). These findings are consistent with the belief that increases in myelination result in improved processing of information (Paus, 2005), supporting more efficient cognitive function.

In the context of childhood brain insult such as traumatic brain injury, multiple sclerosis and acute disseminated encephalomyelitis, disruption to myelination processes likely contributes to decreased conduction velocity, increased refractory periods after synaptic firing, more frequent conduction failures, temporal dispersion of impulses and increased susceptibility to

extraneous influences (Konner, 1991). In keeping with the key role of myelination for efficient information processing, each of these conditions has been characterised by deficiencies in processing speed (Anderson et al., 2005a; Deery & Anderson, 2009; Deery, Anderson, Jacobs, Neale, & Kornberg, 2010). Possible origins of myelin deficiencies are amino or organic acid disturbances, congenital hypothyroidism, malnutrition and periventricular leukomalacia (Volpe, 1995; Woodward, Anderson, Austin, Howard, & Inder, 2006b).

Growth spurts and critical periods in development

Brain maturation is not linear, but is punctuated by a series of growth spurts (times associated with rapid development), which are now well established. Over several decades, studies have examined maturation using a variety of methodological approaches, such as brain volume (Giedd et al., 1999), EEG (Hudspeth & Pribram, 1992; Thatcher, 1997) and glucose metabolism (Chugani et al., 1987), with similar distinct growth periods identified. The original work in this domain was based on analyses of human EEG coherence. Using this methodology, Thatcher (1992; 1994; 1997) describes three main growth spurts in brain maturation. An initial growth spurt is recorded between 1.5 and 5 years, a second between 5 and 10 years and a final spurt between 10 and 16 years. In addition, two transitional phases are identified; one occurring between 5 and 7 years in the left hemisphere and another in the right hemisphere between 9 and 11 years. Hudspeth and Pribram (1990; 1992) have documented similar developmental phases using EEG data and an additional spurt between 16 and 19 years. The EEG coherence is interpreted as repetitive sequences of synaptic overproduction followed by synaptic pruning. These growth spurts in development are supported by parallel developmental increments in cognitive skills, through infancy and into adolescence.

While this fine-tuning occurs, other more macro-level changes are in train, probably reflecting the accumulation of growth processes. Recently developed experimental techniques have identified a series of growth spurts throughout pre- and post-natal development, rather than a gradual, continuous developmental progression, with anterior regions the last to reach maturity (Fuster, 1993; Jernigan & Tallal, 1990; Kolb & Fantie, 1989; Risser & Edgell, 1988). The earliest of these spurts has been documented at around 24–25 weeks of gestation, coinciding with the completion of neuronal generation. A further spurt occurs during the first year of life due to dendritic and synaptic development and myelination. Later spurts have been identified between 7 and 9 years of age, and there is a final spurt at around 16–19 years (Hudspeth & Pribram, 1990; Klinberg et al., 1999; Thatcher, 1997).

Associated with these growth spurts is the concept of '*critical*' *or* '*sensitive*' *periods*, which refer to stages in developmental during which specific cognitive and behavioural domains may experience major progression. While not yet fully understood, these critical periods are hallmarks of early development, which result in either particularly good or, conversely, particularly poor

outcomes (Kolb, Monfils, & Sherren, 2008). They mark phases of increased plasticity, when specific brain circuits are maximally sensitive to acquiring certain kinds of information, or even need that information to be consolidated so that the system involved can establish interconnections with other systems (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Hensch, 2004; Stein & Hoffman, 2003; Thomas & Johnson, 2008; Uylings, 2006).

Within the context of healthy development, critical periods are also times when neural networks are particularly sensitive to positive environmental influences, such as learning and instruction, or negative influences, such as neglect and abuse. Brain disruption or insult during a critical period is thought to be particularly detrimental, causing a cessation of development or altering its course. If this progression does not occur appropriately, it may never occur and there may be delay in ongoing development of damaged brain regions or asynchrony with respect to the sequential establishment of neural connections (Johnson, 2009; Kolb, Monfils, & Sherren, 2008; Schneider & Koch, 2005).

The concept of critical periods has been best established for the visual system. For example, impaired vision during early life due to ocular disorders causes disparate images to be transmitted to visual cortices, resulting in reorganisation of visual pathways and permanent amblyopia. Similar conditions later in childhood, when the visual system is more mature, have no such consequences (Johnson, 2009; Majdan & Shatz, 2006; Tagawa, Kanold, Majdan, & Shatz, 2005). Within the motor system, a similar 'critical period' is described, with young children being better able to compensate for damage to the motor cortex. Several researchers report that, following large early unilateral lesions in the motor cortex, neuronal representation of the primary motor region is reorganised to the ipsilateral region, so that motor representations are accommodated in the undamaged hemisphere (Carr, Harrison, Evans, & Stephens, 1993; Kuhnke, Juenger, Walther, Berweck et al., 2008; Wilke, Staudt, Juenger, Grodd et al., 2009). These examples highlight the potential interactions between timing of injury and functional domain.

Critical periods for more complex neurobehavioural domains are less well studied, although work from our research team has identified differentially poor outcomes, including compromised intellectual ability, language, memory, attention and executive function, for children sustaining either focal or diffuse brain insult before two years of age (Anderson et al., 2005a; Anderson, Catroppa et al., 2009; Anderson, Spencer-Smith et al., 2009; Anderson, Spencer-Smith et al., 2010). However, many questions remain; for example, are there different critical periods for different neurobehavioural domains? Do some skills have shorter critical periods? Are some functions less likely to be influenced by plasticity processes?

Influences on brain development

Clearly, brain development is complex, with a range of developmental mechanisms occurring both in sequence and simultaneously. While development appears to follow a fairly fixed, genetically specified pattern, a number

of factors can interfere with this process, potentially causing irreversible change to these processes and to the final outcome.

The most common causes of prenatal pathology identified to date include biological agents such as genetic factors and intrauterine trauma (infections, toxins, injury). These factors, if acting while structural development is in progress, may lead to structural malformations and cerebral reorganisation. For example, contraction of rubella during the first trimester of pregnancy has been shown to have a significant impact on the structure and function of the CNS. Similarly, a range of environmental agents can influence development prenatally. Maternal nutrition, maternal alcohol intake and drug addiction and maternal stress have also been implicated in anomalous CNS development.

Post-natal development, while susceptible to the effects of biological risks such as infection, is also subject to disruption due to external trauma (Pozo & Goda, 2010). Research from our laboratory has provided evidence that such agents have the greatest impact on younger children, when the brain is developing most rapidly. For example, acquired brain injury, either focal or diffuse in nature, in preschool children will lead to more severe and persistent cognitive disability than similar injuries in older children (Anderson & Moore, 1995; Anderson, Spencer-Smith et al., 2009; Deery et al., 2010; Deery & Anderson, 2009; Lo, Gordon, Hajek, Gomes et al., 2014; Long, Anderson, Jacobs, Mackay et al., 2011). Brain irradiation for the treatment of leukaemia leads to significant neurobehavioural sequelae in children treated prior to age five, while older children exhibit no such impairment (Anderson, Smibert, Ekert, & Godber, 1994). These findings are supported by other research groups (Ewing-Cobbs et al., 1997; Taylor & Alden, 1997). Recent population-based studies have also detected poorer cognitive and behavioural function in the context of early exposure to a range of environmental toxins, such as lead, polychlorinated biphenyls, methylmercury and environmental tobacco smoke (Symeonides, Ponsonby, Vuillermin, Anderson, & Sly, 2013). Table 2.2 provides a list of factors that may be responsible for disruption of CNS development.

Environmental factors, both distal (e.g., socioeconomic status, ethnicity, parent education) and proximal (e.g., family function, parent mental health, parenting style), also need to be considered in the developmental equation. Quality of the mother–child relationship, level of stimulation available to the child, social support structures and access to resources may all impact on development, with children from disadvantaged environments more highly represented in special education classes and at the lower end of the IQ distribution (Aylward, 1997). When such factors are linked to biological vulnerabilities, authors have argued that a '*double hazard effect*' may result (Breslau, 1990; Taylor & Alden, 1997). Thus, children with severe brain insults who come from disadvantaged environments will show particularly poor outcomes when compared to those with mild insults and from well-resourced families, which show best outcomes. The possibility of an active role for the environment

Table 2.2 Risk factors for anomalies in brain development

Prenatal factors
Maternal stress and age
Maternal health (e.g., history of infection, rubella, cytomegalovirus, AIDS, herpes simplex)
Nutrition – diet, malnutrition
Maternal drug and alcohol addiction – smoking, alcohol, marijuana, cocaine, heroin
Environmental toxins – lead, radiation, trauma
Post-natal factors
Birth complications
Nutrition
Environmental toxins – lead, radiation, trauma
Cerebral infection
Environment/experience

in enhancing development and maximising recovery in children with early brain insult argues for the importance of appropriate intervention and management. Further, it suggests that environment may be a critical modifiable risk factor for these children and families.

Conclusions

The specific details of normal brain development are rapidly becoming better understood, with new technologies enabling researchers to study the immature brain more directly. As a result, a number of developmental principles are emerging that demonstrate that early brain maturation is not a simple, linear progression. Rather, there is a gradual 'fine-tuning' of the cerebral system, characterised by initial neural growth, later specification and ultimate connectivity within and between functional systems, until optimal efficiency is achieved. This process is highly complex and tightly defined with respect to timing. Any interruption may divert the expected developmental course and ultimate outcome. Research indicates that prenatal development occurs largely according to a biologically predetermined template, with neurons generated, transported and aggregated into set neural systems via a complex and sophisticated series of developmental stages. Disruptions, either biological or environmental, occurring during this period may lead to alterations in the structural brain formation. Post-natal development may also be prespecified, although perhaps to a lesser extent. The brain is vulnerable to the influence of environmental and experiential factors throughout development into early adulthood. The consequences of this disruption may be qualitatively different, depending upon the timing and nature of disruption, with dysfunction of the elaboration and connectivity of the brain more likely post-natally.

3 Cognitive and social development

The period from birth to adulthood is characterised by dramatic progression across cognitive and social domains. This is a rich and complex process, vulnerable to external influences. Contemporary models view the child as an active participant, seeking out knowledge and skills and using past experience to understand and integrate new information, thus developing more sophisticated repertoires. Not surprisingly, attempts to increase our understanding of cognitive and social development have flourished, with cognitive, social and developmental psychologists, linguists and neuroscientists, to name but a subset, all participating in the endeavour. In this chapter, we do not attempt to address this vast literature, but rather to draw out some aspects specifically relevant in the context of early brain insult. The focus of discussion will be on the development of information processing skills, incorporating attention, memory, processing speed, executive skills and social cognition, abilities that are frequently compromised in the context of neurodevelopmental disorders and brain insults acquired during childhood. We also explore the links between acquisition of cognitive and social skills, associated parallels in brain maturation and the possible impact of cerebral insult on the subsequent development and consolidation of these processes.

When considering developmental processes and timelines, it is important to note that the study of relationships between age and cognitive skills is limited due to the imprecise markers available to map development stage. While chronological age is generally employed as an index of developmental stage, there exist significant individual differences in maturation at any given age, which means that this approach lacks precision. For example, as indicated in Table 3.1, the exact timing of the emergence of most functional abilities cannot be accurately determined, with considerable variation in the timing of skill acquisition across the normal population. Where interruption occurs in this developmental process, variability is increased, so that developmental predictions become even less reliable. Similarly, measures employed to examine developmental processes are usually multidimensional, tapping into a range of skills and complicating the ability of the clinician or scientist to address isolated cognitive abilities. For many cognitive abilities, our understanding of mature cognitive processes is incomplete, and descriptions

Table 3.1 Development of motor and perceptual skills through early childhood

Age	*Motor function*	*Visual function*	*Communication/social function*
Birth–6 weeks	Reflex sucking, rooting, swallowing Infantile grasping	Turns head, blinks to light Follows dangling ball briefly Fixes on mother's face from 3 weeks	Eye-to-eye contact Turns head to speaker
6 weeks–3 months	Increasing neck control, extends and turns neck when prone Unable to take weight on legs Finger play	Preoccupation with human face Follows dangling ball attentively Defensive blink Converges eyes for finger play	Smiles when played with
3–6 months	Grasps objects with both hands Extends arms to be lifted Takes weight on legs Rolls and sits with support	Visually alert for near and far Turns to objects in visual field Regards small objects Reaches and grasps toys	Localises sounds Loud vocalisations to others Primitive articulated sounds Noisy cries/protests when distressed Laughs aloud and shows pleasure
6–12 months	Sits independently Crawls Thumb–forefinger grasp Pulls to stand Reaches for toys without falling	Follows dangling ball in all directions Looks for fallen or hidden toys Anticipates rotating ball Increased attention span for visual stimuli	Babbles using strings of syllables Smiles at self in mirror Responds to name and familiar sounds Imitates sounds and gestures Increased reserve with strangers Demonstrates affection Seeks attention via gestures and vocalisation
1–2 years	Walks independently Crawls upstairs Kneels without support Able to release objects from grasp	Full adult visual acuity Picks up threads and small pellets	Expresses two to four words with meaning Understands several nouns Conversation-like jargon

(*continued*)

Table 3.1 (Cont.)

Age	*Motor function*	*Visual function*	*Communication/social function*
2–3 years	Runs safely Climbs on furniture Walks up and down stairs Bends and picks up objects Turns knobs Able to partially dress	Can match objects and pictures	Two- to three-word sentences Uses pronouns accurately Points to body parts Obeys simple commands Plays simple games Symbolic play emerges
3–5 years	Peddles tricycle Runs on tip-toe Climbs ladders and trees Drawing skills emerge	Recognises letters and numbers	Speech fully intelligible Extensive vocabulary Asks questions Recites nursery rhymes Plays with others
5+ years	Dresses and undresses independently Skips and hops Ties shoelaces	–	Repeats digits Names colours Gives personal details (e.g., name) Narrates/retells stories Correct grammatical usage

of the development of these skills are in their infancy. These problems are particularly evident in the field of information processing, where even adult models remain controversial.

Within the cognitive development literature, there is ongoing debate with respect to the mechanisms underpinning the maturation of cognitive abilities. Some theorists support domain-specific models and others argue for a more domain-general framework. The domain-specific approach, often applied to language development, is based on a 'modular' or 'localisationist' approach, with individual cognitive skills seen as developing according to a unique timetable and set of rules. In contrast, the domain-general view argues that the emergence of cognitive skills follows a more general blueprint, where the development of specific skills is dependent on a range of cognitive processes, more in keeping with the emergence of functional neural networks. Consistent with this domain-general perspective, information processing skills, including attention, processing speed and memory, are argued to be critical to all aspects of cognitive development (Rose Feldman & Jankowski, 2015; Rose Feldman, Jankowski, & van Rossem, 2012), with these skills measured in infancy shown to be predictive of language, working memory and achievement levels in early adolescence (Gathercole & Pickering, 2000; Rose et al., 2015). It follows that neurodevelopmental disorders and early brain insults that impact a child's information processing skills may underpin cognitive and functional impairments present later in childhood.

The information processing system may be divided into a number of processes or structures, depending on the theoretical perspective taken. For the purpose of the following discussion, we employ a model described by Cowan (1995; 1988), which is primarily structural, and incorporates components of attention, memory, processing speed and central executive. Cowan's model is an integrative, systemic model, in keeping with the domain-general framework at a cognitive level and a neural network model at a brain level (see Figure 3.1). This model postulates that the individual must first attend to

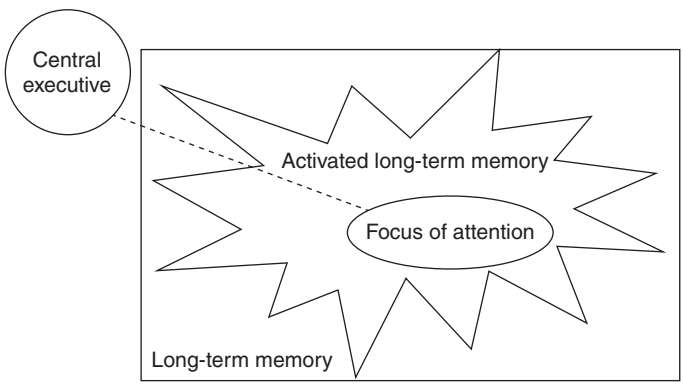


Figure 3.1 Cowan's model of information processing (Cowan, 1999)

information, register and encode it, and then store it in memory, with all these aspects of processing having limited speed and capacity. There are links across each of these steps, and directing the focus of attention and formulating strategies for efficient performance is the 'central executive', which has links with all aspects of the system. Development of these components has follow-on effects to other parts of the system. Conversely, developmental limitations in any of these components will reduce the efficiency of the system as a whole.

Attention

From a functional perspective, attentional skills are of particular significance during childhood, being critical for the development of neurocognitive systems, which in turn influence adaptive, social and academic functioning (Anderson P. J., 2002; Anderson V., 2010). If attentional skills are impaired, then children may be less able to learn and acquire skills from their environment, to function independently in day-to-day life and to make use of both formal instruction and incidental environmental learning. Accurate mapping of a child's attentional profile may enable the implementation of appropriate and accurately targeted intervention.

Theoretical models of attention

It is generally agreed that attention is represented by an integrated neural system, involving contributions from a range of structures, including the brainstem, reticular activating system and posterior and anterior cerebral regions (Mirsky, 1996; Stuss, 1999; 2006). Developmental research demonstrates that the young child has a limited attentional capacity, possibly reflecting the immaturity of these underlying neural substrates, such as unmyelinated axons and developing frontal lobes (Anderson, Anderson, Jacobs, & Spencer-Smith, 2008; Anderson, Anderson et al., 2001; McKay, Halperin, Schwartz, & Sharma, 1994). The development of attention is characterised by a systematic increase in the child's ability to override innate response tendencies and replace them with more appropriate ones in situations where it is advantageous to do so. Increases in attentional capacity depend on the ability to transmit information both within the cortex and via subcortical–cortical connections (Kinsbourne, 1996). It is argued (Hudspeth & Pribram, 1990; Klinberg et al., 1999; Thatcher, 1991) that the development of these tracts occurs in a set order, and within a set time frame, with anterior–posterior connections not fully developed until late childhood. Consistent with such a perspective are observations from the developmental psychology literature that attentional skills improve with age (Cooley & Morris, 1990; McKay et al., 1994; Waber, de Moor, Forbes, Almli et al., 2007; Welsh, Pennington, & Grossier, 1991), with different developmental trajectories identified for the separate elements of attention.

One of the earliest neuropsychological models of attention was postulated by Alexander Luria (1973), based on his work with focal lesions in adults.