Development of Human Brain Functions

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Aspects of postnatal human brain development are reviewed. The development of brain function has commonly been characterized in terms of the unfolding of a maturational sequence. In contrast, we argue that postnatal functional brain development occurs through a dynamic process of emerging patterns of interactions between different brain regions. Some of these processes may also be characteristic of perceptual and motor skill learning in adults. Possible implications of these views for our understanding of developmental disorders are raised. Biol Psychiatry 2003;54:1312–1316 © 2003 Society of Biological Psychiatry

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Introduction

Understanding the functional development of the human brain is critical for social, educational, and clinical policies. Given its importance, it is surprising that until recently very little was known about the topic; however, with the advent of suitable methods for investigating brain function in infants and children, this area of neuroscience is now making rapid progress. A critical focus of current research is the question of how the development of brain structure (neuroanatomy) relates to the emerging motor, perceptual, and cognitive functions during childhood. Another issue central to this topic concerns the developmental origin of specialized structures and processing within the brain. One perspective on this second issue is that functional specialization of regions of the cerebral cortex arises mainly through intrinsic genetic and molecular mechanisms and that experience merely plays a role in the final fine-tuning. An alternative view is that at least some aspects of human functional brain development involve a prolonged process of functional specialization that is heavily shaped by postnatal experience. A parallel debate to that among developmental neuroscientists rages among developmental psychologists. Some developmental psychologists argue that the human infant is born with innate modules and core knowledge relevant to the physical and social world. In contrast, others propose that many of the changes in behavior observed during infancy are the result of general mechanisms of learning and plasticity. In this article, I will outline these different viewpoints on typical human functional brain development and briefly discuss implications for our understanding of certain developmental disorders and the consequences of perinatal brain damage.

The Structural Development of the Human Brain

While the developmental neuroanatomy of the mammalian brain has been researched for decades, at this point relatively few studies have focused on human postnatal development. In general, human brain development appears to follow the same sequence of events observed in other primates but on a slower time schedule. One model of genetic control predicts that the more delayed the general time course of brain development in a species, the larger the relative volume of the later developing structures (such as the cerebral cortex and particularly the frontal cortex) (Clancy et al 2000). In accordance with this general prediction, the slowed rate of development in humans is associated with a relatively larger volume of cortex and an especially large frontal cortex. An additional important benefit of a slowed time course of brain development is that it potentially allows a prolonged postnatal period during which interaction with the environment can contribute to the tuning and shaping of circuitry.

There are a number of ways to study postnatal neuroanatomical development in humans. Postmortem analyses have been conducted, albeit usually on small sample sizes. Developmental positron emission tomography (PET) and magnetic resonance imaging (MRI) studies are becoming more common but are sometimes restricted to infants with suspected clinical symptoms (for detailed review of techniques currently available, see Casey and de Haan 2002). One conclusion that can be drawn at this point is that around the time of birth in humans most neurons have migrated to their appropriate locations within the cortex, hippocampus, cerebellum, and other structures (although some neurogenesis continues into adulthood). Also at birth, subcortical structures are clearly definable and closely resemble their adult forms. While the major landmarks (sulci, gyri) of the cerebral cortex are present, it remains relatively immature at birth in terms of its interregional and intraregional connectivity.
The fourfold increase in the total volume of the brain from birth to teenage years is not uniform. For example, while there is a rapid increase in synaptogenesis around the time of birth for all cortical areas studied, the timing of the most rapid burst of synapse formation and the final peak density occurs at different ages in different areas (Huttenlocher and Dabholkar 1997). In the visual cortex, there is a rapid burst of synapse formation at 3 to 4 months, and the maximum density of around 150% of adult level is reached between 4 and 12 months. Synaptogenesis also starts at the same time within the prefrontal cortex, but the density increases much more slowly and does not reach its peak until well after the first year. This differential time course of development of cortical regions is also observable in the living human brain using PET (Chugani et al 1987). During the first weeks after birth, glucose uptake is highest in sensorimotor cortex, thalamus, brainstem, and the cerebellar vermis. By 3 months, there are considerable rises in the parietal, temporal, and occipital cortices; basal ganglia; and cerebellar cortex, while such rises are not found in the frontal and dorsolateral occipital cortex until approximately 6 to 8 months. There is a continuing rise in overall resting brain metabolism (glucose uptake) after the first year of life, with a peak approximately 150% above adult levels achieved around 4 to 5 years of age for some cortical areas. As in other mammals, regressive events are also observed during human brain development. For example, PET studies reveal that while the overall level of glucose uptake reaches a peak during early childhood which is much higher than that observed in adults, the rates return to adult levels after about 9 years of age. A corresponding “rise and fall” in synaptic density (synapses per neuron) is observed with the density falling to adult levels at different ages for different cortical regions during later childhood.

In addition to the formation of dendritic trees and their associated synapses, most fibers become myelinated during postnatal development. Structural MRI images reveal that the general appearance of brain cortex is similar to that of adults by 2 years of age and that all major fiber tracts can be observed by 3 years of age (Matsuzawa et al 2001). Increases in white matter extend through adolescence into adulthood, particularly in frontal brain regions (Giedd et al 1999).

The Functional Development of the Human Brain

Relating the evidence discussed above on the neuroanatomical development of the brain to the remarkable changes in motor, perceptual, and cognitive abilities during the first decade or so of human life remains a challenging question. Considerable knowledge about the cognitive and perceptual abilities of human infants and children has accrued as a result of behavioral testing (see Johnson and Mareschal 2001 for recent review). While controversies remain, one theme that emerges from these studies is the active role played by the infant, toddler, or child in attending to novel and socially relevant stimuli and events. Thus, far from being a passive learner or blank slate, the developing infant can be viewed as an active participant in the latter stages of its own brain development.

To date, much of the research attempting to relate brain to behavioral development in humans has been from a maturational viewpoint in which the goal is to relate the maturation of particular regions of the brain, usually regions of cerebral cortex, to newly emerging sensory, motor, and cognitive functions (Figure 1A). Evidence concerning the differential neuroanatomical development of cortical regions reviewed earlier is used to determine an age when a particular region is likely to become functional. Success in a new behavioral task at this age is then attributed to the maturation of a new brain region. By this view, functional brain development is the reverse of adult neuropsychology, with the difference that specific brain regions are added in instead of being damaged. Despite the intuitive appeal of the maturational approach, it does not successfully explain some aspects of human functional brain development. For example, recent evidence suggests that some of the regions that are slowest to develop by neuroanatomical criteria show activity from shortly after birth (see below). Further, where functional activity has been assessed by functional magnetic resonance imaging (fMRI) during a behavioral transition, multiple cortical and subcortical areas appear to change their response pattern (Luna et al 2001), rather than one or two previously silent regions becoming active (mature).

In contrast to the above approach (in which intraregional connectivity matures), an alternative viewpoint, interactive specialization, assumes that postnatal functional brain development, at least within the cerebral cortex, involves a process of organizing patterns of interregional interactions (Johnson 2000) (Figure 1B). According to this view, the response properties of a specific region are partly determined by its patterns of connectivity to other regions and their patterns of activity. During postnatal development, changes in the response properties of cortical regions occur as they interact and compete with each other to acquire their role in new computational abilities. By this view, some cortical regions may begin with poorly defined functions and consequently are partially activated in a wide range of different contexts and tasks. During development, activity-dependent interactions between regions sharpen up the functions of regions such that their activity becomes restricted to a narrower set of circumstances (e.g., a region originally activated by a
A wide variety of visual objects may come to confine its response to upright human faces). The onset of new behavioral competencies during infancy will therefore be associated with changes in activity over several regions and not just by the onset of activity in one or more additional region(s). In further contrast to the maturational approach, this view predicts that during infancy, patterns of cortical activation during behavioral tasks may be more extensive than those observed in adults. Additionally, within broad constraints, successful behavior in the same tasks can be supported by different patterns of cortical activation in infants and adults.

Recent evidence does, in fact, indicate that the same behavior in infants and adults can be mediated by different structures and pathways and that there are dynamic changes in the cortical processing of stimuli during development. Experiments with scalp recorded electrical potentials have suggested that there is increasing spatial localization of selective processing with age or experience of a stimulus class. For example, for word recognition, differences between known words and control stimuli are initially found over large areas, but this difference narrows to the leads over the left temporal lobe only when vocabulary reaches around 200 words, irrespective of maturational age (Neville et al 1992). In parallel with changes in the patterns of regional activation are changes in the “tuning” of individual regions. For example, when event-related potentials (ERPs) are recorded during passive exposure to

Figure 1. A hypothetical illustration of three accounts of the neural basis of an advance in behavioral abilities in infants. (A) Represents a maturational view in which maturation of one region (in this case the dorsolateral prefrontal cortex) enables new behavioral abilities to appear. (B) Illustrates an interactive specialization view in which the onset of a new behavioral ability is due to changes in the interactions between regions that were already partially active. By this view, several regions adjust their functionality together to enable new computations. (C) Shows a third perspective, skill learning, in which certain regions become active during the acquisition of a range of new skills throughout the life span. The activation of some of these skill acquisition regions declines as expertise is developed. Reprinted with permission from Johnson (2001) by Nature Reviews Neuroscience. © 2001 Macmillan Magazines Ltd.
faces, the resulting component that is sensitive to upright human faces (the “n170”) in adults is much more broadly tuned in its response in infants. Specifically, in adults, the n170 shows a different amplitude and latency to human upright faces than to animal or inverted faces. In infants, the equivalent ERP component responds similarly to upright and inverted human faces (de Haan et al. 2002). This evidence for dynamic changes in cortical processing during infancy is consistent with a process in which interregional interactions help to shape intraregional connectivity, such that several regions together come to support particular perceptual and cognitive functions.

A third perspective on human functional brain development (termed skill learning) involves the proposal that the brain regions active in infants during the onset of new perceptual or behavioral abilities are similar, or identical to, those involved in complex skill acquisition in adults (Figure 1C). With regard to perceptual expertise, Gauthier et al. (1999) have shown that extensive training of adults with artificial objects (called “greebles”) eventually results in activation of a cortical region previously associated with face processing, the fusiform face area. This suggests that the region is normally activated by faces in adults, not because it is prespecified for faces, but due to our extensive expertise with that class of stimulus. Further, it encourages parallels with the development of face processing skills in infants (Gauthier and Nelson 2001). The extent to which parallels can be drawn between adult expertise and infant development remains unclear. Future experiments will need to trace in more detail changes in the patterns of cortical activation during training in adults and development in infants.

The differences between the three viewpoints on functional brain development described above can be illustrated by consideration of the prefrontal cortex. By neuroanatomical criteria, this region of the brain is the slowest part of the brain to develop, with detectable changes still occurring into the teenage years (Giedd et al. 1999).

According to some, maturation within the frontal lobes is related to the onset of the ability to successfully reach for desirable objects toward the end of the first year. Infants younger than 9 months often fail to accurately retrieve a hidden object after a short delay period if the object’s location is changed from one where it was previously successfully retrieved. Young infants tend to perseverate by reaching to the hiding location where the object was found on the immediately preceding trial. This error is similar to those made by human adults with frontal lesions and monkeys with lesions to the dorsolateral prefrontal cortex, leading to the proposal that the maturation of this region in human infants allows them to retain information over space and time and to inhibit prepotent responses (Diamond 2001).

Conclusions and Implications for Atypical Development

The three perspectives on human functional brain development discussed above have different implications for our understanding of developmental disorders and the effects of brain damage over the years of life. By the maturational view, genetic disorders could potentially lead to focal cortical damage and consequently to selective cognitive, motor, or perceptual disorders. Symptoms of these disorders would first become evident at the normal age of maturation of the regions concerned; however, recent reviews have concluded that there are few, if any, human developmental abnormalities of genetic origin that only affect one or two specific regions of cortex (Johnson et al. 2002). Rather, structural and functional neuroimaging usually reveal subtle but widespread differences in the brains of groups with developmental disorders. Relatedly, claims of domain-specific cognitive deficits in syndromes such as autism and Williams syndrome have been challenged and replaced with hypotheses about different styles or modes of processing (Karmiloff-Smith 1998). Finally, it is difficult to explain reports of recovery of functions following early brain damage by the maturational view without recourse to additional special mechanisms of plasticity.

According to the interactive specialization view, developmental disorders of genetic etiology will often involve disruption of the typical biases and interactions between regions that give rise to adult patterns of cortical functional specialization. By this view, subtle symptoms
should be evident from birth, but these will become compounded through the infant’s abnor-
mal interactions with its environment. While there are currently few behavioral studies of
developmental disorders during infancy, those that do exist suggest discontinuities in the
patterns of behavioral and cognitive deficits through postnatal development. For example, in
one such disorder, Williams syndrome, adults present with behavioral deficits in number tasks but show surprising proficiency in some aspects of language. A question recently investigated is whether this pattern of specific deficits is also observed in Williams syndrome infants, as would be expected if they have a damaged innate module for numbers. Standard infant paradigms for assessing number and object naming skills were used with toddlers with Williams syndrome (Paterson et al 1999). The toddlers did not show the same behavioral profile as observed in adults with the syndrome, indicating that the profile of behavioral deficits in developmental disorders can change during ontogeny and that it is not appropriate to characterize such deficits in terms of damage to domain-specific modules. From the interactive specialization perspective, it may also be easier to understand recovery of function following early damage since the same mechanisms that ensure specialization during the typical developmental trajectory could ensure a different pattern of specialization.

Further assessment of the three perspectives on human functional brain development presented in this article will require more improved methods for noninvasive functional imaging methods, such as near infrared spectroscopy (NIRS)/optical imaging, and more detailed computational models that generate predictions about both neuroanatomy and behavior (Casey and de Haan 2002). Whatever the outcome of these investigations, a better understanding of functional brain development in human infants and children may have profound consequences for educational, clinical, and social policies.

References


