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Brain Plasticity, Learning, and Developmental Disabilities

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This is a time of significant gains in methodological development for examining the developing human brain. New efforts are underway to unify the understanding of the development of brain anatomy with physiological, cellular and molecular processes that influence behavioral development. This special issue provides animal models of behavior and brain development, applications of noninvasive imaging and genetic methods to human brain development and behavior, and select reviews of how these models and methods have been applied to the examination of developmental disabilities. This issue reflects a sampling of current approaches to the study of brain plasticity, development and learning in typically and atypically developing humans and animals.
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We are in an explosive era of methodological development that has opened new doors for examining the developing human brain in vivo. Functional neuroimaging is providing new insights into the dynamics of neural circuits involved in cognitive and emotional development and genomic research is producing an abundance of new target molecules for the treatment of developmental brain disorders. With this progress, new efforts are underway to unify the understanding of functional brain anatomy with physiological, cellular and molecular processes that influence behavioral development. Such a unified understanding of mechanisms involved in cognitive and emotional development may open up new avenues for therapeutic intervention for clinical populations at the pharmacological, genetic and behavioral levels.

Recent progress in the field of developmental neuroscience is most evident in the growing number of biological studies on human brain development. Perhaps the most obvious examples are those involving noninvasive magnetic resonance imaging. Although it is true that progress in imaging methods offers a new window into the developing human brain [Casey, 2002; Casey and de Haan, 2002], other methods including animal models, computational modeling, lesion studies, and genetics, remain essential in constraining the interpretation of imaging data, informing theories of behavioral and brain development, and encouraging new interventions for atypically developing populations [Casey and Munakata, 2002; Johnson, 2001; Posner et al., 2001].

This issue highlights the importance of a converging methods approach to the study of brain development, plasticity and developmental disabilities. Brain plasticity and learning are enhanced in the immature organism relative to the mature one in the speed, quantity and quality of learning and change following experience. This type of learning has been described in the context of sensitive or critical periods—a phase of development when the brain is especially sensitive to modification by experience. Understanding the timing of early events on later development—aberrant or typical, will no doubt be informative for the development of interventions and treatments for developmental disabilities.

The significance and lasting effects of early experiences on the developing system have been characterized in a number of animal models of learning. Wilbrecht and Nottebohm show the powerful effects of timing of specific experiences on the development of song learning in zebra finches. These birds show a critical period for song memorization that occurs only a few weeks after birth and ends during puberty. Exposure to the species specific song before or after this period has little effect as the nervous system must be in a receptive state and sufficient experience must occur if the song is to be "crystallized" in memory. If, however, the songbird is deprived of hearing their species-specific song until puberty, then the critical period appears to extend remaining open for slightly longer periods of development. Experiences encountered after the critical period is closed (e.g., once the bird has received adequate experience and/or a neural pathway is irreversibly committed to a particular pattern of neuronal connectivity) have minimal effect, although Wilbrecht and Nottebohm describe experiences following song crystallization (e.g., deafening) that can result in modifications in the learned song and have been linked to changes in neurogenesis over the life span. Thus, this paper provides a number of examples showing clear interactions between experiences and genetically programmed processes that occur in this system and most likely apply to certain aspects of human learning and language. Wilbrecht and Nottebohm attempt to link the song learning literature with the developmental literature on human speech perception and production, showing similarities and differences in both the timing and plasticity of learning.

A provocative position paper by McEwen emphasizes the significance and lasting effects of early experiences on the developing system in potentially detrimental ways. McEwen ar-

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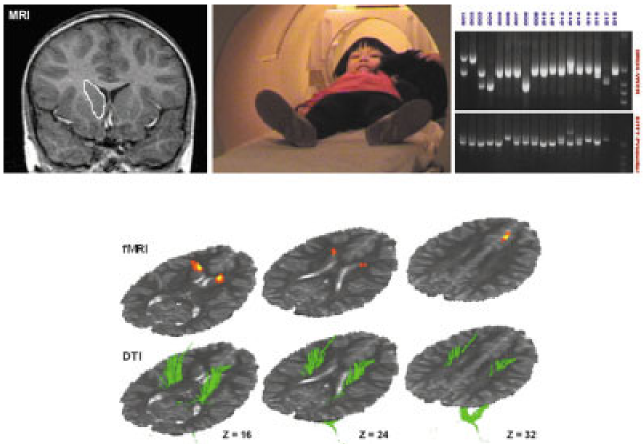

Fig. 1. An illustration of several different noninvasive tools currently being used to study human brain development, learning and plasticity. From top left to right to bottom are images of an MRI, a child in a MRI simulator, and DNA samples collected from cheek swabs, images from a fMRI study and DTI images, respectively.

gues that the child's early life has profound effects on physical as well as mental health, and argues that unstable parent-child relationships, can lead to behavioral disorders, and increased mortality and morbidity from a wide variety of common diseases later in life. This position, which is largely grounded in animal models of maternal-infant interaction, suggests that long-term unstable, early relationships are just as important to consider as clear cases of child abuse. The timing of these experiences appear to be key for defining times in development for intervening to prevent or reverse the effects of adverse early life experiences. Translational approaches such as McEwen's provide the basis for potential mechanisms of environmental and developmental determinants of individual differences in human stress reactivity, as well as anxiety, depression and related systemic disorders. These first two papers lay the critical foundation of translational evidence for how early experiences can have a profound impact, both positive and negative on the developing organism.

Developments in the human genome project and in magnetic resonance imaging methods provide us with the opportunity to more directly examine the effects of early experience on gene expression and plasticity in the developing human brain. A collection of papers describes the use of these methodologies in typically and atypically developing populations. Each paper presents a different method, from structural and functional magnetic resonance imaging (MRI) as described by both Kennedy et al. and Davidson et al., to white matter fiber tracking using diffusion tensor imaging (DTI) by Watts et al., to applications of human genetics in understanding very basic aspects of human brain development and behavior (see Fossella et al., also this issue). Figure 1 illustrates these very different techniques as a collage of images. Each of these methods together, rather than individually, can help inform and constrain our theories of biological mechanisms of human brain development and behavior and how this development may go awry in the context of developmental disabilities such as ADHD (Durston), reading disorder (McCandliss and Noble) and autism (Eigsti and Shapiro).

The last three papers of this special issue focus on developmental disabilities and the previously described models and methods for identifying biological substrates underlying these disorders. Durston provides an overview of the neurobiology of ADHD covering clinical, pharmacological, and genetic studies but emphasizing how functional neuroimaging has informed the field on the biological substrates of this disorder. This review will no doubt serve as a reference for scientists in reviewing the imaging studies of this disorder. Eigsti and Shapiro provide an excellent overview of autism spectrum disorders providing evidence for different etiologies (both genetic and environmental). They provide a nice review of the structural and functional imaging work currently being done in this area (see Kennedy et al. and Davidson et al. for more detailed description of these methods) in addition to discussing animal models of autism. Finally, McCandliss and Noble provide an overview of the current imaging literature on reading disorder. They propose a *cascading model* for the developmental progression of this disorder, in which individual differences in brain areas associated with phonological processing influence the specialization of visual areas involved in the rapid processing of written words. This work is especially exciting in the context of successful interventions that show normalization of brain activity in these brain regions and abilities with behavioral interventions.

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