Neural and Cognitive Plasticity

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Abstract

Modern humans spend much of their early lives participating in formal educational programs designed to increase their cognitive competencies. Despite this concerted effort to maximize individuals intellectual capacities, scientists and educators know relatively little about the neural factors that determine when and how learning experiences lead to improvements in cognitive abilities. Current theories of how brains are changed by learning focus on incremental adjustments to connections between neurons that are driven by increases in neural activity. This article summarizes past theoretical and experimental research on the relationship between neural plasticity and experience-dependent changes in cognition, briefly describes recent technological advances in measuring and inducing brain plasticity mechanisms, and outlines key questions that researchers must address to provide a more complete understanding of the factors that enable people to learn new cognitive skills. Answering such questions will require the combined efforts of neuroscientists, psychologists, and educational researchers, as well as the development of new technologies for monitoring neural changes in humans and other animals as they learn to perform a variety of cognitive tasks.

INTRODUCTION

The intellectual capacities of adult humans depend on numerous cognitive skills acquired through years of practice, including reading, writing, and problem-solving abilities. Although it is well known that individuals vary considerably in their capacity to gain proficiency in such skills, the specific qualities of brain structure and function that enable certain individuals to excel in situations where others struggle remain mysterious. Historically, cognitive prowess has been viewed as an intrinsic trait, a kind of mental talent endowed at birth. More recently, however, it has become clear that how a person's brain functions can be strongly experience-dependent and that the structure of brain circuitry is much more dynamic than previously assumed. Here, I summarize seminal ideas and findings that have led to this new understanding of how experience changes brain function, and consider

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how brain plasticity may contribute to (or constrain) an individual's ability to master cognitive skills.

Past studies of brain plasticity have focused on changes that occur during development, in response to brain injuries, and during learning. For the past century, scientists have heavily emphasized changes that occur in the connections between neurons. Such changes are possible because of *neural plasticity*, which is the capacity of neurons to morph over time. Neuroscience studies have revealed that neural circuits can be highly mutable, even in adults, and that changes in circuitry are correlated with changes in functional capacity. Psychological studies of learning and cognition have long assumed that learning experiences can generate internal traces of those experiences, but it has only been recently that researchers have gained access to technologies that enable them to monitor and manipulate brain changes in parallel with changes in behavior. Studies of *cognitive plasticity*, the capacity of individuals to acquire or improve cognitive skills, seek to identify the factors that determine the range of plasticity as well as ways of expanding this range.

Understanding the relationship between neural and cognitive plasticity is key for maximizing the benefits of educational and rehabilitation programs, as well as for understanding the neural substrates of cognitive abilities. Identifying how variations in brain structure and function contribute to individual differences in cognitive capacity will require the development of advanced technologies for measuring and modifying brain structure and activity, as well as collaborative interdisciplinary efforts between psychologists, educators, rehabilitation scientists, and neuroscientists.

FOUNDATIONAL RESEARCH

BRAIN PLASTICITY

The phenomenon of neural plasticity was hypothesized long before any empirical evidence of developmental or experiential changes in neural circuits was collected. William James (1890) popularized the use of the term plasticity as a property of neural circuits and theorized that all perceptual and cognitive abilities were a function of experience-driven changes in neural circuits that occurred continuously throughout an organism's life. The neuroanatomist Ramón y Cajal proposed that neurons were connected by discrete junctions (synapses) and suggested that plasticity of such connections might be an important component of regenerative processes in the nervous system (DeFelipe, 2006; Stahnisch & Nitsch, 2002). Cajal described neural plasticity as a process that enabled the brain to compensate for damaged circuits, whereas James theorized that changes in neural circuits were an inherent feature of their normal functioning and a fundamental component of all learning and memory abilities.

Cognitive Change

A third perspective on neural plasticity came from researchers studying the early development of behavior (Bischof, 1983). Lorenz (1937) observed that young birds would preferentially follow moving objects that they experienced soon after hatching, including specific people, and that this preference persisted throughout development. This type of early imprinting suggested that experiences within a developmentally restricted period (referred to as a critical or sensitive period) could have profound impacts on an individual's brain and behavior. It was later found that preferences created during such sensitive periods were largely irreversible (Bischof, 1983). Studies of imprinting in birds thus provided the first clear evidence that behavioral plasticity could vary considerably across an organism's lifespan and strong indications that experience could lead to significant shifts in the way that an individual's brain responded to highly specific events such as the visual features associated with a particular human.

Early theories of learning assumed that the acquisition of new behavioral patterns required the modification of cortical circuits (Pavlov, 1927). However, some initial neuroscience studies raised doubts about the contributions of cortical plasticity and theories of learning quickly became divorced from any assumptions about underlying neural substrates (Thompson, 1965). Studies of perceptual learning in the late 1960s set the stage for renewed interest in links between neural plasticity and learning mechanisms (Hall, 1991). In particular, Gibson and Walk's (1956) demonstrations that adults could improve their ability to distinguish visual stimuli simply by being repeatedly exposed to those stimuli revived questions about the underlying mechanisms of perceptual skill acquisition. Such behavioral results, in combination with increasing knowledge of the cortical substrates of perception, ultimately reunited the study of learning and cognition with neurobiological studies of cortical plasticity as originally conceived by James and Pavlov.

MEASURING NEURAL CORRELATES OF LEARNING

A key breakthrough in scientific studies of experience-dependent neural plasticity came when Hubel and Wiesel (1970) showed that the firing patterns of visual cortical neurons could be systematically changed by controlling the early visual experiences of kittens. They found that some neurons responded most strongly to specific visual inputs such as lines oriented at a particular angle. In other words, the neurons acted as if they were detecting visual features. Hubel and Wiesel showed that the selectivity of cortical neurons could be biased toward particular features by limiting what kittens saw. These studies established that processing of specific visual inputs early in development could change how cortical circuits functioned, as suggested by earlier studies of imprinting.

Hebb (1949) noted that rats raised by children as pets seemed to have a greater capacity to learn than his laboratory rats. This observation was later confirmed in studies comparing the maze learning abilities of rats raised in enriched environments to those of rats raised in standard laboratory housing (Rosenzweig, 1984). Researchers found that the brains of enriched rats contained cortical neurons with more extensive connections than seen in the brains of rats raised in more sterile environments (Globus, Rosenzweig, Bennett, & Diamond, 1973; Greenough, West, & DeVoogd, 1978); overall brain volume was also greater. Thus, differences in early experiences can not only change the response properties of cortical neurons, they may also lead to structural changes in neural circuits that are correlated with individual differences in learning capacity.

Studies of neural plasticity initially focused on developmental plasticity and effects of the environment on cortical structure and function. In contrast, links between associative learning and neural plasticity were sparse until the early 1970s when researchers discovered techniques for inducing long-lasting changes in the electrical activity of mammalian hippocampal circuits (Bliss & Lomo, 1973), and for observing changes in simple neural circuits of sea snails that were associated with incremental changes in learned responses (Kandel & Schwartz, 1982). The availability of these new methods for inducing and measuring changes in the neural circuits of adult animals led to a renaissance of research on the neural substrates of learning mechanisms. However, the range of learned skills that could be explored using both techniques was severely limited. Consequently, the increased understanding of mechanisms of synaptic plasticity derived from these new methods provided few insights into the factors that constrain an individual's learning capacity.

The kinds of neural plasticity postulated by James and Cajal were first demonstrated in adult monkeys. Merzenich and colleagues showed that reducing the functionality of a monkey's hand by removing a finger, or by surgically joining two fingers, led to rapid and extensive changes in cortical representations of the affected finger (Merzenich *et al.*, 1983). They interpreted these changes as evidence of compensatory plasticity within the cortex that served to counteract the loss of function. Subsequent studies showed that when monkeys learned to make fine distinctions between tactile or auditory stimuli, changes in cortical sensitivities were observed (Recanzone, Merzenich, Jenkins, Grajski, & Dinse, 1992), suggesting that learning experiences could change sensory cortical processing in adults. Such learning-related changes in cortical sensitivities were also reported during learning by nonprimates (Weinberger & Diamond, 1987). Taub (1980) found that monkeys that lost the use of an arm after sensation in that arm was surgically blocked could be rehabilitated if they were forced to use the disabled arm. Recovery was mediated in part by cortical reorganization (Taub, Uswatte, & Elbert, 2002). Collectively, these studies with adult mammals provided convincing evidence that plasticity in cortical circuits contributed to learning-related changes in perceptual and motor abilities.

MEASURING COGNITIVE PLASTICITY IN HUMANS

Unlike neural plasticity research, which historically has focused primarily on the developing brains of nonhumans, cognitive plasticity studies have emphasized the intellectual capacities of humans, concentrating heavily on factors that led to cognitive deficits at later stages of the lifespan. Baltes (1987) proposed that there were large variations in the capacity of elderly individuals to benefit from cognitive training and showed that extended training on a cognitive task could increase an older adult's abilities to levels closer to those seen in younger adults. He also developed techniques for measuring differences in individual learning capacity in an effort to identify the range of learning abilities and the biological and sociocultural limits on what individuals can learn. Studies of cognitive plasticity build on a long history of efforts to understand the factors that constrain human intellectual abilities (Mercado, 2008), but shift the emphasis from one-shot measures of cognitive performance to more longitudinal measures of changes in cognitive capacity over time.

CUTTING-EDGE RESEARCH

In the past, observations of neural plasticity have been limited to either imaging of microscopic structural features within post-mortem brain tissue or recordings of electrical activity from neurons in animals or brain tissue. Recently, however, new techniques for genetically engineering brain structure in animal models and for imaging tissue with lasers has made it possible to measure and modify changes in neural circuits with unprecedented precision. For instance, *optogenetics* enables researchers to visualize dynamic structural changes in synapses, dendrites, and dendritic spines in behaving animals (Bernstein & Boyden, 2011; Fenno, Yizhar, & Deisseroth, 2011). Used in combination with sophisticated laser technologies (Holtmaat, Randall, & Cane, 2013; Knott & Holtmaat, 2008), researchers can now artificially stimulate and inhibit specific types of neurons in particular areas (Andrasfalvy, Zemelman, Tang, & Vaziri, 2010; Smith & Graybiel, 2013), and can also remove parts of individual neurons, including pruning individual axons, dendrites, and dendritic spines (Holtmaat *et al*., 2013). Furthermore, light-based manipulations tend to cause less damage than more traditional electrophysiological and pharmacological techniques, increasing the repeatability of manipulations to neural circuits (Smith & Graybiel, 2013). In some cases, this has made it possible to use colored light to control an organism's developmental trajectory (Schultheis, Liewald, Bamberg, Nagel, & Gottschalk, 2011). Techniques involving introducing nanoparticles into the membranes of neurons provide yet another way of precisely controlling the activity of individual neurons (Huang, Delikanli, Zeng, Ferkey, & Pralle, 2010). These new technologies provide a wealth of opportunities for exploring detailed interactions within neural circuits as well as how synapses are affected by different experiences.

The most impressive examples of neural plasticity occur during the early stages of development, as noted in the description of sensitive periods. Originally, periods of increased sensitivity were thought to be limited to specific stages along an individual's developmental trajectory. Recent research has revealed, however, that it is possible to manipulate the timing, duration, and closure of critical periods in sensory systems and that in some cases such periods can be reactivated in adulthood (Hensch, 2004; Hooks & Chen, 2007). Surprisingly, researchers have discovered that reactivation of critical periods in adults does not require invasive surgery, neurostimulation, or pharmacological interventions, but can be achieved simply by systematically changing the sensory stimulation that an individual receives (Duffy & Mitchell, 2013; He, Hodos, & Quinlan, 2006; de Villers-Sidani, Simpson, Lu, Lin, & Merzenich, 2008; Zhou, Panizzutti, de Villers-Sidani, Madeira, & Merzenich, 2011). The ability to control levels of brain plasticity has important implications for the development of new educational strategies, therapies, and approaches to minimizing deficits associated with cognitive aging. As techniques for controlling brain plasticity become more sophisticated, this will afford new opportunities for studying how variations in neural plasticity impact an individual's ability to learn new cognitive skills.

The capacity for brain plasticity to vary over time, either as a function of development, experience, or artificial manipulations has been described as *metaplasticity* (Abraham, 2008; Hulme, Jones, & Abraham, 2013; Sehgal, Song, Ehlers, & Moyer, 2013). Recent research suggests that mechanisms of metaplasticity provide a way for brains to dynamically adjust the capacity of neural circuits to change, thereby potentially increasing or decreasing learning capacity in a context-dependent manner (Hulme *et al*., 2013). Degradation of neural plasticity within and across individuals may be associated with abnormalities in learning abilities (Dovgopoly & Mercado, 2013), and a loss of cognitive abilities (Hulme *et al.*, 2013). Conversely, techniques for globally increasing neural plasticity, such as those described in relation to sensitive periods, may potentially provide new ways of enhancing rehabilitation after brain damage. In addition to possible implications for treating disorders, manipulations of metaplasticity are also becoming more relevant for the general population. Specifically, there is increasing interest in the potential for typically functioning individuals to use drugs to enhance their learning capacity (Greely *et al.*, 2008; Smith & Farah, 2011). Researchers are also beginning to explore new techniques for noninvasively modulating metaplasticity in adults, such as transcranial magnetic and electrical stimulation (Cappelletti *et al.*, 2013; Kadosh, Levy, O'Shea, Shea, & Savulescu, 2012). Such studies suggest that the relative benefits and costs of artificially controlling levels of neural plasticity vary considerably across individuals and that extensive research will be needed to determine how one might use manipulations of metaplasticity to optimize an individual's learning potential without leading to unintended negative consequences.

Neuroimaging studies of cognitive processing have focused heavily on localizing brain regions that are differentially activated during the performance of specific tasks, including cognitive skills such as reading (Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003), calculating (Butterworth & Walsh, 2011), and musical processing (Ellis *et al.*, 2012). There has been developing interest in understanding how activation in such regions changes with practice (Chein & Schneider, 2005; Ellis *et al.*, 2012; Ischebeck *et al.*, 2006), and most recently in how cognitive training can change brain structure in adults (He *et al.*, 2006; Lovden, Wenger, Martensson, Lindenberger, & Backman, 2013; Welcome, Chiarello, Thompson, & Sowell, 2011). More attention is also being given to identifying the role of genetics versus experience in determining individual variations in cognitive plasticity (He *et al.*, 2006; Mercado, 2008; Pinel & Dehaene, 2013; Welcome *et al.*, 2011), and to clarifying the role of neural plasticity in cognitive aging (Greenwood & Parasuraman, 2010). Future efforts that combine interventions such as neurostimulation and cognitive training with neuroimaging (e.g., Cappelletti *et al.*, 2013) will be important for understanding how processing can be modified in human brains.

KEY ISSUES FOR FUTURE RESEARCH

The dynamic nature of neural processes undoubtedly shapes the ways in which people and other animals are able to think and learn. Although neuroscientists have conclusively established that experience can modify neural circuits, the understanding of how such changes may impact cognitive processes remains limited. A basic assumption of current educational systems is that schooling at any age can promote positive changes in intellectual competence and that accumulation of knowledge, in particular, is critical to maximizing an individual's intellectual potential. However, essentially nothing is known about the direct impact of this practice on brain circuitry and function, making it difficult to evaluate the actual neural costs or benefits of current educational approaches. Furthermore, it is now known that levels of neural plasticity are themselves dependent on experience, such that periods of high plasticity can be either shortened or extended depending on the types of events that an individual experiences. Discovering new ways of fostering and assessing the brain changes that give rise to improvements in cognitive abilities is a major challenge for future research on the efficacy of different educational approaches.

A key question that researchers have yet to adequately address is what specific factors determine when and how much neural circuits change. While it is known that a structured sequence of gene expression gives rise to the basic organizational structure of each individual's brain, it is less clear how sensitive different time points along these trajectories might be to different environmental influences. Similarly, the extent to which an individual's cognitive abilities might be enhanced (or degraded) through targeted behavioral, pharmaceutical, or technological interventions delivered at particular points in development is unknown. Ethical considerations preclude detailed studies of such issues in humans, making it important to develop new ways of investigating processes of neural and cognitive plasticity in nonhumans. A major challenge for this approach is to discover ways of increasing the complexity of cognitive skills that can be learned by animals so that cognitive training in animals leads to mental processing that more closely approximates the kinds of cognitive acts typically engaged in by modern humans. This may also require creating new kinds of animals (e.g., through genetic engineering or neuroengineering) with neural circuitry and brain organization that is more similar to that of humans (an approach which raises its own set of ethical dilemmas).

Along with efforts to clarify how changes in neural plasticity can naturally impact levels of cognitive plasticity, there is interest in developing techniques for artificially accelerating brain changes, including changes that may increase the efficacy of compensatory responses to brain damage or the benefits of behavioral training for cognitive performance. More refined techniques for controlling when particular circuits become engaged, and to what extent, can profoundly impact how rapidly neural circuits reorganize as well as which circuits change. Given the large individual differences in brain circuits across the lifespan and between individuals, techniques for directly measuring the impact of different interventions and for adaptively customizing treatments based on the efficacy of a particular approach are sorely needed. It will also be important to develop models of the long-term impact of artificially remodeling neural circuits to determine when such interventions might lead to unintended negative side effects.

The potential benefits of understanding mechanisms of neural and cognitive plasticity are far reaching in both educational and medical contexts. Such knowledge is also fundamentally important for understanding human cognition more generally. Philosophers, theologians, and scientists alike have often pointed to the superior intellectual capacities of humans as evidence of their unique status among living things, and theories abound about the properties of human brains and minds that confer humans with these enhanced abilities. The current consensus view is that human brains can give rise to cognitive processes that the brains of other animals cannot. However, whether such constraints arise because of fundamental differences in neural architectures or because of more subtle differences in the availability or capacity of particular circuitry remains a topic of debate. Consequently, it remains to be seen what type of brain circuits are necessary to endow an individual with a given level of cognitive plasticity or what levels of plasticity are necessary for an individual to learn any given cognitive skill at a level comparable to modern humans.

Many of the cognitive skills commonly taught in elementary schools are relatively recent cultural inventions that arose through social trial-and-error long before there was any scientific awareness of the role of brain circuitry in cognition. As scientific understanding of the neural constraints on cognition grows, it is likely that new ways of overcoming existing constraints on cognitive development will be discovered, as well as new cognitive skills that enable humans to think in ways that they have never thought before.

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