INSIGHT INTO NEURAL PLASTICITY: AN OVERVIEW

S. Sarangi, A. P. K. Mahapatra, A. K. Kundu and S. Mohapatra

Department of Veterinary Physiology,

College of Veterinary Science and Animal Husbandry,

OUAT, Bhubaneswar, Odisha, India

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Corresponding Author : subhashreesarangi2010@gmail.com

ABSTRACT

Plasticity is a prominent feature of mammalian brain, particularly the visual cortex. Although such neural changes are most evident during development, adult cortical circuits can be modified by a variety of manipulations, such as perceptual learning and visual deprivation. Elucidating the underlying mechanisms at cellular and synaptic levels is an essential step in understanding neural plasticity in mature animal. Notable differences between developmental and adult plasticity may be attributed to developmental cortical changes at multiple levels. These range from shifts in molecular profiles of cortical neurons to changes in spatiotemporal dynamics of network activity. In this review, we have discussed earlier developments, recent progress and remaining challenges in understanding neural plasticity as a whole. Optical imaging and multi electrode recording techniques have greatly expanded our ability to study neuronal populations in awake behaving animals which will ultimately allow us to understand how cortical plasticity operates in natural sensory and behavioural contexts.

KEYWORDS: Cortical Remapping, Synaptic Pruning, Neurogenesis, Traumatic brain injury (TBI), Medial preoptic area (mPOA), Lesioned rats.

INTRODUCTION

Neural plasticity or cortical remapping describes how experiences reorganize neural pathways and synapses in the brain which are due to changes in behavior, environment and neural processes, as well as changes resulting from physical injury (Pascual-Leone *et al.*, 2011). Long lasting functional changes in the brain occur when we learn new things or memorize new information. These changes in neural connections refer to the brain's unique ability to constantly change, grow, and remap itself over the course of a lifetime. The "plastic" in this sense refers to "mouldable," rather than to the family of products derived from petrochemicals. This distinctive trait makes the brain a very valuable organ, as it can constantly adapt itself to deal with new input and information. All animals possess this characteristic to some extent, although most studies have focused specifically on the workings of the human brain.

EARLY DEVELOPMENT: TOWARDS A BEGINNING

Until around the 1970s, an accepted idea across neuroscience was that the nervous system was essentially fixed throughout adulthood, both in terms of brain functions, as well as the idea that it was impossible for new neurons to develop after birth. Italian anatomist Malacarne (1793) carried experiments in which he paired rats, trained one of the pair extensively for years, and then dissected both. He observed that the cerebellums of the trained rats were substantially larger. The idea that the brain and its functions are not fixed throughout adulthood was proposed in 1890 by William James in *The Principles of Psychology*, though the idea was largely neglected (James, 1890). Lashley *et al.* (1923) conducted experiments on rhesus monkeys demonstrating changes in neuronal pathways and gave evidence of plasticity which was not widely accepted by neuroscientists. Bach-y-Rita (1969), the father of sensory substitution and brain plasticity, invented a device named

"Blind Port" that allowed blind people to read, perceive shadows, and distinguish between close and distant objects. He thought, "We see with our brains, not with our eyes". Michael Merzenich (1998) a neuroscientist who has been one of the pioneers of neuroplasticity for over three decades has made some of "the most ambitious claims for the field - that brain exercises may be as useful as drugs to treat diseases as severe as schizophrenia - that plasticity exists from cradle to the grave, and that radical improvements in cognitive functioning - how we learn, think, perceive, and remember are possible even in the elderly (Buonomano and Merzenich, 1998). Merzenich's work was affected by a crucial discovery made by Hubel and Wiesel (1970) in their work with kittens. The experiment involved sewing one eye shut and recording the cortical brain maps. Hubel and Wiesel (1970) saw that the portion of the kitten's brain associated with the shut eye was not idle, as expected. Instead, it processed visual information from the open eye (Hubel and Wiesel, 1970).

UNDERLYING MECHANISMS

The brain is composed of approximately 100 billion neurons. Early scientists believed that neurogenesis, or the creation of new neurons, stopped shortly after birth. Today, it is understood that the brain possesses the remarkable capacity to reorganize pathways, create new connections and in some cases, even create new neurons. There are some factors which govern neural plasticity. Firstly, neuroplasticity includes several different processes that take place throughout the lifetime. It does not consist of a single type of morphological change, but rather includes several different processes that occur throughout an individual's lifetime. Many types of brain cells are involved in neuroplasticity, including neurons, glia, and vascular cells. Secondly, neuroplasticity has a clear age-dependent determinant. Although plasticity occurs over an individual's lifetime, different types of plasticity dominate during certain periods of one's life and are less prevalent during other periods. Thirdly, neuroplasticity occurs in the brain under two primary conditions, the first one during normal brain development when the immature brain first begins to process sensory information through adulthood (developmental plasticity and plasticity of learning and memory), and the second one as an adaptive mechanism to compensate for lost function and/or to maximize remaining functions in the event of brain injury. Fourthly, environment plays an essential role in the process, but genetics can also have an influence. In addition to genetic factors, the brain is shaped by the characteristics of an individual's environment and by the actions of the same individual.

Developmental Plasticity: Synaptic Pruning

Following birth, the brain of a newborn is flooded with information from its sense organs. This sensory information must somehow make it back to the brain where it can be processed. To do so, nerve cells must make connections with one another, transmitting the impulses to the brain. Like the basic telephone trunk lines strung between cities, the newborn's genes instruct the "pathway" to the correct area of the brain from a particular nerve cell.

Over the first few years of life, the brain grows rapidly. As each neuron matures, it sends out multiple branches i.e.axons, (which send information out) and dendrites (which take in information), increasing the number of synaptic contacts and laying the specific connections from house to house, or in the case of the brain, from neuron to neuron. At birth, every neuron in the cerebral cortex has an estimated 2,500 synapses; by age of three, this number has grown to a whopping 15,000 synapses per neuron. The average adult, however, has about half that number of synapses. Why? Because as one gains new experiences, some connections are strengthened while others are eliminated. This process is known as synaptic pruning. Neurons that are used frequently develop stronger connections and those that are rarely or never used eventually die. By developing new connections and pruning away weak ones, the brain is able to adapt to the changing environment.

Plasticity of Learning and Memory

It was once believed that as we aged, the brain's networks became fixed. In the past two decades, however, an enormous amount of research has revealed that the brain never stops changing and adjusting. Learning is defined as the ability to acquire new knowledge or skills through instruction or experience. Memory is the process by which that knowledge is retained over time. The capacity of the brain to change with learning is plasticity. So how does the brain change with learning? There appears to be at least two types of modifications that occur in the brain with learning, first a change in the internal structure of the neurons, the most noticeable being in the area of synapses, and second an increase in the number of synapses between neurons. Initially, newly learned data are "stored" in short-term memory, which is a temporary ability to recall a few pieces of information. Some evidence supports the concept that short-term memory depends upon electrical and chemical events in the brain as opposed to structural changes such as the formation of new synapses. After a period of time, information may be moved into a more permanent type of memory, long-term memory, which is the result of anatomical or biochemical changes that occur in the brain.

Injury-induced Plasticity: Plasticity and Brain Repair

During brain repair following injury, plastic changes are geared towards maximizing function in spite of the damaged brain. In studies involving rats in which one area of the brain was damaged, brain cells surrounding the damaged area underwent changes in their function and shape that allowed them to take on the functions of the damaged cells. This phenomenon is clearly indicated in male Wistar rats. Even after bilateral destruction of neurons in the mPOA, following intracerebral injection of N-methyl D-aspartic acid (NMDA), the rest of the brain including the left over mPOA had the ability to increase the quantity of sleep that was reduced by cold exposure (Mahapatra *et al.*, 2005).

RECENT DEVELOPMENTS

There is strong evidence that neurogenesis (birth of brain cells) occurs in the adult, mammalian brain—and such changes can persist well into old age (Rakic, 2002). The evidence for neurogenesis is mainly restricted to the hippocampus and olfactory bulb, but current research has revealed that other parts of the brain, including the cerebellum, may be involved as well (Ponti et al., 2008). In the rest of the brain, neurons can die, but they cannot be created. The manner in which experience can influence the synaptic organization of the brain is also the basis for a number of theories of brain function including the general theory of mind and epistemology referred to as Neural Darwinism and developed by immunologist Nobel laureate Gerald Edelman. Robot assisted therapy is an emerging technique, which is also hypothesized to work by way of neuroplasticity, though there is currently insufficient evidence to determine the exact mechanisms of change when using this method.

One of the most recent applications of neuroplasticity involves work done by a team of doctors and scientist at Emory University, specifically Cutler *el al.* (2007) and Wright *et al.* (2007) noticed that female mice seemed to recover from brain injuries better than male mice. Also in females, he noticed that at certain points in the estrus cycle females recovered even more may be due to high levels of progesterone and showed that administration of progesterone after traumatic brain injury (TBI) and stroke reduces edema, inflammation, and neuronal cell death, and enhance spatial reference memory and sensory motor recovery" (Cutler *et al.*, 2007).

Michael Merzenich developed a series of "plasticity-based computer programs known as Fast ForWord" which offers seven brain exercises to help with the language and learning deficits of dyslexia. The data collected from the study indicated that a neuroplasticity-based program could notably improve cognitive function and memory in adults with ARCD (Merzenich *et al.*, 1984). Binocular vision improvements and stereopsis recovery are now active areas of scientific and clinical research.

Implantation of a sensory prosthesis, in patients with congenital hearing impairment, has shown to activate the auditory system and help in its functional maturation (Kral and Sharma, 2012). Due to a sensitive period for plasticity, there is also a sensitive period for such intervention within the first 2–4 years of life.

The experience of Phantom limbs is a phenomenon in which a person continues to feel pain or sensation within a part of their body which has been amputated. This is strangely common occurring in 60-80% of amputees (Beaumont *et al.*, 2011). An explanation for this refers to the concept of neuroplasticity, as the cortical maps of the removed limbs are believed to have become engaged with the area around them in the postcentral gyrus. Moseley and Brugger (2009) carried out a remarkable experiment in which they encouraged arm amputee subjects to use visual imagery to contort their phantom limbs into impossible configurations. This experiment suggests that the subjects had modified the neural representation of their phantom limbs and generated the motor commands needed to execute impossible movements in the absence of feedback from the body.

Individuals who suffer from chronic pain experience prolonged pain at sites that may have been previously injured, yet are otherwise currently healthy. This phenomenon is related to neuroplasticity due to a maladaptive reorganization of nervous system, both peripherally and centrally. During the period of tissue damage, noxious stimuli and inflammation cause an elevation of nociceptive input from the periphery to the central nervous system. Prolonged nociception from periphery will then elicit a neuroplastic response at the cortical level to change its somatotopic organization for the painful site, inducing central sensitization (Seifert and Maihöfner, 2011).

In a study, Yu-Fan *et al.*, (2009) made two groups of mice swim a water maze, and then in a separate trial subjected them to an unpleasant stimulus to see how quickly they would learn to move away from it. Then, over the next four weeks they allowed one group of mice to run inside their rodent wheels, an activity most mice enjoy, while they forced the other group to work harder on mini treadmills at a speed and duration controlled by the scientists. They then tested both groups again to track their learning skills and memory. Both groups of mice improved their performances in the water maze from the earlier trial. But only the extra-worked treadmill runners were better in the avoidance task, a skill that, according to neuroscientists, demands a more complicated cognitive response. The mice that were forced to run on the treadmills showed evidence of molecular changes in several portions of their brains when viewed under a microscope, while the voluntary wheel-runners had changes in only one area.

CONCLUSION

Decades of research have now shown that substantial changes occur in the lowest neocortical processing areas, and that these changes can profoundly alter the pattern of neuronal activation in response to experience. Neuroscientific research indicates that experience can actually change both the brain's physical structure (anatomy), i.e., structural plasticity and functional organization (physiology) otherwise called functional plasticity as seen in mPOA lesioned rats exposed to acute and then chronic mild cold ambient temperature. Neuroscientists are currently engaged in a reconciliation of critical period studies demonstrating the immutability of the brain after development with the more recent research showing how the brain can, and does, change, and how the brain shapes in the way in which one wants to shape it, for the good, or the bad.

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