Neuroplasticity (Neuroplasticity, 2010)

From Wikipedia

Neuroplasticity challenges the idea that brain functions are fixed in certain locations.

**Neuroplasticity** (also referred to as brain plasticity, cortical plasticity or cortical re-mapping) is the changing of neurons, the organization of their networks, and their function via new experiences. This idea was first proposed in 1890 by William James in *The Principles of Psychology*, though the idea was largely neglected for the next fifty years. The first person to use the term neural plasticity appears to have been the Polish neuroscientist Jerzy Konorski.

The brain consists of nerve cells (or "neurons") and glial cells which are interconnected, and learning may happen through change in the strength of the connections, by adding or removing connections, or by adding new cells. "Plasticity" relates to learning by adding or removing connections, or adding cells. During the 20th century, the consensus was that lower brain and neocortical areas were immutable in structure after childhood, meaning learning only happens by changing of connection strength, whereas areas related to memory formation, such as the hippocampus and dentate gyrus, where new neurons continue to be produced into adulthood, were highly plastic. This belief is being challenged by new findings, suggesting all areas of the brain are plastic even after childhood. Hubel and Wiesel had demonstrated that ocular dominance columns in the lowest neocortical visual area, V1, were largely immutable after the critical period in development. Critical periods also were studied with respect to language; the resulting data suggested that sensory pathways were fixed after the critical period. However, studies determined that environmental changes could alter behavior and cognition by modifying connections between existing neurons and via neurogenesis in the hippocampus and other parts of the brain, including the cerebellum.

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. According to the theory of neuroplasticity, thinking, learning, and acting
actually change both the brain's physical structure (anatomy) and functional organization (physiology) from top to bottom. Neuroscientists are presently engaged in a reconciliation of critical period studies demonstrating the immutability of the brain after development with the new findings on neuroplasticity, which reveal the mutability of both structural and functional aspects. A substantial paradigm shift is now under way: Canadian psychiatrist Norman Doidge has in fact stated that neuroplasticity is "one of the most extraordinary discoveries of the twentieth century."

**Neurobiology**

**Cortical maps**

Cortical organization, especially for the sensory systems, is often described in terms of maps. For example, sensory information from the foot projects to one cortical site and the projections from the hand target in another site. As the result of this somatotopic organization of sensory inputs to the cortex, cortical representation of the body resembles a map (or homunculus).

In the late 1970s and early 1980s, several groups began exploring the impacts of removing portions of the sensory inputs. Michael Merzenich and Jon Kaas and Doug Rasmusson used the cortical map as their dependent variable. They found—and this has been since corroborated by a wide range of labs—that if the cortical map is deprived of its input it will become activated at a later time in response to other, usually adjacent inputs. At least in the somatic sensory system, in which this phenomenon has been most thoroughly investigated, JT Wall and J Xu have traced the mechanisms underlying this plasticity. Re-organization is not cortically emergent, but occurs at every level in the processing hierarchy; this produces the map changes observed in the cerebral cortex.

Merzenich and William Jenkins (1990) initiated studies relating sensory experience, without pathological perturbation, to cortically observed plasticity in the primate somatosensory system, with the finding that sensory sites activated in an attended operant behavior increase in their cortical representation. Shortly thereafter, Ford Ebner and colleagues (1994) made similar efforts in the rodent whisker barrel cortex (also somatic sensory system). These two groups largely diverged over the years. The rodent whisker barrel efforts became a focus for Ebner, Matthew Diamond, Michael Armstrong-James, Robert Sachdev, Kevin Fox and great inroads were made in identifying the locus of change as being at cortical synapses expressing NMDA receptors, and in implicating cholinergic inputs as necessary for normal expression. However, the rodent studies were poorly focused on the behavioral end, and Ron Frostig and Daniel Polley (1999, 2004) identified behavioral manipulations as causing a substantial impact on the cortical plasticity in that system.

Merzenich and DT Blake (2002, 2005, 2006) went on to use cortical implants to study the evolution of plasticity in both the somatosensory and auditory systems. Both systems show similar changes with respect to behavior. When a stimulus is cognitively associated with reinforcement, its cortical representation is strengthened and enlarged. In some cases, cortical representations can increase two to threefold in 1–2 days at the time at which a new sensory motor behavior is first acquired, and changes are largely finished within at most a few weeks.
Control studies show that these changes are not caused by sensory experience alone: they require learning about the sensory experience, and are strongest for the stimuli that are associated with reward, and occur with equal ease in operant and classical conditioning behaviors.

An interesting phenomenon involving cortical maps is the incidence of phantom limbs (see Ramachandran for review). This is most commonly described in people that have undergone amputations in hands, arms, and legs, but it is not limited to extremities. The phantom limb feeling, which is thought to result from disorganization in the brain map and the inability to receive input from the targeted area, may be annoying or painful. Incidentally, it is more common after unexpected losses than planned amputations. There is a high correlation with the extent of physical remapping and the extent of phantom pain. As it fades, it is a fascinating functional example of new neural connections in the human adult brain.

The concept of plasticity can be applied to molecular as well as to environmental events. The phenomenon itself is complex and can involve many levels of organization. To some extent the term itself has lost its explanatory value because almost any changes in brain activity can be attributed to some sort of "plasticity". For example, the term is used prevalently in studies of axon guidance during development, short-term visual adaptation to motion or contours, maturation of cortical maps, recovery after amputation or stroke, and changes that occur in normal learning in the adult. Plasticity in more recent writing is frequently described as a property of the central nervous system with the term reorganization used to introduce the specific types of changes observed including axonal sprouting, long-term potentiation or the expression of plasticity related genomic responses Pinaud.

Norman Doidge, following the lead of Michael Merzenich, separates manifestations of neuroplasticity into adaptations that have positive or negative behavioral consequences. For example, if an organism can recover after a stroke to normal levels of performance, that adaptiveness could be considered an example of "positive plasticity". An excessive level of neuronal growth leading to spasticity or tonic paralysis, or an excessive release of neurotransmitters in response to injury which could kill nerve cells; this would have to be considered a "negative" plasticity. In addition, drug addiction and obsessive-compulsive disorder are deemed examples of "negative plasticity" by Dr. Doidge, as the synaptic rewiring resulting in these behaviors is also highly maladaptive.

A 2005 study found that the effects of neuroplasticity were even more rapidly than previously expected. Medical students' brains were imaged during the period when they were studying for their exams. In a matter of months, the students' gray matter increased significantly in the posterior and lateral parietal cortex.

**History**

**Proposal**

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.
The idea that the brain and its functions are not fixed throughout adulthood was first proposed in 1890 by William James in *The Principles of Psychology*, though the idea was largely neglected.

**Research and discovery**

In 1923, Karl Lashley conducted experiments on rhesus monkeys which demonstrated changes in neuronal pathways, which he concluded to be evidence of plasticity, although despite this, as well as further examples of research suggesting this, the idea of neuroplasticity was not widely accepted by neuroscientists. However, more significant evidence began to be produced in the 1960s and after, notably from scientists including Paul Bach-y-Rita, Michael Merzenich along with Jon Kaas, as well as several others. [13][14]

In the 1960s, Paul Bach-y-Rita invented a device that allowed blind people to read, perceive shadows, and distinguish between close and distant objects. This “machine was one of the first and boldest applications of neuroplasticity.” The patient sat in an electrically stimulated chair that had a large camera behind it which scanned the area, sending electrical signals of the image to four hundred vibrating stimulators on the chair against the patient’s skin. The six subjects of the experiment were eventually able to recognize a picture of the supermodel Twiggy. It must be emphasized that these people were congenitally blind and had previously not been able to see. Bach-y-Rita believed in sensory substitution; if one sense is damaged, your other senses can sometimes take over. He thought skin and its touch receptors could act as a retina (using one sense for another). In order for the brain to interpret tactile information and convert it into visual information, it has to learn something new and adapt to the new signals. The brain's capacity to adapt implied that it possessed plasticity. He thought, “We see with our brains, not with our eyes.”

A tragic stroke that left his father paralyzed inspired Bach-y-Rita to study brain rehabilitation. His brother, a physician, worked tirelessly to develop therapeutic measures which were so successful that the father recovered complete functionality by age 68 and was able to live a normal, active life which even included mountain climbing. “His father’s story was firsthand evidence that a ‘late recovery’ could occur even with a massive lesion in an elderly person.” He found more evidence of this possible brain reorganization with Shepherd Ivory Franz’s work. One study involved stroke patients who were able to recover through the use of brain stimulating exercises after having been paralyzed for years. “Franz understood the importance of interesting, motivating rehabilitation: ‘Under conditions of interest, such as that of competition, the resulting movement may be much more efficiently carried out than in the dull, routine training in the laboratory'(Franz, 1921, pg.93).” This notion has led to motivational rehabilitation programs that are used today.

Michael Merzenich is a neuroscientist who has been one of the pioneers of brain plasticity for over three decades. He 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.” Merzenich’s work was affected by a crucial discovery made by David Hubel and Torsten Wiesel in their work with kittens. The experiment involved sewing one eye shut and recording the cortical brain maps.
Hubel and Wiesel 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. It was “… as though the brain didn’t want to waste any ‘cortical real estate’ and had found a way to rewire itself.” This implied brain plasticity during the critical period. However, Merzenich argued that brain plasticity could occur beyond the critical period. His first encounter with adult plasticity came when he was engaged in a postdoctoral study with Clinton Woosley. The experiment was based on observation of what occurred in the brain when one peripheral nerve was cut and subsequently regenerated. The two scientists micromapped the hand maps of monkey brains before and after cutting a peripheral nerve and sewing the ends together. Afterwards, the hand map in the brain that was expected to be jumbled was nearly normal. This was a substantial breakthrough. Merzenich asserted that “if the brain map could normalize its structure in response to abnormal input, the prevailing view that we are born with a hardwired system had to be wrong. The brain had to be plastic.”

Richard Davidson

Richard Davidson is a Harvard-trained neuroscientist at the University of Wisconsin–Madison's W.M. Keck Laboratory for Functional Brain Imaging and Behavior. He has led experiments in cooperation with the Dalai Lama on effects of meditation on the brain. His results suggest "alterations in patterns of brain function assessed with functional magnetic resonance imaging (fMRI), changes in the cortical evoked response to visual stimuli that reflect the impact of meditation on attention, and alterations in amplitude and synchrony of high-frequency oscillations that probably play an important role in connectivity among widespread circuitry in the brain."

Applications and examples

Treatment of brain damage

A surprising consequence of neuroplasticity is that the brain activity associated with a given function can move to a different location; this can result from normal experience and also occurs in the process of recovery from brain injury. Neuroplasticity is the fundamental issue that supports the scientific basis for treatment of acquired brain injury with goal-directed experiential therapeutic programs in the context of rehabilitation approaches to the functional consequences of the injury.

The adult brain is not "hard-wired" with fixed and immutable neuronal circuits. There are many instances of cortical and subcortical rewiring of neuronal circuits in response to training as well as in response to injury. There is solid evidence that neurogenesis, the formation of new nerve cells, occurs in the adult, mammalian brain—and such changes can persist well into old age. 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. In the rest of the brain, neurons can die, but they cannot be created. However, there is now ample evidence for the active, experience-dependent re-organization of the synaptic networks of the brain involving multiple inter-related structures including the cerebral cortex. The specific details of how this process occurs at the molecular and ultrastructural levels are topics of active
neuroscience research. 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. The concept of neuroplasticity is also central to theories of memory and learning that are associated with experience-driven alteration of synaptic structure and function in studies of classical conditioning in invertebrate animal models such as Aplysia. This latter program of neuroscience research has emanated from the ground-breaking work of another Nobel laureate, Eric Kandel, and his colleagues at Columbia University College of Physicians and Surgeons.

**Treatment of learning difficulties**

Michael Merzenich developed a series of “plasticity-based computer programs known as Fast ForWord.” FastForWord offers seven brain exercises to help with the language and learning deficits of dyslexia. In a recent study, experimental training was done in adults to see if it would help to counteract the negative plasticity that results from age-related cognitive decline (ARCD). The ET design included six exercises designed to reverse the dysfunctions caused by ARCD in cognition, memory, motor control, and so on. After use of the ET program for 8–10 weeks, there was a “significant increase in task-specific performance.” The data collected from the study indicated that a brain plasticity-based program could notably improve cognitive function and memory in adults with ARCD.