

Neural Plasticity: Merzenich, Taub, and Greenough

BY ERIN CLIFFORD

Introduction

The study of neural plasticity has important implications for psychological development. Plasticity refers to the brain's ability to change and reorganize in response to some change in input from internal or external sources. Three types of plasticity, "experience-independent" (Shatz, 1992), "experience-expectant," and "experience-dependent" are utilized in normal development (Black & Greenough, 1997). Three of the leading researchers who have studied the mechanisms and effects of experience-dependent plasticity are Michael Merzenich, Edward Taub, and William Greenough. This paper will attempt to present their respective findings in a concise manner relevant to the study of human development.

Experience-independent plasticity

Experience-independent plasticity refers to changes in the brain which are not the result of external environmental changes or influence. The brain sculpts itself in part through spontaneous, internally-generated activity which occurs independently of any outside influence. One of the best known examples of experience-independent plasticity is the formation of layers in the lateral geniculate nucleus of the thalamus, the brain structure which relays signals to the visual cortex (Shatz, 1992). Alternating, eye-specific layers form in the lateral geniculate nucleus prior to the development of light receptors. In order to form the layers correctly, ganglion cells in the retina fire in such a way

so as to correlate their timing with the cells adjacent to each other, but not with those far away or in the other eye.

According to the theory of Hebbian plasticity, connections between neurons are strengthened or weakened based on the similarities or differences in the timing of their presynaptic and postsynaptic activity. Certain synapses, called "Hebbian synapses," become stronger when presynaptic and postsynaptic neurons are active simultaneously (Hebb, 1949, cited in Buonomano & Greenough, 1998). These synapses also respond to asynchrony in paired neurons' activities; the synaptic connection between two neurons which do not fire simultaneously can weaken or disappear entirely (Shatz, 1992). The relative timing of neurons firing in the lateral geniculate nucleus strengthens or weakens their intraconnections, and so determines their relative positions, forming the necessary eye-specific layers.

Ganglion cells use Hebbian synapses to organize the layers of the lateral geniculate nucleus by firing in waves of activity across the eye. These waves of action potentials are structured so that the whole retina is not active at once, but cells located spatially near each other are very likely to fire simultaneously and so strengthen the connections between the cells in the lateral geniculate nucleus which receive their signals. The waves seem to be random in timing and in direction, so cells which

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are located spatially far apart or on different eyes are not at all likely to fire at the same time, and so the connections between them should be subsequently weakened or removed. These waves can be recorded in retinas that have been detached from the eye and brain and kept alive in a solution of fluids, demonstrating the independence of the activity from external stimuli.

Experience-independent plasticity is similar to other kinds of plasticity in that it lowers the amount of the genome that neural development monopolizes; if plasticity did not exist, every neuron, every axonal projection, would have to be coded for specifically in the genome, leaving nothing to chance or experience (Shatz, 1992). The principal way of sculpting the complex features of the brain is to produce rough neural structures and then await input from the internal or external environment which can be counted upon,

in the organism's normal environment, to refine those structures in a way that is similar across individuals in a species. Many organisms, including humans, overproduce neurons and synapses and later cull those connections that are not used. By using the developing brain's capacity for plasticity, genes can code for randomness in projections rather than specificity, and either cause self-generated internal activity (experience-independent plasticity) or wait for external stimulation (experience-expectant plasticity) to precisely sculpt the needed connections.

Experience-expectant plasticity

Experience-expectant plasticity occurs when the brain uses input from the external environment to effect normal developmental changes in its structure. One example of experience-expectant sculpting is the formation of the ocular dominance columns in the visual cortex. The ocular dominance columns in an adult mammal are organized in alternating "stripes," each stripe receiving input from either the right or the left visual field. These columns are not fully developed when an infant is born; the visual cortex organizes itself according to the input it receives through the left and right visual fields. For example, if a cat is visually deprived from birth, its visual cortex does not develop neatly into the typical left-right striped pattern; instead, the axons projecting to the visual cortex from the separate fields can overlap with each other (Hubel & Wiesel, 1962).

Similarly, in humans, childhood cataracts can cause permanent blindness if not treated properly, while the same cataracts in adults cause visual impairment only until they are removed through surgery (von Senden, 1932). This suggests a sensitive period for the development of the visual cortex, during which the absence of the experiential input needed to refine the pattern of connections can cause damage much more severe than in an adult brain (Shatz, 1992).

Experience-expectant plasticity is perhaps the simplest type of plasticity to manipulate. If the expected, normal input from the environment is not present or is blocked experimentally or accidentally in the course of development, the feature which needed that input to develop will mature abnormally or not at all. Learning more about experience-expectant plasticity in the developing brain might help researchers overcome the adverse effects of accidental deprivation of input in human fetuses, infants, and children. If researchers understood exactly how deprivation engenders abnormal brain development, they could perhaps use the

brain's plasticity to reverse the effects of deprivation or to provide the correct type of artificial input to replace the normal, expected experience necessary for development.

Experience-dependent plasticity

Experience-dependent plasticity occurs in features of the brain that may not need experience to develop but can be changed or modified by it. If a modification to the internal or external environment produces change in a feature of the brain, that feature is said to possess experience-dependent plasticity. Learning is a form of experience-dependent plasticity, inasmuch as it is reflected in changes in the learner's brain (Greenough & Black, 1997). The physical changes which take place during learning are most likely caused at the neuronal level by Hebbian plasticity, strengthening or weakening synapses depending on the relative timing of the neurons' activity (as explained above). If two stimuli always appear together, the neurons receiving input from those paired stimuli consistently fire together, and the connection between them is strengthened. Thus, a type of learning, an increase in the association of two temporally paired stimuli, occurs. These changes in neuronal connections could lead to changes in the topography of the overall cortical structure. In primates, connections in the visual, auditory, and somatosensory cortices can be influenced by experience, and some subcortical structures may also be shaped by some degree of experience-dependent plasticity (Pons et al., 1991).

The existence of plasticity demonstrates that the development of the brain is not dictated solely by genes; the plasticity that the brain retains after birth ensures that each individual's brain is unique, even if two (or more) individuals have identical sets of genes. Experience-dependent plasticity allows the brain to respond flexibly to unanticipated changes in input (an important trait in a changing environment) and to allocate its limited area efficiently according to the input it receives from various sources. Michael Merzenich, Edward Taub, and William Greenough all deal primarily with experience-dependent plasticity.

Merzenich: Experience affects cortical representations

Merzenich demonstrated some of the effects of action on the adult primate brain. If a body part becomes less or more active, such as by deafferentation or by

repeated use in learning paradigms, its topographical representation in the somatosensory cortex shrinks or enlarges, respectively (Recanzone et al., 1992; Merzenich et al., 1983a,b; Buonomano & Merzenich, 1998). Often, these changes cause proportional enlargement or shrinkage of adjacent cortical representational areas, apparently in order to utilize cortical space and neurons more efficiently.

Two of Merzenich's experiments demonstrating the effects of repeated action and attention or persistent inaction on the somatosensory cortex involved the fingers of owl monkeys, which are topographically represented in Area 3b of the somatosensory cortex. In one experiment, Merzenich measured the cortical representations of the hand in three groups of owl monkeys (Recanzone et al., 1992). One group was trained in a frequency discrimination task in which they learned to discriminate between increasingly similar frequencies of a fluttering stimulus applied to a consistent area of skin on one finger. Another group was passively stimulated, with no learning, and a third group was not stimulated at all. After several weeks of training, Merzenich and his colleagues inserted microelectrodes into the relevant sections of each monkey's somatosensory cortex to measure the neurons' activity during differential stimulation of areas of skin on the fingers.

When they mapped the representations of the cutaneous inputs onto the somatosensory cortex for the three groups, they found no change in the cortical representations of the control group with who had experienced no prior stimulation, and only minimal enlargement of the cortical area representing the stimulated skin in the untrained, stimulated monkeys. In the trained monkeys, however, that cortical area was significantly (1.5 to >3 times) larger than in the controls. In addition to the original representational area, an additional 1-2 mm of cortex, which had previously received input from other parts of the hand, now received inputs from the trained section of skin. The increased use of a body part and attention to the input resulting from that use effectively altered the structure of the somatosensory cortex. Other experiments have been done replicating these results for the auditory cortex (Recanzone et al., 1993). Merzenich's finding implies that use may help determine the proportional allotment of topographical representations in the somatosensory cortex.

In a converse manipulation, Merzenich transected the median nerves of a group of monkeys, removing all of the normal input from the ventral portions of the thumb and the first two fingers to the somaten-

sory cortex (Areas 3b and 1) (Merzenich et al., 1983a,b, cited in Buonomano & Merzenich, 1998). Immediate changes in the cortical representations of these areas were apparent; adjacent cortical representations of other parts of the fingers and hand encroached on the area which had previously represented the deafferented parts, and this reorganization continued and increased for several weeks. This finding reiterates the importance of continued use in maintaining normal topographical cortical representations. Experience-dependent plasticity confers a definite advantage on the organism by allowing parts of the brain which are initially abnormal or deficient to sometimes be corrected through experience.

Taub: Unused cortical area is taken over by adjacent representations

Taub, like Merzenich, studied the effects of use/disuse on the brain. Taub provided one of the most dramatic examples to date regarding the possible extent of encroachment by adjacent areas into an unused area of the somatosensory cortex. He studied monkeys 12 years after they had received deafferentations of one or both of their upper limbs (Pons et al., 1991). Prior to this experiment, the greatest cortical reorganization that had been demonstrated amounted to only about 1-2 mm of encroachment in the cortex, leaving substantial areas bereft of any responsive properties after amputation or deafferentation of their inputs. Surprisingly, Taub's monkeys' somatosensory cortices were completely responsive. There were no areas which did not respond to stimulation; the entire area which had previously represented the upper limb(s) now responded to stimulation of other areas whose representations had been adjacent to the upper limbs' representations in the cortex. This amounted to an encroachment of 10-14 mm, demonstrating cortical representational plasticity of at least one order of magnitude greater than previously thought possible.

Taub's data disproved a previous theory (cited in Pons et al., 1991) regarding the mechanisms underlying cortical plasticity. The "unmasking" theory holds that plasticity is due to the arborization of single axons projecting from the thalamus to different representational areas of the cortex (see Ramachandran et al., 1992). Under this theory, plasticity is caused by the transfer of input from the same axon into two cortical areas, the area to which it would normally go and another area, which normally inhibits this axon's input,

but which now accepts it for lack of its normal input. The extent of arborization of the thalamocortical axons is about 1-2 mm, so that theory fit with previous data, but was disproved as a primary source of cortical plasticity by Taub's data, which demonstrated plasticity of at least 10-14 mm, too great to be caused by arborization of single axons. Taub (Pons et al., 1991) suggests that much of the observed reorganization may be due to changes not in the cortex itself, but in subcortical structures, such as the brainstem and thalamus. He explains that small changes in the mapping of features in the brainstem translate into larger changes as the representations increase in size sequentially in the thalamus and cortex, so that arborization or axonal sprouting could indeed be culpable for plasticity, but not as directly as previously thought. Instead, Taub proposes a theory of an unnamed type of subcortical plasticity, which has yet to be directly documented, but which would yield plasticity in the overall brain much greater than previously thought possible. In any case, Taub's data demonstrates that the brain has a great potential for change.

William Greenough: Rich early environment creates neurons for learning

Greenough's work clearly shows that an organism's environment during infancy and childhood can influence brain structure. Greenough and his colleagues raised two groups of young, post-weaning rats, ages 28-32 days, in two very different environments (Comery et al., 1995, 1996). One group was put in individual cages and provided with only food and water, while the other group was put in cages together with other rats and a multitude of toys and interesting, changing stimuli to explore. When Greenough examined their brains thirty days later, he found an important discrepancy: The rats reared in the complex environment had 60% more multiple-headed dendritic spines on neurons of the striatum than the control rats. This neurological change is a type of experience-dependent neural plasticity, and the specific type of change, the appearance of more multiple-headed dendritic spines,

may create the potential for further neural plasticity in the form of learning.

The finding of Greenough and his colleagues disproves the general assumption that any new synapses added as a result of experience are equivalent to previously extant synapses (Comery et al., 1996). Rats reared in a complex environment (EC) had a 30% higher density of multiple-headed spines than the controls, meaning that a given synapse in an EC rat's brain was more likely to be connected to a dendrite with more than one head. Greenough and his colleagues (Comery et al., 1996) refer to a recent theory which states that synaptic configurations involving multiple associated contacts may facilitate plastic change. Multiple-headed spines may indicate the presence of parallel connections between neurons. These connections could strengthen or weaken existing connections or could connect to a new synapse, altering the pattern of connections between the neurons. Such changes in the neural web of connections could aid learning, especially under the theory of Hebbian plasticity (Hebb, 1949, cited in Buonomano & Merzenich, 1998). The strong connections between temporally associated synapses could form the neural basis for learning, and multiple-headed spines could aid the brain in making and strengthening such connections.

Synaptic contacts involving those spines seem more prevalent in rats who have had more opportunity for exploration of new stimuli and social contacts, those reared in the EC. It seems that rats exposed to a complex, interesting environment, which facilitates learning and multiple connections early in life, might gain an edge in learning later, due to their relative abundance of multiple-headed spines (although testing on the rats' actual ability to learn has yet to be done).

Further testing with the two groups of adult rats might be able to determine whether the EC rats are truly better learners than the controls. If

rats with more multiple-headed dendritic spines were able to learn tasks more easily than controls, it might be concluded that the rearing environment could affect the capacity for learning by providing the brain with the opportunity to create more parallel neural connections and strengthen existing ones by the principle of Hebbian plasticity. Developmental experiments

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with new rats could discover if more time in, or earlier exposure to, the differentiated environments further increases the EC rats' number of multiple-headed dendritic spines or learning capacities in relation to the controls. If age at exposure was relevant, that data could suggest the existence of a sensitive period for the development of the neuronal changes described above. Experimenters might be encouraged to attempt further studies of human developmental environments and their impact on learning, using data from these experiments to help create a time frame for their studies.

Conclusion

Merzenich and Greenough have researched some effects of externally caused experience-dependent neural plasticity: Merzenich studied how the brain is altered in response to changes in the body, and Greenough studied how the brain is altered in response to the external environment. Taub discovered some larger-than-expected changes in the brain's topography and theorized about the underlying mechanisms of plasticity. These three researchers have made substantial additions to the body of literature concerning experience-dependent plasticity, and their findings may help others develop ways to use the brain's potential for change to help those people with neural deficits redesign their own minds.

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