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# Experience shapes the brain's circuitry throughout adulthood

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The adult brain, long considered to be fixed in its wiring, is in fact remarkably dynamic. Neuroscientists once thought that the brain's wiring was fixed early in life, during a critical period beyond which changes were impossible. Recent discoveries have challenged that view, and now, research by scientists at Rockefeller University suggests that circuits in the adult brain are continually modified by experience.

The researchers, led by Charles D. Gilbert, Arthur and Janet Ross Professor and head of the Laboratory of Neurobiology, observed how neurons responsible for receiving input from a mouse's whiskers shift their relationships with one another after single whiskers are removed. The experiments explain how the circuitry of a region of the mouse brain called the somatosensory cortex, which processes input from the various systems in the body that respond to the sense of touch, can change. The findings will be published next week in the online, open access journal PLoS Biology.

The Gilbert lab has been studying changing neuronal connections for several years. Their approach, in which the scientists use a viral labeling system to attach fluorescent proteins to individual neurons and then image individual synapses in an intact, living brain with a high-resolution two-photon microscope, has provided several important clues to understanding the dynamics of the brain's wiring. Students in the Gilbert lab, Dan Stettler and Homare (Matias) Yamahachi, in collaboration with Winfried Denk at the Max Planck Institute in Heidelberg, previously followed the same neurons week after week in the primary visual cortex of adult monkeys. They found that the circuits of the visual cortex are highly dynamic, turning over synapses at a rate of seven percent per week. These changes occurred without any learning regimen or physical manipulations to the neurons.

Last year, Yamahachi, together with Sally Marik and Justin McManus, showed that when sensory experience is altered, even more dramatic changes in cortical circuits occur, with very rapid alterations in circuitry involving an exuberant growth of new connections paralleled by a pruning of old connections. These studies and others by the Gilbert lab have begun to show that there are underlying dynamics in the sensory cortex and it's not a fixed system, as has long been believed.

In the new study, Marik and other members of the Gilbert lab looked at excitatory and inhibitory neurons within the mouse cortex during periods of sensory deprivation to determine how experience shapes different components of cortical circuitry. For this study they used the whisker-barrel system in adult mice. The barrel cortex, part of the somatosensory cortex, receives sensory input from the animal's whiskers. Scientists have shown that after a row of whiskers is removed, barrels shift their representation to adjacent intact whiskers.

Marik, together with Yamahachi and McManus, found that after a whisker was plucked excitatory connections projecting into the deprived barrels underwent exuberant and rapid axonal sprouting. This axonal restructuring occurred rapidly — within minutes or hours after whiskers were plucked — and continued over the course of several weeks. At the same time that excitatory connections were invading the deprived columns, there was a reciprocal outgrowth of the axons of inhibitory neurons from the deprived to the non-deprived barrels. This suggests that the process of reshaping cortical circuits maintains the balance between excitation and inhibition that exists in the normal cortex.

"Previously we showed changes only in excitatory connections," Gilbert says. "We've now demonstrated a parallel involvement of inhibitory connections, and we think that inhibition may play a role equal in importance to excitation in inducing changes in cortical functional maps."

The new study also showed that changes in the inhibitory circuits preceded those seen in the excitatory connections, suggesting that the inhibitory changes may mediate the excitatory ones. This process, Gilbert says, mimics what happens in the brain during early postnatal development.

"It's surprising that the primary visual or somatosensory cortices are involved in plasticity and capable of establishing new memories, which previously had been considered to be a specialized function of higher brain centers," Gilbert says. "We are just beginning to tease apart the mechanisms of adult cortical plasticity. We hope to determine whether the circuit changes associated with recovery of function following lesions to the central and peripheral nervous systems also occur under normal conditions of perceptual learning."

**More information:** Marik SA, Yamahachi H, McManus JNJ, Szabo G, Gilbert CD (2010) Axonal Dynamics of Excitatory and Inhibitory Neurons in Somatosensory Cortex. PloS Biol 8(6): e1000395. doi:10.1371/journal.pbio.1000395

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