Revealing the machinery underlying the 'plastic' juvenile brain

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Among the central mysteries of neurobiology is what properties of the young brain enable it to so adeptly wire itself to adapt to experience—a quality known as plasticity. The extraordinary plasticity of the young brain occurs only during a narrow window of time known as the critical period. For example, children deprived of normal visual stimulation during an early critical period of the first few years of life suffer the permanent visual impairment of amblyopia.

Now, researchers comparing the genetic machinery of juvenile and adult mouse brains undergoing visual experience have uncovered differences in genetic activity that appear to be central to this plasticity.

Tommaso Pizzorusso and colleagues published their findings in the March 1, 2007 issue of the journal *Neuron*, published by Cell Press.

In their experiments, after keeping juvenile and adult mice in the dark for three days, the researchers exposed the animals to episodes of normal light and analyzed the response in the genetic machinery of the visual cortex in each animal's brain.

They found that the brains of the juvenile mice showed activation of specific genetic mechanisms that the adult brains did not. Specifically, the researchers found that visual experience in the juvenile brains triggered telltale chemical alterations in substances called histones that were not triggered in the adult brains.

Such histones are protein components of the spools around which DNA winds in chromosomes, and alterations of histones can render the DNA accessible to the machinery that activates genes. The researchers also found that the visual stimulation activated genes known to regulate the transcription of other genes. Transcription is the process of copying DNA genes into RNA, which acts as a blueprint for making proteins.

As a test to determine whether such histone modification functionally affected plasticity, the researchers administered a drug to adult mice that would increase chemical modification of histone. They found that such adult mice, indeed, showed an increase in a form of visual plasticity.

"Our results show that visual experience differently activates intracellular signaling pathways that control gene expression in the visual cortex of juvenile and adult mice, and that this developmental downregulation could regulate the developmental reduction of plasticity occurring in the adult visual cortex," concluded Pizzorusso and colleagues. They also concluded that the closure of the critical period was associated with a decrease in the ability of visual experience to drive the histone modifications that are necessary for neural rewiring.

The researchers concluded that the mechanism they discovered "might be important for plasticity in the visual cortex during the critical period, and its downregulation could be involved in the closure of the critical period."

They wrote that "Thus, multiple molecular mechanisms acting at different levels—extracellularly, on the cell membrane, and intracellularly—might contribute to the developmental downregulation of plasticity occurring in coincidence with the closure of the critical period."

Source: Cell Press