

Seeing a brain as it learns to see

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A brain isn't born fully organized. It builds its abilities through experience, making physical connections between neurons and organizing circuits to store and retrieve information in milliseconds for years afterwards.

Now that process has been caught in the act for the first time by a Duke University research team that watched a naïve brain organize itself to interpret images of motion.

"This is the first time that anyone has been able to watch as visual experience selectively shapes the functional properties of individual neurons," said David Fitzpatrick, professor of neurobiology and director of the Duke Institute for Brain Sciences. "These results emphasize just how important experience is for the early development of brain circuits." The group's findings appear online Oct. 22 in the journal *Nature*.

Using an advanced imaging system that can see changes in calcium levels within individual neurons as an indication of electrical activity, the team has been able to see inside the brain of a one-month old ferret as it opened its eyes for the first time and learned how to interpret moving images.

They watched the brain learning how to see. As a ferret learned to discriminate one pattern of motion from another over the course of a few hours, the researchers could see large numbers of individual neurons in the visual cortex develop specific responses and become organized into functional assemblies called cortical columns. Additional

experiments confirmed that the changes were dependent on the neurons being activated by the animal's experience with moving visual images.

The measurements were made using something called "in vivo two-photon laser scanning microscopy," which allows researchers to focus on a virtual slice of living tissue a few microns thick, and up to 300 microns below the surface of the brain. By scanning at multiple depths, the researchers were able to examine the properties of hundreds of neurons in a single animal. A fluorescent dye sensitive to calcium allowed the scientists to detect changes in the activity of individual neurons as the learning occurred.

Ferrets are born with their eyes closed and remain so for the first 30 days or so, Fitzpatrick explained. What the Duke team saw happening as the animals opened their eyes and watched moving images for the first time was the emergence of columns of neurons sensitive to a particular feature of the visual stimulus: its direction of motion.

In visual areas of the mature brain, individual neurons are programmed to be most responsive to a particular direction of motion. Some are most responsive to left-to-right motion, for example, and others will be most responsive to down-to-up or right-to-left and so on. As signals from a visual stimulus enter these brain centers for interpretation, the entire collection of neurons that has been programmed to detect motion will fire signals to cast their votes, in effect, on which direction the stimulus is moving. Those neurons which are programmed to be most responsive to the direction the stimulus is actually moving cast the loudest votes.

"Before experience with a moving stimulus, individual neurons respond almost equally to opposite directions of motion and there is little order in the way they are arranged," Fitzpatrick said. "But as a result of experience with moving images, their response to a particular direction of motion strengthens and they begin to act like their neighbors, forming

columns of neurons with similar preferences. We have been able to visualize the self-organizing process by which the brain uses experience to guide the construction of circuits that are critical for interpreting moving stimuli."

The scientists next have to figure out how neurons end up preferring one motion direction over another, and what aspects of the circuit are altered to create the direction-selective responses.

Fitzpatrick is confident that the findings from these experiments can be generalized to other brain regions and will be of value in understanding neurological and psychiatric disorders.

"Many people don't realize that the vast majority of cortical connections are being formed at a time when experience can influence neural activity," he said. "Understanding how experience shapes the architecture of developing neural circuits, and identifying the underlying cellular and molecular mechanisms could provide the key to a number of developmental brain disorders."

Source: Duke University

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