Studies show importance of visual stimulation in wiring up species' brains to see

June 5 2011

Any parent knows that newborns still have a lot of neurological work to do to attain fully acute vision. In a wide variety of nascent animals, genes provide them with only a rough wiring plan and then leave it to the developing nervous system to do its own finish work. Two studies by Brown University researchers provide new evidence of a role for exposure to light in the environment as mouse pups and tadpoles organize and refine the circuitry of their vision systems.

"Through a combination of light-independent and light-dependent processes, the visual system is getting tuned up over time," said David Berson, professor of neuroscience.

His new work, published in advance online June 5 in Nature Neuroscience, offers the surprising result that light exposure can enhance how well mice can organize the nerve endings from their left eye and their right eye in an area of the brain where they start out somewhat jumbled. Neuroscientists had thought that mammals were unable to see at this stage, but a new type of light-sensitive cell that Berson discovered a decade ago turns out to let in the light.

Meanwhile, Berson's colleague Carlos Aizenman, assistant professor of neuroscience, co-authored a paper online May 31 in the Journal of Neuroscience showing that newborn tadpoles depend on light to coordinate and improve the response speed, strength and reliability of a network of neurons in a vision-processing region of their brains.

"This is how activity is allowing visual circuits to refine and sort themselves out," said Aizenman. "Activity is fine-tuning all these connections. It's making the circuit function in a much more efficient, synchronous way."

Not completely blind mice

Berson, postdoctoral scholar Jordan Renna, and former postdoctoral researcher Shijun Weng conducted several experiments in newborn mice to see whether light influences the process by which the mice rewire to distinguish between their eyes.

"For certain functions, the brain wants to keep track of which eye is which," Berson said. Among those functions are the perception of depth and distance.

At a circuit level, the brain keeps signals from the two eyes distinct by segregating their nerve endings into separate regions in the dorsal lateral geniculate nucleus (dLGN), a key waystation on the path to the visual cortex and conscious visual perception. Scientists have long known this sorting-out process depends on waves of activity that spontaneously excite cells in the inner retina. They did not know until now that the waves are influenced by a light-sensitive type of cell called intrinsically photosensitive retinal ganglion cells (ipRGCs).

About a decade ago, a team Berson led at Brown discovered the ipRGCs, which are the first light-sensitive cells to develop in the eye. They reside in the inner retina, the home of retinal cells that send visual information directly to the brain. The outer retina is where the more familiar rods and cones sense light. Early in life, when the brain is segregating nerve endings into distinct regions in the dLGN, the two retinal layers are not connected, so until ipRGCs were discovered there was no reason to believe that light would affect the sorting process.

The new research doesn't say anything definitive about the consequences of light exposure at this stage for eyesight in adults, especially given that some mammals (such as monkeys) experience this developmental stage in utero.

"Whether different animals in nature are exposed to enough light to induce a change in segregation patterns is unclear," Renna said.

But the research shows that light exposure does improve how well the sorting goes, Berson said, and the work advances neuroscientists' understanding of the eye-distinction process, which is widely studied as a model of "activity-driven" neural development.

To assess the effect of light on retinal waves, Renna used electrodes to record the activity of cells in the inner retinas of newborn mice, first recording in the dark, then in the light, and then again in the dark. In every case retinas experienced waves, but when the retinas were exposed to light, the waves lasted about 50 percent longer.

Renna then tested whether the light-sensitive cells were really creating this wave-lengthening effect by repeating the study in "knock-out" mice in which the ability of the ipRGCs to sense light had been genetically abolished. With the cells disabled, exposure to light no longer made any difference in the duration of the waves.

Finally, to assess the effect of light on the left-right sorting process in the dLGN, Renna examined the tissues from normal mice and the mice whose ipRGCs couldn't sense light. In each case he fluorescently labeled the nerve endings from one eye red and the other green. A computer comparison of the tissues showed that the normal mice developed a higher degree of segregation between red and green than the knockout mice. In other words, the ability of ipRGCs to sense light improved sorting out one eye from another in the dLGN.

Twinkling tadpoles

In his study, Aizenman collaborated with Arto Nurmikko, professor of engineering and physics, to investigate the function of in the optic tectum of tadpole brains. They flooded the tectal neurons in live tadpoles with a molecule that makes calcium ions fluoresce. As whole networks of neurons became active, they'd take in the ions and glow. The researchers recorded the tadpoles with a high-resolution, high-speed camera that could capture the millisecond-to-millisecond activity of the neurons.

Led in the lab by engineering graduate student Heng Xu, the lead author, and postdoctoral researcher Arseny Khakhalin, the team reared some young tadpoles under normal conditions of 12 hours of light and 12 hours of darkness during the crucial days of development when the tectum is developing. They reared others in the dark, and still others with a chemical that blocks the activity of NMDA receptors, a subtype of receptor to the neurotransmitter glutamate, that is known to promote neural rewiring.

Then they exposed all the tadpoles, however they were reared, to blue LED light flashes delivered via a fiber optic cable mounted next to the eye.

What they found over the course of several experiments was that the neural networks in the tectums of tadpoles reared under normal conditions developed a faster, more cohesive, and stronger response (in terms of the number of neurons) to light.

The tectal neural networks of tadpoles kept in the dark during development failed to progress at all. Those whose NMDA receptors were blocked occupied a middle ground, showing more progress than dark-reared tadpoles but less than normal tadpoles. Tadpoles, they

found, train their brains with the light they see.

Aizenman said he hopes the calcium ion imaging technique will prove useful in a wide variety of other neuroscience experiments, including studying how tadpoles neurally encode behaviors such as fleeing when they see certain stimuli.

In the meantime, his team and Berson's have added to the understanding scientists have been building of how creatures turn the somewhat mushy approximations of their brains at birth into high-functioning animal minds.

"That's what everybody is after," Aizenman said. "How do you get this fine-tuned, finely wired brain in the first place?"

Provided by Brown University