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As Life Slips by: Why Eye Movement Doesn't Blur the Picture

Two specific proteins bind during development to stabilize the brain cells that allow us to see things clearly, even as we move

Researchers at University of California, San Diego School of Medicine and Shiley Eye Institute have identified the molecular "glue" that builds the brain connections that keep visual images clear and still, even as objects or your eyes move. Using mouse models, the researchers demonstrate that image stabilization depends upon two proteins, Contactin-4 and amyloid precursor protein, binding during embryonic development. The study is published May 7 by *Neuron*.

Researchers discover how the eye and brain keep images still even as we move, unlike a camera's blur.

"In the visual system, precise connections between your eyes and brain help you see specific things and make sure those images are clear and crisp," said senior author Andrew D. Huberman, PhD, assistant professor of neurosciences, neurobiology and ophthalmology. "Sensors in the eye also detect movement and connect to the brain in just the right way to tell your eyes to move in the right direction without blurring images, the way a camera does if you try to take a picture while moving. Until now, we didn't really understand how the eye and brain control that on a molecular level."

To determine exactly how your eyes and brain work together to keep things steady, Huberman, lead author Jessica Osterhout and team labeled specific sets of neurons in the brain that make specific connections — a technique pioneered by Huberman's lab. This approach allows researchers to look at individual components of the visual network and eventually identify the exact genes those cells switch on during development, as they make the appropriate connections.

From this, the team found Contactin-4, an adhesion molecule. They determined that Conactin-4's expression is very specific to those cells in the eye involved in image stabilization. When the researchers mutated Contactin-4, the circuit didn't form properly and visual cells didn't talk to the brain correctly. On the other hand, when they added Contactin-4 to a cell that doesn't normally produce it, that one additional protein was all the cell needed make the circuits for a steady eye-brain connection.

Then the team went looking for proteins that bind Contactin-4. They uncovered amyloid precursor protein, which has been widely studied for its role in Alzheimer's disease, but is also known to be an important factor in normal brain development. If amyloid precursor protein isn't available, the researchers discovered, Contactin-4 can't control development of the visual circuitry.

Based upon these findings, Huberman and colleagues hypothesize that there are also very specific sets of genes that make sure the correct neurons make the correct connections in other aspects of neural circuitry, in addition to vision. And these genes are very likely important for accurate sensory perception and behavior.

Next, Huberman and his team plan to take a closer look at how these genes and precise neural connections go wrong in cognitive diseases. For example, since the Contactin-4 gene is located in a cluster of genes that have been implicated in some forms of autism, they want to know if aberrations in that particular gene might play a role in development of the disease.

"My lab is also interested in figuring out how to reconnect or regenerate circuits damaged by injury or disease," Huberman said.

Co-authors of this study include Benjamin K. Stafford, and Phong L. Nguyen, UC San Diego; Yoshihiro Yoshihara, RIKEN Brain Science Institute.

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