Adaptive optics helps reveal what the eyes tell the brain

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When photoreceptors in the retina of the eye detect light, they relay the information toward the brain's primary visual cortex for image processing. Scientists at the Howard Hughes Medical Institute's Janelia Research Campus who are studying the visual system in mice have now discovered that the input received by the visual cortex is tuned to signal the orientation and direction of movement of a visual stimulus.

The finding is surprising, says Na Ji, the Janelia group leader who led the research, because researchers have long thought that these features were absent from the information that enters the primary visual cortex, and that the orientation and direction of a stimulus must therefore be determined through neuronal computation within this part of the brain. Ji and her colleagues reported their findings as an Advance Online Publication of the journal *Nature Neuroscience* on December 21, 2015.

The visual system is sensitive to the orientation of the edges within an image, Ji says, explaining that this is why we immediately recognize objects in simple line drawings or cartoons, even if the images lack color or detail. Likewise, the system is sensitive to motion – a moving object attracts our attention even within a crowded scene.

Scientists have long known that there are neurons in the visual cortex whose activity corresponds to specific orientations or directions of movement. Nobel Prize-winning neuroscientists Torsten Wiesel and the late David Hubel first found such cells during the 1950s and 1960s by studying visual processing in cats. But evidence also seemed to suggest that the signals that arrive at the primary visual cortex—relayed from the retina by way of a brain structure called the thalamus—did not explicitly communicate orientation or direction of movement. Instead, the thalamic relay cells appeared to be equally responsive to visual stimuli regardless of these features. "For many years, people have thought that this selectivity is generated inside the cortex itself," Ji says.

A few years ago, other scientists found orientation-selective cells in the thalamus of mice, but it was unknown whether that information was relayed to the visual cortex. Ji, who not only studies neural circuits but also develops new imaging technologies to advance those studies, was in a unique position to examine those inputs more closely.

Microscope images of structures in the brain have typically been obscured by the surrounding tissue, which bends and scatters light as it passes through. So while cells themselves appear distinct, their finer structures—including the branches and protrusions through which they communicate with other cells—cannot be discerned. But since 2010, first with Janelia group leader and Nobel laureate Eric Betzig and then leading her own team, Ji has developed a number of solutions to this problem. Their approaches rely on adaptive optics, which corrects for aberrations in a microscope image. Although adaptive optics is relatively new to microscopy, its application has long been used by astronomers to correct telescope images for aberrations introduced as light passes through the Earth's turbulent atmosphere. Ji's adaptive optics innovations allowed her team to see structures deeper in the brain. More broadly, Janelia is at the forefront of applying adaptive optics to various imaging techniques.

Using adaptive optics, Ji and her team were able to find and measure activity at about 28,000 spots where cells from the thalamus delivered input to cells in the primary visual cortex. They tested the responses at these inputs as mice were presented with images of drifting black bars.

About half of the thalamic inputs in the fourth layer of the visual cortex—where most thalamic inputs are received—were active only when the black bar had a particular orientation, with some cells preferring horizontal bars and other cells preferring vertical bars. Adaptive optics was essential here, Ji says—without it the same experiments would have indicated that only 9 percent of inputs communicated orientation information.

About half of the orientation-sensitive inputs were also selective for stimuli moving in a particular direction. Many were particularly sensitive to movement from behind toward the animal's front, which would be particularly important signals for an animal that needs to know when it is being pursued by predators. Not all directions of movement were represented by the thalamic inputs, however.

Once they had established that input into the visual cortex carries information about direction and orientation, Ji and her team investigated how that information was represented as the information passed through other regions of the visual cortex. They found that cells in layer 4 not only retained this information, but also passed along new information about direction that had not been provided by thalamic inputs. "Some neurons in layer 4 may directly inherit tuning from their inputs," Ji says, "while others likely generate their selectivity by performing computations on the visual information arriving on their inputs."

Further experiments showed that the increased sensitivity to stimuli moving from back to front is lost by the time the information reaches the next step of visual processing in layer 2/3 of the cortex, allowing for more equal representation of all components of an image. However, Ji and her colleagues saw this bias reemerge in layer 5, the part of the visual cortex that sends information on to other parts of the brain. This might represent a shortcut by which the visual system can rapidly alert other parts of the brain to crucial information, enabling a mouse to react to movement from behind without waiting for the cortex to calculate which direction the stimulus is moving, she says.

More information: Wenzhi Sun et al. Thalamus provides layer 4 of primary visual cortex with orientation- and direction-tuned inputs, *Nature Neuroscience* (2015). DOI: 10.1038/nn.4196

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