Bright lights, not-so-big pupils

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A team of Johns Hopkins neuroscientists has worked out how some newly discovered light sensors in the eye detect light and communicate with the brain. The report appears online this week in *Nature*.

These light sensors are a small number of nerve cells in the retina that contain melanopsin molecules. Unlike conventional light-sensing cells in the retina—rods and cones—melanopsin-containing cells are not used for seeing images; instead, they monitor light levels to adjust the body's clock and control constriction of the pupils in the eye, among other functions.

"These melanopsin-containing cells are the only other known photoreceptor besides rods and cones in mammals, and the question is, 'How do they work?'" says Michael Do, Ph.D., a postdoctoral fellow in neuroscience at Hopkins. "We want to understand some fundamental information, like their sensitivity to light and their communication to the brain."

Using mice, the team first tested the light sensitivity of these cells by flashing light at the cells and recording the electrical current generated by one cell. They found that these cells are very insensitive to light, in contrast to rods, which are very sensitive and therefore enable us to see in dim light at night, for example. According to Do, the melanopsin-containing cells are less sensitive than cones, which are responsible for our vision in daylight.

"The next question was, What makes them so insensitive to light?

Perhaps each photon they capture elicits a tiny electrical signal. Then there would have to be bright light—giving lots of captured photons—for a signal large enough to influence the brain. Another possibility is that these cells capture photons poorly," says Do.

To figure this out, the team flashed dim light at the cells. The light was so dim that, on average, only a single melanopsin molecule in each cell was activated by capturing a photon. They found that each activated melanopsin molecule triggered a large electrical signal. Moreover, to their surprise, the cell transmits this single-photon signal all the way to the brain.

Yet the large signal generated by these cells seemed incongruous with their need for such bright light. "We thought maybe they need so much light because each cell might also contain very few melanopsin molecules, decreasing their ability to capture photons," says King-Wai Yau, Ph.D., a professor of neuroscience at Hopkins. When they did the calculations, the research team found that melanopsin molecules are 5,000 times sparser than other light-capturing molecules used for image-forming vision.

"It appears that these cells capture very little light. However, once captured, the light is very effective in producing a signal large enough to go straight to the brain," says Yau. "The signal is also very slow, so it is not intended for detecting very brief changes in ambient light, but slow changes over time instead."

Curious about how these cells bear on behavior, the researchers examined pupil constriction in mice that had been genetically altered to be free of rod and cone function in order to focus on activity resulting from only melanopsin-containing cells. Flashing light at mice sitting in the dark, the team measured the degree of pupil constriction. They found that, on average, roughly 500 light-activated melanopsin molecules are

enough to trigger a pupil response. "But it takes a lot of light to activate 500 molecules of melanopsin," says Yau. "Thus, the pupils close maximally only in bright light."

"In terms of controlling the pupils and the body clock, it makes sense to have a sensor that responds slowly and only to large light changes," says Yau. "You wouldn't want your body to think every cloud passing through the sky is nightfall."

"These melanopsin-containing cells signal light to many different parts of the brain to drive different behaviors, from setting the circadian clock to affecting mood and movement," says Do. "I want to know how these signals are processed and whether they are abnormal in disorders like seasonal affective disorder and jetlag—this is what we hope to tackle next."

On the Web:
neuroscience.jhu.edu/KingWaiYau.php
neuroscience.jhu.edu/
www.nature.com/nature/index.html

Source: Johns Hopkins Medical Institutions