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HOW DOES LIGHT AFFECT THE BODY'S INTERNAL CLOCK?

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Have you ever wondered why you are active during the day and sleepy at night? Why are some animals like owls and mice the opposite? A big reason for this is called circadian photoreception, which is the way we synchronize the body's internal, 24-h clock to the light cycle outside. This process starts in the eye. In this article, we discuss the characteristics of circadian photoreception and the scientists that helped us understand this process. We explore the key parts involved in circadian photoreception: photopigments, which are the pigments in the eye that change when they absorb light and are each found in their own cells. Last, we examine ganglion cells, which are special cells in the eye that send information to the brain.

CIRCADIAN PHOTORECEPTION

The way we synchronize the body's internal, 24-h clock to the light cycle outside.

Why are you active during the day and sleepy at night? This cycle happens due to a process called **circadian photoreception**, which is the way we synchronize the body's internal, 24-h clock to the light and dark periods outside. Photoreception means that a biological system is sensing light. Circadian means a rhythm which is close

BIOLOGICAL CLOCK

An organism's internal clock that maintains its circadian rhythm.

PHOTORECEPTOR

A special type of cell that responds to light. Photoreceptors include rods and cones.

PHOTOPIGMENT

Pigments that chemically change when they absorb light.

to 24-h. So, circadian photoreception is how the **biological clock** of the brain, a special part of brain called the SCN, synchronizes its 24-h rhythm to the sunrise. The biological clock of the brain is in turn responsible for maintaining many circadian rhythms: mental, physical, and behavioral changes linked to the 24-h clock. Circadian photoreception is a part of the visual system, so it is related to processes happening in the eyes. Normally, when you think of the eyes, you think about vision. **Photoreceptors** are a special type of nerve cells in the eyes that respond to light. In the daytime, we use photoreceptors called cones. In the nighttime, when there is little light, we use another type of photoreceptors, called rods. Rods and cones contain **photopigments**, special pigments that change when they absorb light. Each photoreceptor cell contains only one type, or color, of photopigment.

CHARACTERISTICS OF CIRCADIAN PHOTORECEPTION

Scientists learned that circadian photoreception requires the eyes. How did they test this? They used mice, since mice are similar to humans in terms of genetics and behaviors. Mice and humans have the same photopigments in the same types of cells. The cells even look the same and are the same size. Scientists removed the cells that connect the mice's eyes to their brains. Then, they tested those mice to see if they still woke up at "sunrise." They did not! However, the mice still had regular sleep cycles, but they went to sleep and woke up independent of the sunrise. As a result, scientists concluded that *at least part* of circadian photoreception must take place in the eye [1]. Later, scientists showed that some people who were completely blind still synchronized their sleep cycles with light cycles [2]! This was early evidence that humans, like mice, had extra photoreceptors in addition to the ones used for sight. Scientists also found a pathway that connects the eye to the biological clock in the brain, which is different from the part of the brain that allows us to see. This biological clock in the brain is called the SCN, which stands for the **suprachiasmatic nucleus** (Figure 1). Although the SCN is a small brain region, it is very important and is connected to multiple other brain regions [3].

SUPRACHIASMATIC NUCLEUS (SCN)

A small brain region above the roof of the mouth that receives light information from the eye and controls circadian rhythms.

To understand more about circadian photoreception, researchers placed mice in three different conditions. They placed some mice in conditions that corresponded to light in the daytime and dark in the nighttime and recorded their activity. The mice ran on their running wheels only at night. Then, they placed mice only in the dark. Even though there was no sunlight telling the mice what time it was, the mice followed their biological clock [4]. This means that they woke up and went to sleep with a daily rhythm, but that rhythm no longer matched the clock on the wall.

Last, the scientists flashed a small amount of light on the mice during the constant darkness. Then, they placed the mice in the dark again.

Figure 1

The suprachiasmatic nucleus (SCN) is the biological clock of the brain in both humans and mice. Light is detected by our eyes and the information is sent to our brains through optic nerves. The brain's central clock, the suprachiasmatic nucleus is found where the nerves from the two eyes come together above the roof of your mouth. This is the same in humans and mice.

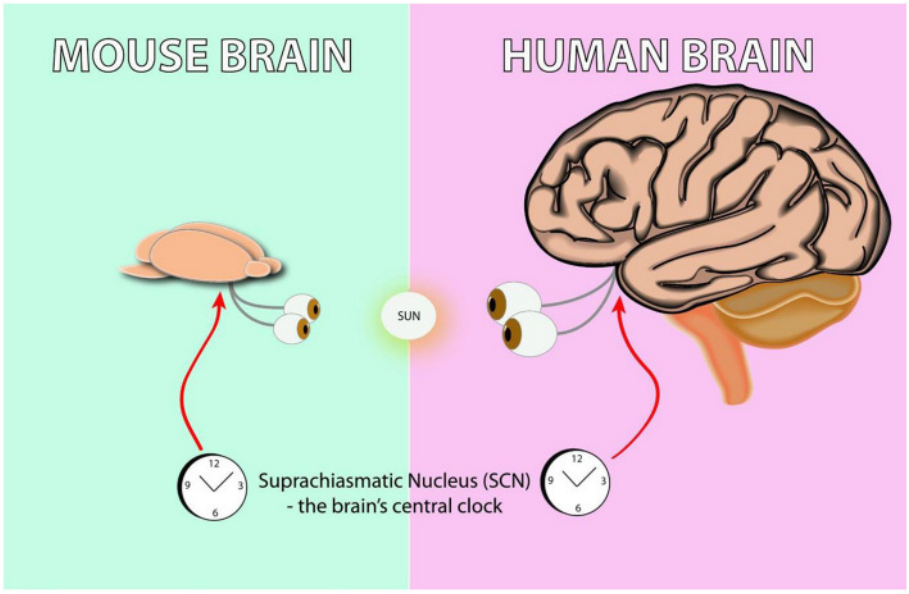

Figure 1

They found that, the next day, the mice got up a few hours earlier and, for the rest of the experiment, the mice woke up at this new earlier time. They concluded that the mice's sleep/wake cycles had been reset. The flashing light changed the time they woke up. Additionally, if they gave the same light flash at a different time of day, the mice woke up a few hours later the following day. Again, their internal clocks were reset [5].

Next, researchers wanted to test whether the strength of the light and the length of time they shined light on the mice influenced the results. They found that the circadian photoreception system in mice requires more light to get activated than rods do—rods become activated with very little light. The amount of light needed for circadian photoreception in mice is just above the strength of moonlight. This makes sense because mice are nocturnal animals (animals that wake up at night). When mice are awake in the moonlight, they do not want the moonlight to reset their internal clocks because they are already waking up at the right time (Figure 2). Instead, they use the little bit of light they see at sunset and sunrise to set their clocks.

The researchers also found that the circadian photoreception system seems to count the number of light flashes it detects over long periods. This is different from the way rods and cones work. The circadian photoreception system can measure the amount of light coming into the eyes. So, a bright light over a short time might have the same effect as a dimmer light shining over a long time [6].

Figure 2

This mouse is in the moonlight. Moonlight is not strong enough to reset the mouse's biological clock. Humans, however, are awake during the day. This means that any light we see at night *can* reset our circadian photoreception. When you go to bed, do you watch TV or use an electronic device? This light might be bright enough to interfere with circadian photoreception. Instead, you could read a book!

Figure 2

MELANOPSIN: A NEW PHOTOPIGMENT

Scientists wanted to find out exactly where the photoreceptors responsible for circadian photoreception were located. Most scientists assumed the rods or cones were responsible, but they had to test this idea.

Clyde Keeler was one of the first researchers to find mice that did not have rods and cones, which means that those mice were blind. But Keeler found that these mice could still respond to the amount of light by changing the size of their pupils [7]. Later, Melanie Freedman and Russel Foster completed a similar experiment. They found that blind mice could still respond to the strength of light and change their bedtimes accordingly. They concluded that there must be another photopigment in the retina—but other scientists wanted more proof [8].

Foster's student, Ignacio Provencio, helped find proof for a new photopigment. This new photopigment, called **melanopsin**, was different from the photopigments present in rods and cones. The discovery of this photopigment in frog skin helped prove that Foster was correct.

Provencio discovered that melanopsin was found in **ganglion cells** located in the innermost layer of the eye (Figure 3) [9]. Ganglion cells are special cells that send information to the brain. Normally, ganglion cells, which get information about light from rods and cones, do not directly respond to light. However, scientist David Berson found that ganglion cells containing melanopsin *do* directly respond to light. Scientists gave these ganglion cells a special name: **intrinsically photosensitive retinal ganglion cells** (**ipRGCs**). While this name sounds complicated, once we break it down, it is easy

MELANOPSIN

A photopigment that is most sensitive to blue light and is important for circadian photoreception.

GANGLION CELLS

Cells that make up the innermost part of retina. Branches from these cells form a nerve that goes into the brain to send information about light.

INTRINSICALLY PHOTOSENSITIVE RETINAL GANGLION CELLS (IPRGCS)

Ganglion cells that are sensitive to light because they contain the photopigment melanopsin.

RETINA

The thin, light-sensitive tissue that lines the inside of the eye.

to understand. Intrinsically means "by nature." Photosensitive means "sensitive to light." Retinal refers to where the cells are found, in the **retina**. The last piece is the type of cell—ganglion cells [10].

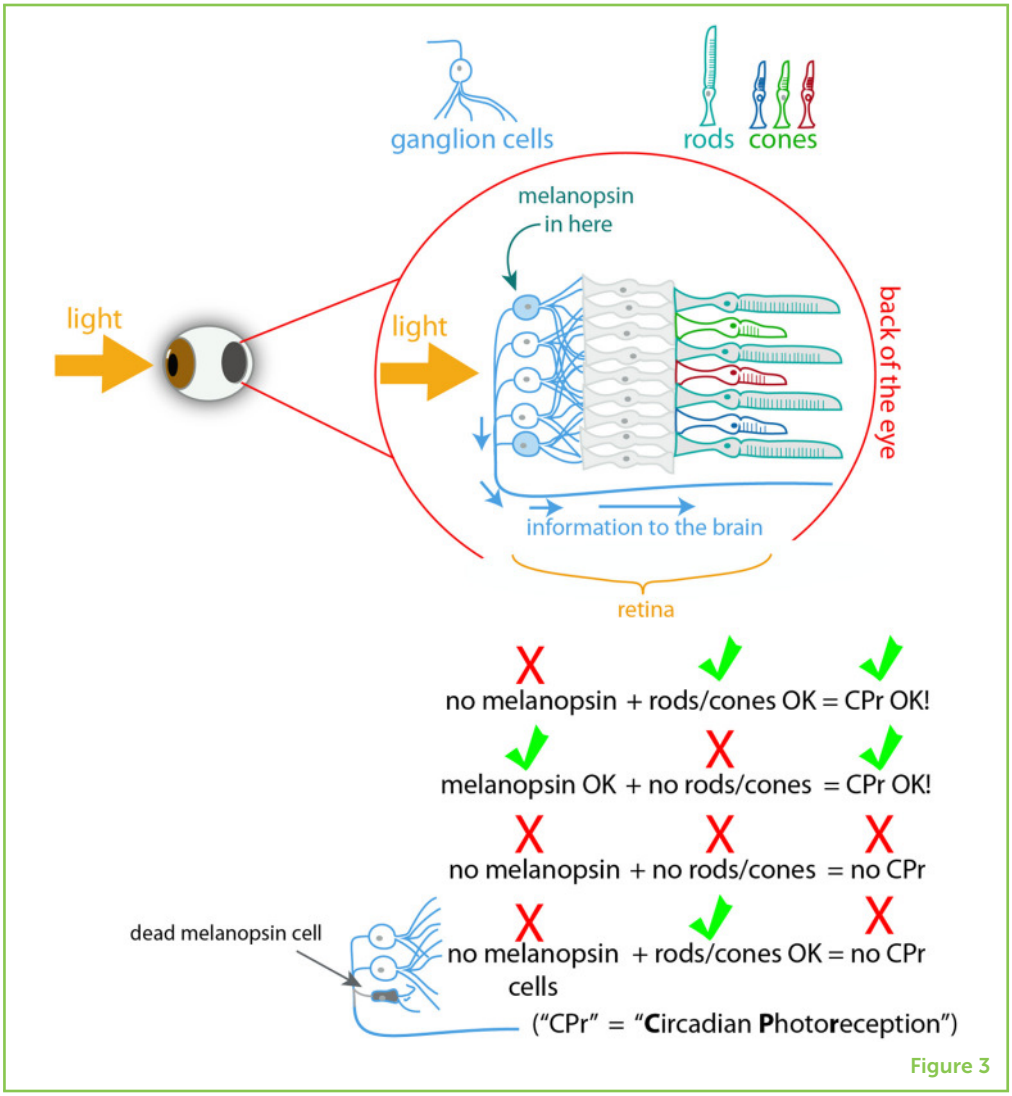

Figure 3

Along the inside of the eye (along the backs and sides) is a thin tissue called the retina. Light shines through the ganglion cells in the retina to the rods and cones at the back of the eye. The rods and cones send the light information back to the ganglion cells, which then send the information to the brain. Some ganglion cells called ipRGCs respond directly to light and do not need the rods and cones to talk to the brain. It is the melanopsin inside the ipRGCs that is actually detecting the light. The retina can use either melanopsin or rods and cones to achieve circadian photoreception (CPr). If the ipRGCs themselves are dead, then there is no circadian photoreception.

HOW DO IPRGCS, RODS, AND CONES WORK TOGETHER?

Scientists found that ipRGCs use the same pathway from the eye to the brain that the circadian photoreception system uses [10, 11]. They also found that ipRGCs need about the same amount of light to get activated as humans and mice need to set their internal clocks [12]. Additionally, ipRGCs seem to count the number of light flashes they get over long periods. This means that ipRGCs count light flashes: For example, short, bright light and long, dim light would lead to the same number of light flashes. This was a really big deal in the visual science community because it challenged the persisting idea that photoreception occurs only in rods and cones!

Although we know that ipRGCs respond to light, they are also connected to the other photoreceptors, like rods and cones. The bottom of Figure 3 summarizes how these structures work together.

When researchers remove melanopsin, circadian photoreception still happens. This means that melanopsin is not necessary for circadian photoreception because the rods and cones can take over. When rods and cones are removed, circadian photoreception also still happens. This means that rods and cones are not necessary for circadian photoreception because melanopsin can take over. When melanopsin, rods, and cones are all removed, circadian photoreception does *not* happen [13]. So, those three photoreceptors are necessary parts of the circadian photoreception system. If ipRGCs themselves are removed, rather than just turning off their photopigments, there is also no circadian photoreception. This means that the melanopsin-expressing ipRGCs are the only pathway through which information from the eye gets to the brain's biological clock. ipRGCs can catch light using any of the three photopigments: rods, cones, or melanopsin [14].

CONCLUSION

Circadian photoreception is the name for the process by which we match the body's internal, 24-h clock to the light cycle outside, and it starts in the eyes. The discovery of circadian photoreception led to the discovery of a new photopigment, melanopsin, which was revolutionary for visual science. Before this, scientists thought that rods and cones were the only photopigments in humans. Circadian photoreception depends on melanopsin-containing cells called ipRGCs, which form the only pathway by which information moves from the eye to the biological clock in the brain. Because this is separate from our vision, this means that our brains are paying attention to light that we do not "see." Our eyes are setting the alarm clocks in our SCN, and our SCN are waking us up at the right time.

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YOUNG REVIEWERS

ABHAY, AGE: 10

I am a fourth-grader who loves movies and reading. I am a big fan of movie franchises such as Marvel and Star Wars and book collections such as Geronimo Stilton. You will almost always find me with a book. The favorite ways I like to spend my time doing are making family trees, drawing, reading, and watching tv. My ambition when I grow up is to become a fashion designer.

APARNA, AGE: 12

I am a 12 year old girl and my interests are science, music and art! I am also a sports enthusiast who loves any type of action. Other interests include playing violin, drawing, and making new friends. I love the Harry Potter book series and the movies as well. My dream is to become a neurologist one day and help find cures to diseases.

KAVISH, AGE: 9

I am a curious, fun-loving, little fourth grader who is interested in various topics. I like to spend my time writing stories and poems, drawing, singing, and dancing. But I love playing above all of them. I love Science and dogs, though my parents do not allow. I enjoy observing, experimenting, and discussing all aspects of nature. I would like to become a scientist when I grow up and help the mankind.

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