

In 1958, J. Woodland Hastings and Beatrice M. Sweeney tested the ability of different wavelengths of light—corresponding to different colors—to shift the circadian rhythm in the photosynthetic marine dinoflagellate *Gonyaulax polyedra*. The greatest power to reset the organism's daily meter lay in the blues, with a precipitous decline into the greens and a modest boost in the reds.

Hastings and Sweeney's paper, published in the December 1958 *Biological Bulletin*, gathered dust for decades. No one thought these findings might hold any relevance for humans, whose circadian rhythms were then widely believed to be relatively insensitive to light.

But scientific discoveries in the past two decades have changed all that. Not only does light reset the human circadian rhythm, but the same blue light that has the strongest impact on dinoflagellates has equal power to reset our own clocks—although most visible wavelengths can reset the clock, the blues do the job with the greatest efficiency.

Now researchers are finding increasingly that an out-of-phase circadian rhythm is a health hazard. "Maintaining synchronized circadian rhythms is important to health and well-being," says Dieter Kunz, director of the Sleep Research and Clinical Chronobiology Research Group at Charité-Universitätsmedizin Berlin. "A growing body of evidence suggests that a desynchronization of circadian rhythms may play a role in various tumoral diseases, diabetes, obesity, and depression."

Shift workers, whom Kunz calls "a model for internal desynchronization," are known to experience increased morbidity and mortality for a number of diseases, including cardiovascular disorders and cancer. In fact, in 2007, the World Health Organization decreed that shift work is a risk factor for breast cancer, and on that basis, in 2009, the Danish government began compensating some female shift workers with breast cancer.

At the same time, researchers have repeatedly shown that bright white light has the power to mitigate depression and other maladies of mood. An

emergent recent literature suggests that blue light may be particularly potent for such applications.

Unraveling the Mysteries of Circadian Rhythm

In the absence of normal cues of nightfall and daybreak, the circadian rhythm "runs free" and has been found to average about 24.25 hours. Night owls' endogenous cycles typically run slightly longer, and morning people may cycle short of 24 hours. Exposure to the normal day/night cycle keeps people entrained (or aligned) on 24 hours through daily resetting, or switches them to new cycles when they cross time zones, almost the way you might reset your watch.

For many years it was thought that social interaction was the major force involved in resetting humans' internal clock—in this regard, uniquely among the kingdoms of life, humans were thought to be relatively insensitive to light. In one study, researchers at the Max Planck Institute for Behavioral Physiology, led by Jurgen Aschoff and Rütger Wever, built a soundproof underground bunker in which subjects could be insulated from time cues. They even wrapped the bunker in copper wire, like the coils on an electric motor, to prevent the possibility that external electromagnetic forces, which might vary with time of day, might somehow cue time. Subjects' responses to potential external cues or to their own endogenous rhythms were assessed by observing their sleep/wake cycles and various physiologic measures that cycle with circadian rhythm, such as body temperature, which rises during the day and falls at night.

Subjects were exposed to external circadian cues for 9 days, with light, temperature, and noise ebbing and flowing on 24-hour cycles. Under these circumstances, subjects showed 24-hour rhythms, as described in the January 1970 issue of the *European Journal of Physiology*. Then all external cues were removed. Subjects ate and turned lights on and off when they felt like it. Under these "free-running" conditions, the typical subject's sleep/wake cycle exceeded 24 hours. Once the experimenters re-imposed the 24-hour cycle of light and dark, however, subjects' bodies re-established a 24-hour circadian rhythm.

The 1998 discovery of a new photoreceptor in the eye—which later turned out to be especially sensitive to blue light—revolutionized the way we think about how circadian rhythm is entrained. Today we understand that blue light has many unique physiologic effects.