BIOLOGICAL IMPLICATIONS OF CIRCADIAN DISRUPTION

Life on Earth has evolved under a consistent cycle of light and darkness caused by the Earth's rotation around its axis. This has led to a 24-hour circadian system in most organisms, ranging all the way from fungi to humans. With the advent of electric light in the 19th century, cycles of light and darkness have drastically changed. Shift workers and others exposed to high levels of light at night are at increased risk of health problems, including metabolic syndrome, depression, sleep disorders, dementia, heart disease, and cancer. This book describes how the circadian system regulates physiology and behavior and considers the important health repercussions of chronic disruption of the circadian system in our increasingly lit world. The research summarized here will interest students in psychology, biology, neuroscience, immunology, medicine, and ecology.

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A Modern Health Challenge

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Preface

In 1998, researchers had a simple question: Is there a relationship between night-shift work and type 2 diabetes? To investigate, 178,000 female nurses were monitored because nursing involves a lot of night shifts. At the start of the study, none of the nurses had type 2 diabetes. Working night shifts over the next decade, the researchers reported, sharply increased the nurses' risk of type 2 diabetes – and the more years they worked the night shift, the higher their diabetes rates became.

Other researchers explored whether night shift work clouds people's thinking. They compared 1,500 night-shift and 1,500 day-shift workers in France. Even when the researchers controlled for sleep deprivation, people who had worked night shifts – including well before the study – scored lower on tests of memory, brain-processing speed, and overall cognitive capacity than people who worked day shifts of the same jobs. And the declines were even worse for people who had worked nights for a decade or more. These long-term shift workers had cognitive deficits equal to 6.5 years of age-related decline.

The Centers for Disease Control and Prevention (CDC) monitors the weight of Americans, and their data show that there has been a sharp increase in obesity. From 2000 to 2018, the prevalence of obesity increased from 30.5 percent to 42.4 percent. This is an increase of 12 percent in less than 20 years! Developing countries like Mexico, India, and China have shown even steeper increases in obesity. In 1985, obesity was almost nonexistent in India. Now approximately 20 percent of its people are obese – despite having the largest underfed population after China.

What do these serious problems have in common? Exposure to light at night, social jetlag, shift work, or, more broadly stated, disruption of the circadian system. Research data from our labs and the laboratories of the contributing authors to this book suggest there is a connection between disruptions of our body's 24-hour internal timekeeping system and a host of problems such as obesity and metabolic syndrome, major depression, bipolar depressive disorder, seasonal affective disorder, sleep disorders, common problems with learning and memory, Alzheimer's disease and other forms of dementia, sundowning syndrome, cancer, heart disease, hypertension, heart attacks, and strokes. Even exposure to the equivalent of a child's night light can impact everything from how well our brains function every day to how well our bodies recover from injury.

How does disrupting our body clocks connect to all these problems? Our body's internal clock regulates a number of essential functions throughout our body, regulating when we eat, sleep, and even when we most efficiently fight off infections. Disrupting circadian rhythms can impair these essential functions. How does the circadian system get disrupted? Primarily by exposure to light at the "wrong" time of day (see Chapter 1). In this book, our authors will present their research data that explain how and why disruption of circadian rhythms influences a broad range of physiological and behavioral processes.

For the 3–4 billion years before electric light was invented in 1879, life on Earth evolved under the pattern of light during the day and dark at night. Along the way, nearly all organisms, including humans, internalized the temporal rhythm of Earth's rotation and eventually developed self-sustaining biological clocks. These internal rhythms are called circadian rhythms, and the organs that generate them are called circadian clocks. Human's circadian or biological clock is localized in a paired cluster of about 20,000 nerve cells in the hypothalamus at the base of our brain, called the suprachiasmatic nucleus (SCN). The cycle of a circadian clock is approximately 24 hours but seeing light at dawn sets it to precisely 24 hours. Having our clocks set closer to our environment's light–dark rhythms optimizes how our bodies function and how we behave. Circadian clocks are a nearly universal feature of life on this planet, yet over the past century and a half we have managed to manipulate the amount of light in the environment so much that we are constantly disrupting our circadian system.

Apart from shift work, exposure to light at night and circadian rhythm disruption is commonplace in the modern world. People with later chronotype ("night owls") experience misalignment of sleep timing between work and free days when forced to adjust their activities to social (school/working) schedules. The resulting circadian disruption has been termed "social jetlag." Social jetlag is common in adolescents and young adults such as college students, with a reported approximately 75 percent of students experiencing social jetlag. Much like shift workers, college students undergoing social jetlag tend to have worse academic performance, especially in the morning, increased alcohol and substance use, and more depressive symptoms.

We spent centuries battling the night's dangers: predators, crime, fire, ghosts. It makes sense, then, that we eagerly flooded the night with bright electric lights as soon as the technology became available. Unlike earlier ways to create light – torches, fires, oil lamps, candles – electric lights were a dramatic change: safer, cheaper, more reliable, and easier to use. We adopted electric lights long before we understood circadian biology, so we didn't know that we should consider the problems bright artificial light at night could cause for our mental and physical health. It is perhaps not unexpected that there are biological consequences to radically changing from the distinct light–dark cycles life evolved under for billions of years, but we need to be aware of these consequences. The chapters in this book bring together the most reliable research on the different ways disruption of the circadian system affects physiology, behavior, and health.

Broad strategies have been used to study how circadian disruption affects people, including assessments of the negative effects of night-shift work, large-scale epidemiological studies comparing people who are and are not exposed to bright artificial light at night, and controlled laboratory (or cave!) studies that introduce distinct light cycles to people. Our authors will cover these diverse challenges to our biological rhythms to illuminate what science can tell us about how disrupted circadian rhythms affects our health and compromises optimal functioning.

Unfortunately, light pollution is everywhere. In a 2016 *Science* paper, researchers reported there are only three places where the night sky is as it was before electric lights: Chad, Central African Republic, and Madagascar. The countries and territories having the largest area without light pollution are Greenland (only 0.12% does not have pristine skies), Central African Republic (0.29%), Niue (0.45%), Somalia (1.2%), and Mauritania (1.4%). In Singapore, San Marino, Kuwait, Qatar, and Malta, no one can see the Milky Way, and 99 percent of the people in the United Arab Emirates, 98 percent in Israel, and 97 percent in Egypt also cannot see it.

The basics of Circadian Organization are covered in Chapters 1–3. Using light-emitting devices inside is also a significant source of circadian disruption. As we will explain in Chapter 1, not all light affects our circadian systems the same way. We have special receptors in our eyes that feed environmental light information directly to our main biological clock. These receptors have evolved to be activated during the day and not at night – in fact, their activity is what tells our clocks it is daytime. Some are most sensitive to the short (blue) wavelength light we're exposed to during the morning. As the sun sets, we are exposed more to long (reddish) wavelength light. Artificial lights, however, mainly emit short wavelength light. Even though these lights may look white, the primary wavelength is typically in the blue range, especially from fluorescent lights. Although our TVs appear to project all the colors, their light is mostly blue. Think about passing your neighbor's windows at night – the TV glow is blue. Cell phones, e-readers, tablets, computer screens, and other technology also emit primarily short wavelength light. Using them after sunset disrupts the precise circadian organization of our physiology and behavior. We will also describe the basics of circadian biology in Chapter 1.

In Chapter 2, Deborah Joye, Robert Wheeler, and Jennifer Evans provide essential information on how the "core circadian pacemaker" in the suprachiasmatic nucleus of the hypothalamus stays organized and coordinates rhythms throughout our body. Margarita Dubocovich focuses on how light and the circadian system regulate melatonin secretion and the role of melatonin in regulating physiology and behavior in Chapter 3.

In Chapters 4–9 of the book our authors discuss disrupted circadian rhythms and brain function. In Chapter 4, the effects of disrupted circadian rhythms and allostatic load are described by Ilia Karatsoreos. Anthony Rosenthal and Tara LeGates address the downstream effects of disrupted circadian rhythms on mental health in Chapter 5. The role of disrupted circadian rhythms on cognition is portrayed in Chapter 6 by Jacob Moeller and Lance Kriegsfeld. In Chapter 7 the role of disrupted circadian rhythms on aging and Alzheimer's Disease is featured by Marilyn Duncan. The effect of central nervous system injury on circadian rhythms is described by Andrew Gaudet and Emily Greenough in Chapter 8. Alexandra Yaw, Brooke DeVries, and Hanne Hoffmann address the influence of disrupted circadian rhythms on neuroendocrine function in Chapter 9.

Although the primary pacemaker for the circadian system is located in the brain, circadian clocks and their rhythms persist throughout our bodies. Thus, Chapters 10–14 will focus on disordered peripheral physiology in response to disrupted circadian rhythms. In Chapter 10 the effects of disrupted circadian rhythms on metabolic function are described by Deanna Arble. Zhenheng Guo, Tianfei Hou, and Ming Gong describe the effects of disrupted circadian rhythms on blood pressure regulation in Chapter 11. The effects of disrupted circadian rhythms on immune function are covered in Chapter 12 by Louise Ince, Devin Simpkins, and Julie Gibbs. Leandro Brito, Saurabh Thosar, and Matthew Butler describe circadian rhythms and cardiac function in Chapter 13. In Chapter 14 Baharan Fekry and Kristin Eckel-Mahan outline the relationship between disrupted circadian rhythms and cancer.

The final two chapters focus on environmental and ecological influences of disrupted circadian rhythms by light at night. In Chapter 15, Kevin Gaston and Johanna Meijer delve into the broad environmental implications of how our modern light environment disrupts circadian function across species. This chapter will also focus on interventions and solutions for the maladaptive effects of light. Finally, measurement and analysis of nighttime light exposure in the context of epidemiological studies is the topic of Chapter 16, which is coauthored by Xiaozhe Yin and Travis Longcore. Taken together, these chapters provide a comprehensive perspective on the role of disrupted circadian rhythms on physiology, behavior, and health.