

The Lifestyle and Environmental Drivers of Circadian Misalignment and Their Implications for Chronic Diseases

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ABSTRACT

The circadian rhythm is the body's internal clock, regulating vital functions and systems such as sleep cycles, hormone release, appetite, digestion, and temperature. Each organ is influenced by circadian timing, while the master clock resides in the brain. The suprachiasmatic nucleus, a cluster of nerve cells in the hypothalamus, coordinates biological processes in response to daylight and helps regulate the master clock's rhythm. Light signals from the eyes, combined with brain activity, mediate circadian rhythms. However, daily life can disrupt these cycles. This paper reviews common yet detrimental factors that influence the regulation of circadian rhythms. Diet, nutrient intake, and meal timing can disrupt appetite and metabolism. Furthermore, studies have shown that stress, work shifts, screen usage, and poor sleep can all lead to circadian misalignment. This misalignment is associated with chronic health conditions such as obesity, sleep disorders, mental health disorders, heart issues, and cancer.

Keywords: circadian rhythm; circadian misalignment; meal timing; artificial light; shift work; cortisol; mood disorders; metabolic health; chronic disease

INTRODUCTION

Circadian rhythms are controlled by internal clocks in the body that follow a 24-hour cycle. Although circadian rhythms are ongoing innate processes, they are influenced by external cues (1). Circadian rhythms are crucial to regulating numerous body systems, with the main process being the sleep-wake cycle. During the day, signals are sent to the brain, and hormones keep us alert and awake. At night, reduced light triggers the production of melatonin, helping sleep begin. Other processes include the digestive system, cardiovascular system, body temperature, the urinary system, and cognitive function.

These processes include alertness, energy levels, and the 24-hour cycle. Proper timing maintains optimal overall health. Nearly every tissue and organ, including the liver, lungs, heart, pancreas, kidney, and gut, functions under a circadian clock. The master clock, located in the brain, synchronizes with each organ's clock to ensure proper function. The master clock, also known as the suprachiasmatic nucleus (SCN), is a group of nerve cells in the hypothalamus. Intrinsically photosensitive retinal ganglion cells (ipRGCs), which are special cells in the retina, detect light and transmit it to the SCN. Signals are transmitted through the retino-hypothalamic tract and subsequently to the SCN. In contrast to ipRGCs, rods and cones in the retina deliver information to the brain's visual cortex. The ipRGC pathway is not primarily for vision; rather, it is a light-detection system that sends information to the master clock. These specialized cells express melanopsin, a light-sensitive protein that responds to blue light. The amount of light detected by the ipRGCs governs the timing and functionality of

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biological clocks. The body responds to the time of day, so sleep cycles, hormone release, and attentiveness are all regulated to promote wakefulness during the day (2). Other proteins and mechanisms are also involved in synchronizing circadian cycles with day and light. Jeffrey C. Hall, Michael Rosbash, and Michael W. Young received the Nobel Prize in 2017 for their work on circadian rhythms. They discovered that a protein known as PER plays a crucial function in managing the life cycle of fruit flies. In their work, scientists discovered that during the night, PER attaches to another protein called TIM, forming a PER-TIM complex. This compound penetrates the nucleus and prevents further PER generation during the day. PER inhibits its gene transcription. When it becomes daytime, TIM degrades due to light exposure, allowing PER and TIM production to resume, thus completing the cycle. Through this negative feedback loop, PER regulates its transcription. This phenomenon led to additional research into PER proteins and other genes involved in the 24-hour cycle. Specific PERs, or Period proteins, play particular roles in the brain, controlling the body's internal clock and

therefore adjusting physical cycles to match the quantity of light in the environment. When the biological clock desynchronizes from the surrounding environment, the body processes other cycles at the wrong periods. When the SCN does not properly synchronize the body's circadian clock, the functions of other organs can become desynchronized. The brain will continue to send signals for certain functions at particular times, but they may not correspond to the activity being performed during the day. For example, if a person moves across significantly different time zones, the body's clock may remain tuned to the previous location's light cycles. This may cause jet lag, excessive tiredness, or waking earlier or later than the current time zone cycle (3).

Misalignment of circadian rhythms with the diurnal light cycles can lead to significant health issues. These encompass profound fatigue, emotional fluctuations, gastrointestinal disturbances, sleep disturbances, cognitive difficulties, and an elevated risk of chronic health issues. In addition to inadequate sleep, other daily occurrences may interfere with biological rhythms (Table 1). The timing, type, and frequency of food

Table 1. Summary of key studies on circadian disruption and health-related outcomes.

Factor examined	Study	Study design / model	Key finding	Relevance to circadian disruption
General circadian rhythm regulation	Vitaterna <i>et al.</i> (1)	Review of circadian rhythm biology	Circadian rhythms regulate sleep-wake cycles, hormone release, metabolism, and other physiological systems.	Provides background on why circadian alignment is important for overall health.
Light exposure	LeGates <i>et al.</i> (2)	Review of light, sleep, and affect	Light signals influence the suprachiasmatic nucleus and affect sleep, circadian timing, and mood.	Supports the role of light as a major environmental cue for circadian regulation.
Circadian disruption and mental health	Walker <i>et al.</i> (3)	Review of circadian rhythm disruption and mental health	Circadian disruption is associated with sleep problems and mental health disorders.	Explains the link between misaligned biological rhythms and psychological outcomes.
Meal timing	Vahlhaus <i>et al.</i> (5)	Human study using eating timing, sleep-wake timing, and glucose measures	Later eating in relation to the internal clock was associated with lower insulin sensitivity.	Shows that meal timing can disrupt metabolic regulation and increase health risk.
High-fat diet	Kohsaka <i>et al.</i> (6)	Mouse model comparing regular chow and high-fat diet	A high-fat diet disrupted behavioral and molecular circadian rhythms.	Demonstrates that diet composition can alter biological clock function.
Emerging mood disorders	Carpenter <i>et al.</i> (7)	Human study of youth with emerging mood disorders	About 23% of individuals with emerging mood disorders showed evidence of internal circadian misalignment.	Supports the connection between mood symptoms and altered circadian markers.

Continued Table 1. Summary of key studies on circadian disruption and health-related outcomes.

Factor examined	Study	Study design / model	Key finding	Relevance to circadian disruption
Shift work and cortisol	Huang <i>et al.</i> (8)	Multicenter study of midwives in Southeast China	Irregular shift workers showed less daily variation in cortisol rhythm.	Suggests that irregular work schedules can weaken normal hormone rhythms.
Neurodegenerative disease	Namgyal and Lim (9)	Review of circadian dysfunction in neurodegenerative diseases	Circadian dysfunction and neurodegenerative disorders may influence each other bidirectionally.	Shows that circadian disruption may be both a symptom and contributing factor in neurological disease.
Brain disorder incidence	Chen <i>et al.</i> (10)	Prospective cohort study using UK Biobank accelerometry data	Weaker circadian rhythms were associated with higher risk of later brain disorders.	Provides large-scale evidence linking rhythm disruption with long-term neurological and psychiatric outcomes.
Seasonal change and shift work	Kim <i>et al.</i> (11)	Study of medical interns using wearable data	Seasonal differences influenced adaptation to shift work and circadian misalignment.	Shows that environmental seasonality can affect how well the body adapts to altered schedules.
Traumatic brain injury	Kuo <i>et al.</i> (12)	Mouse model of traumatic brain injury	Traumatic brain injury disrupted molecular clock gene expression and body temperature rhythms.	Supports the idea that brain injury can directly impair circadian regulation.
Acute subdural hematoma definition	Karibe <i>et al.</i> (13)	Review of acute subdural hematoma management	Acute subdural hematoma involves bleeding between the brain surface and its outer covering.	Used only to clarify the injury model, not as evidence for circadian disruption.

intake are crucial factors that may influence circadian rhythms. The body and digestive system operate most effectively during daylight hours as a result of circadian rhythms. Consuming food late at night, during diminished light, may result in insufficient digestion due to the digestive system's unfamiliarity with eating at that hour. Moreover, diets heavy in fat and sugar convey erroneous signals to the SCN. An inadequate diet may diminish tissue sensitivity or disrupt the cycle's synchronization. Dietary stimulants, including caffeine and alcohol, disrupt circadian rhythms. Poor dietary habits increase the likelihood of weight gain and the onset of chronic diseases, including diabetes. Artificial illumination, especially during nocturnal hours from mobile devices and televisions, disrupts circadian rhythms and diminishes melatonin synthesis. The eyes perceive light from phones, erroneously perceiving it as sunshine and transmitting misleading signals to the brain. Stress is an additional factor that might result in misalignment. Excessive activation of the brain's stress response mechanism disrupts the body's natural, healthy rhythms. Cortisol, sometimes referred to as the stress

hormone, reaches its peak levels in the body during the morning. Frequent stress or stress occurring at atypical periods disrupts the regularity of cortisol output. Researchers have correlated clock misalignment with neurological disorders and sleep disturbances. Multiple ailments induce a feedback loop, including a disrupted circadian rhythm. The ailment alters the circadian rhythm, exacerbating the condition and establishing a challenging cycle to overcome. Individuals afflicted by such disorders endure intense symptoms and have increased vulnerability to chronic conditions resulting from a misaligned circadian rhythm.

DIET: TIMING OF MEALS

While light is the main cue for aligning circadian rhythms, the timing of eating actively disrupts them. Such factors specifically interact with metabolic processes, digestion, energy storage, gut health, and overall health. Specifically, eating late at night sends mixed signals to the suprachiasmatic nucleus and to peripheral metabolic clocks, such as those in the pancreas. At night, the

body slows down digestion, repairs the gut lining, and regulates appetite hormones. Biologically, the gut and digestive system are in a vulnerable state as they are not functioning as efficiently. Eating late at night disrupts the time the body normally uses for repair. Since melatonin levels increase at night, melatonin can bind to pancreatic receptors, signaling them to produce less insulin. Insulin is a hormone produced by the pancreas that allows the body to store glucose from the food consumed in cells. At night, glucose becomes harder to process since the body is less sensitive to the hormone. If a person eats at a time when the body is less sensitive to insulin, a person may experience higher blood sugar spikes and increased fat storage. Signals are sent to the suprachiasmatic nucleus, prompting the body to begin storing glucose and disrupting the cascade of metabolic processes. As a result, individuals become more prone to more severe health conditions. If cycles like these continue, a person may experience weight gain, obesity, or diabetes (4). In the study “Later eating timing in relation to an individual internal clock is associated with lower insulin sensitivity and affected by genetic factors,” conducted by Janna Vahlhaus and other researchers, aimed to investigate the relation between eating timing, the circadian clock and glucose homeostasis (5).

To begin the study, glycemic traits were assessed through the oral glucose tolerance test in 92 adult twins. Glycemic traits are the quantitative measures of blood glucose and insulin regulation, which are crucial indicators of metabolic health. In addition to this information, records of eating timing, frequency, and caloric density were measured over 5 days. The caloric midpoint, or time of day in which 50% of calories were consumed, was measured in relation to their internal clock timing based on their sleep-wake cycle. These intervals were used to measure an individual’s circadian alignment in relation to their eating habits, known as the circadian time of caloric midpoint (CCM). Overall, the study found that participants with a later CCM were associated with poorer insulin sensitivity, meaning their metabolism was less effective at using insulin to benefit their bodies and control blood sugar. If blood sugar levels become dangerously high or low, serious complications can emerge. Associations were also found with a higher BMI and waist circumference. If individuals move most of their caloric intake earlier in the day, it is likely to improve their glucose metabolism. While the timing of eating habits significantly impacts an individual’s overall health, genetic factors also play a crucial role in determining the effectiveness of these interventions.

DIET: COMPOSITION AND HIGH-FAT DIETS

The timing of consumption, along with dietary ingredients, has been shown to influence circadian rhythms. Studies have been undertaken on diets high in fat and sugar because they lack nutrients and are linked to obesity and other health problems. In a study titled “High-Fat Diet Disrupts Behavioral and Molecular Circadian Rhythms in Mice,” researchers examined how different diets affect circadian rhythms at both the behavioral and molecular levels (6). The mice were given two different types of food: one was regular chow (RC) and the other was high-fat chow (HF). This high-fat diet aims to induce obesity in mice, as the expected outcome of feeding them HF diets is to disrupt and slow down their circadian rhythm. Mice were initially provided with a standard chow diet and subjected to normal light cycles for one week before being moved to a setting of perpetual darkness. Some of these mice also transitioned to a high-fat diet. Mice subjected just to food cues for circadian rhythm regulation exhibited an increase in their free-running period within one week when fed high-fat diets. The mice on a standard diet demonstrated a free-running length of around 23.6 hours, whereas the mice on a high-fat diet exhibited a longer free-running period. Throughout the trial, the free-running period of the HF-diet mice progressively lengthened. This indicates that their internal biological clocks are gradually extending due to the HF diet. Consequently, their bodies cannot metabolize food and nutrients as well as those of RC-fed mice (6). Upon completing the study, the researchers gained novel insights about circadian rhythms and nutrition. Initially, as mice were transitioned to completely dark surroundings and their circadian rhythms continued to be disrupted, it became evident that light is not the sole environmental factor influencing these processes. Dietary composition influences the circadian clock, which sleep patterns do not solely govern. This research further demonstrated that circadian disruption may influence the onset of metabolic illnesses.

AFFECTIVE AND PSYCHOLOGICAL DISORDERS

Recent research indicates that mood disorders, including depression, bipolar disorder, and seasonal affective disorder, are bidirectionally associated with circadian misalignment. This establishes a harmful cycle in which mood instability and misaligned

circadian rhythms mutually affect one another, leading to prolonged complications. The suprachiasmatic nucleus regulates sleep cycles, neurotransmitter release, and hormone secretion, all of which directly influence mood. The severity of a mood condition influences the strength of internal rhythm alignment. The study “Evidence for Internal Misalignment of Circadian Rhythms in Youth With Emerging Mood Disorders” looked at biological signs of circadian rhythms in young people (7). In the studied cohort, 69 individuals were identified as having emergent mood disorders, while 19 constituted a control group, with ages ranging from 16 to 35 years. Participants have undergone early intervention mental health treatments, whereas the healthy control group indicated no prior history of a mental health issue before the study. To clinically evaluate each participant and ascertain eligibility for the study, patients were mandated to complete the Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS), and Social and Occupational Functioning Assessment Scale (SOFAS). According to the assessment results, individuals displayed minor depressive symptoms, hypomania, and functional impairment. To record their medical utilization, participants completed a self-report and clinical interview, indicating that 57% had not been utilizing psychotropic drugs. Patients were observed to be experiencing mood-related concerns or to be in the first phases of a mood disorder, including bipolar disorder, depressive disorder, anxiety disorder, or other mental health conditions. This study specifically evaluates the prevalence and severity of circadian misalignment in patients with emerging mood disorders, extending previous research that examined single-phase markers. Observing multiple biological markers yields a more comprehensive understanding of circadian misalignment. To assess circadian misalignment, patients were evaluated according to their dim light melatonin onset (DLMO), peak salivary cortisol (CORT), and minimum core body temperature (TEMP). They were also mandated to wear an actigraphy device to monitor their sleep-wake patterns. The actigraphy evaluation continued for approximately 30 days before patients were transferred to the Brain and Mind Center for an overnight assessment, which included additional criteria used to gauge circadian misalignment. The research indicated that approximately 23% of persons with developing mood disorders displayed evidence of intrinsic circadian misalignment. Phase angles between each of the examined biological indicators were ascertained to arrive at this result. This indicates that

the temporal discrepancies between circadian markers differed from those of a typical patient. The phase angles of their research demonstrated that the timing of their circadian rhythms fell beyond the standard norms. It was demonstrated that internal circadian rhythms are not well aligned with environmental cues in individuals exhibiting the start of mood disorders or minor symptoms thereof. Although individual results varied, the aggregate data from patients indicated a disruption of the normal circadian alignment. This study lacks longitudinal results of this method, which are essential for a comprehensive understanding of circadian misalignment in individuals with developing mood disorders.

STRESS

Stress is characterized by the body’s inherent response to difficulties. Such activities initiate a cascade of hormone release, including adrenaline, noradrenaline, and subsequently cortisol. This phenomenon is referred to as the “fight-or-flight” reaction, enabling the body to remain vigilant, tighten muscles, and enhance sensory perception, all of which are essential in stressful circumstances. Extended periods of stress, however, produce detrimental impacts on the body. They exacerbate diminished work performance, vulnerability to infections, and an elevated risk of developing cardiovascular or mental disorders. Cortisol is a corticosteroid hormone commonly recognized as a marker for stress. Cortisol levels are generally elevated upon waking and diminished after bedtime. During stress, the brain transmits messages to the adrenal glands, which then secrete these chemicals.

This normal rhythm often varies when circadian rhythms are disrupted or when the body is under prolonged stress. The study titled “The association between circadian rhythm of cortisol and shift work regularity among midwives—A multicenter study in Southeast China” investigated this relationship among midwives in Southeast China (8). Midwives must ensure the health and safety of both the infant and the mother during their employment, which requires the ability to function in high-pressure situations. This study specifically evaluated midwives’ work shifts in relation to their circadian cortisol rhythm. The study used two groups, totaling 86 participants. One adhered to a consistent schedule with regular night-shift patterns in the month preceding the trial. The other group experienced erratic shifts, characterized by

often varying night shifts in the months leading up to the study. Each group dedicated a comparable number of hours daily. Four urine samples were obtained from each midwife over two days, and thereafter analyzed for cortisol levels and imbalances within each group. Upon completion of the trial, it was determined that all midwives exhibited a consistent cortisol secretion schedule, with peak levels occurring in the morning and minimal amounts observed prior to nighttime. Notwithstanding this observation, midwives within the regular-shift cohort exhibited a broader range of cortisol fluctuations. Irregular shift workers exhibited less variability in their cortisol levels throughout the day, indicating disruption of the cortisol secretion rhythm. This condition is termed circadian blunting: a reduction in the differentiation of biological functions. Cortisol continues to be synthesized in the irregular shift group; however, temporal signals from the suprachiasmatic nucleus are inhibited. Their brain exhibited restricted regulation over the timing of cortisol level peaks or reductions. This process is influenced by numerous factors, including irregular light exposure and fluctuating sleep habits, which disrupt the master clock. This study revealed that irregular schedules and disrupted circadian rhythms diminish the body's regulation of stress chemicals. Conversely, regular work shifts establish a distinct cortisol rhythm that the body instinctively follows throughout the day.

RISK OF DEVELOPING NEUROLOGICAL AND MENTAL HEALTH DISORDERS

Neurological illnesses affect the central nervous system, including the brain, spinal cord, and peripheral nervous system. They produce a range of symptoms and stem from various etiologies in each patient. Generally, they induce motor and cognitive impairments. Alzheimer's disease is a neurological ailment that progressively deteriorates memory and cognitive abilities. The illness has catastrophic repercussions, hindering daily activities. Parkinson's disease is a neurological ailment characterized by diminished mobility resulting from the degeneration of dopamine-producing neurons. Parkinson's disease results in bradykinesia, tremors, and rigidity in movement. Individuals afflicted by such disorders also exhibit dysregulated circadian rhythms (9). They interfere with the body's natural circadian rhythm, leading to disrupted sleep and diurnal drowsiness. A bidirectional association exists, since a disrupted circadian rhythm has been recognized as a contributing

factor to many conditions.

The study "Association of Circadian Rhythms with Brain Disorder Incidents: A Prospective Cohort Study of 72,242 Participants" looked at how problems with circadian rhythm relate to the chances of getting long-term brain diseases (10). The study analyzed seven-day accelerometry data from 72,242 individuals in the UK Biobank. Data on daily patterns and biological rhythms were collected over a span of 7 days to formulate a conclusion. The researchers extracted information from the relative amplitude of the data. Participants possessed no antecedent history of neurological disorders. Subsequently, new cases of neurological disorders were monitored for approximately 6.1 years following the 7-day interval. A total of 262 patients were diagnosed with incident dementia, 115 with Alzheimer's disease, 190 with Parkinson's disease, 481 with stroke, 1102 with major depressive disorder, and 1161 with anxiety disorders. Upon completion of the follow-up, it was ascertained that individuals with diminished circadian rhythms exhibited a higher propensity for developing the aforementioned neurological illnesses. Individuals with diminished circadian rhythms exhibited reduced rhythm amplitude, indicating their physiological activity was less pronounced between night and day. The study concludes that circadian rhythm misalignment is not merely a symptom but also a risk factor for the development of certain illnesses. Circadian-targeted medicines have been recognized as promising in reducing future complications for individuals at risk of developing these disorders.

SEASONAL CHANGES

Along with the factors mentioned, the changing seasons can affect an individual's ability to adjust to the light and dark cycles of days. Seasonal changes influence an individual's exposure to natural light. Shorter, and darker winter days are associated with an increase in melatonin production, leading to early sleepiness. Longer, summer days on the other hand, can delay sleep as one is being exposed to more natural light. Such seasonal adjustments can lead to increased sleepiness, poor sleep quality, and in some cases, Seasonal Affective Disorder (SAD). The study, "Seasonal timing and interindividual differences in shiftwork adaptation," by Ruby Kim and other researchers, explores how seasonal cycles and their timing mechanisms affect an individual's ability to adapt to work schedules and the degree of circadian misalignment (11). Researchers collected data from first-

year medical residents located in the US through the Intern Health Study. By wearing FitBit devices, data was collected based on each resident's sleep cycles, heart rate and how it fluctuates throughout the day, and step count for one year. HR-sleep misalignment, defined as the absolute difference between the minimum heart rate and the sleep midpoint of an individual's cycle, was used as the metric to measure circadian misalignment. Data from 3,000 interns were used in 2017 and 2019. The interns took more steps during the summer than during the winter, as well as longer wake periods. While the study's data is primarily insightful, it was not collected in a controlled setting, meaning that other conditions in an individual's life could have affected the results. Individuals who showed stronger seasonal changes in behavior also experienced greater circadian misalignment when working night shifts, especially in winter. Genetic differences in circadian timing influenced sensitivity to light and seasonal cues, which in turn affected how quickly and well their internal clocks adjusted to shift work.

TRAUMATIC BRAIN INJURIES

Traumatic brain injuries can range from mild to severe and are disruptions in normal brain function caused by damage to the head. TBIs can have long-term mental and physical consequences, including headaches, confusion, fatigue, dizziness, and nausea. In severe cases however, symptoms may include seizures, a loss of consciousness, slurred speech, vomiting, and an inability to wake up, which ranges across patients. With these symptoms, disruption of an individual's circadian rhythm may also occur, especially when injury occurs at a critical site that regulates circadian rhythms. If damage occurs in the suprachiasmatic nucleus or hypothalamus, for example, a disrupted circadian rhythm is likely to occur. While these brain regions are crucial for circadian rhythms, damage to any part of the brain will have a significant impact. Trauma to the brain may result in structural damage or inflammation, which will interfere with the molecular clockwork and expression of genes involved. As a result, a person may experience erratic hormone production, especially melatonin, regular sleep-wake disturbances, and decreased alertness. Each factor creates a daunting cycle that is difficult to treat and completely eradicate until the sight of brain injury is fully healed. In the study, "Traumatic brain injury-induced disruption of the circadian clock," researchers studied whether traumatic

brain injuries disrupt the normal cycles of circadian rhythms at the molecular level, by analyzing mice's peripheral blood leukocytes, or white blood cells, and body temperature (12). Previous to this study, it was understood that traumatic brain injuries (TBIs) caused significant changes in sleep cycle, oftentimes leading to insomnia (difficulty sleeping), hypersomnia (excessive sleepiness), or fatigue (extreme tiredness). The gene expression of genes involved in regulating circadian cycles and how they change after TBIs has not yet been studied. The mice used in the study were randomized into two groups. The sham-operated control groups and the acute subdural hematoma (ASDH) group, which is a common consequence of head injuries in people, were included in the study. Acute subdural hematoma is a condition in which bleeding occurs between the brain's surface and its outer covering (13). The control rats also underwent anesthesia, skull opening, and a recovery time but faced no brain injuries. These measures were taken to ensure that differences in the study results were solely due to the lesions the ASDH group suffered, and not to any other factors. All of the mice were kept under 12:12-hour light cycles for about two weeks until the ASDH group of mice were induced with a brain injury under ethical guidelines. Over 48 hours, blood samples were collected from each mouse every 4 hours. The mRNA expression of genes involved in aligning circadian rhythms was quantified. Body temperature of mice was additionally collected as a physiological measurement of each mouse's circadian cycle. The study found that control mice exhibited a robust circadian rhythm, as gene expression showed a clear pattern. In the ASDH mice, gene expression no longer followed a strong, robust pattern. In addition, the sham-operated mice exhibited a normal body temperature rhythm with significant oscillation. The ASDH mice showed lower body temperature amplitudes and a loss of rhythmic significance, supporting the previously noted finding of molecular disruptions. Since the mice's circadian clock at the molecular level isn't expressed properly, the timing of crucial biological processes won't be in tune with the mice's sleep-wake cycles.

CONCLUSION

The disruption of circadian rhythms is a complex mechanism that involves misalignment between an individual's 24-hour biological clock and the light-dark cycles of the environment. The process leads to irregular hormone secretion, a lethargic metabolism system, and

a primarily disturbed sleep-wake cycle. While these are the primary effects of a disrupted circadian rhythm, more serious health issues can arise, along with long-term ones that are difficult to cure. These may include cancer, diabetes, obesity, chronic sleep disorders, or mental health disorders, depending on the severity of the case. There is no single reason for circadian misalignment, as it can result from a variety of factors. The most prominent and most obvious factor is the sleep-wake cycle. If a person does not get an adequate number of hours of sleep to support their lifestyle, it is likely their internal clocks will not be able to keep up and misalign. Another major factor is diet, specifically dietary composition, nutrient intake, and meal timing. Those who eat diets high in fat or too late in the day will send mixed signals to the suprachiasmatic nucleus, resulting in a misaligned circadian rhythm. Research has also indicated that mood disorders, like depression and bipolar disorder are more likely to have their circadian rhythm misaligned. Such effects form a bilateral relationship with circadian rhythms. In a study, it was additionally discovered that 23% of people with developing mood disorders displayed evidence of intrinsic circadian misalignment, meaning those who are not yet diagnosed with a mental health disease but show early signs of it, are likely to have their circadian rhythm misaligned. Stress, or the body's natural reaction to demanding situations, involves a cascade of the secretion of various hormones. If a person undergoes prolonged stress and these hormones are constantly secreted, the body may not recognize the proper times when chemicals like cortisol should be higher or lower. This lack of differentiation is what results in biological clocks to be disrupted. Seasonal changes can also be difficult to adapt to. If a person does not adapt to these changes, their circadian rhythms will be harder to align. Finally, traumatic brain injuries, especially repeated head injuries, cause direct damage to parts of the brain crucial for circadian function. Repeated injuries have been found to reduce the brain's cognitive function and ability to heal once injured. If a certain location in the brain fails to carry out tasks or messages due to injury, then the circadian rhythm will be misaligned.

Maintaining an aligned circadian rhythm becomes more challenging with today's society's growing cognitive and psychological demands. Work schedules, artificial light, and genetics are natural parts of life that contribute to misaligned circadian rhythms. While it is challenging, prioritizing sleep, limiting cortisol level, watching dietary habits, and exercising are ways to

reduce circadian misalignment. In addition, most of the studies presented in this paper involved test subjects that were mice. Although the effects seen in mice could shed light on human biology, variations might exist that result in inaccurate outcomes in humans.

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