The Effects of Circadian Misalignment on Behavior and Cognitive Function

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Abstract

Circadian clocks allow organisms to coordinate and optimize physiological and behavioral activities such as sleep with environmental cues. Regulating circadian rhythms are crucial for maintaining healthy sleep-wake cycles and cognition. This review will examine how cognitive function is affected when circadian misalignment is induced. Modern lifestyle and technology have increased the number of people who are exposed to shift work, jet lag, and artificial light. For example, in industrialized societies, approximately 20% of the population is engaged in shift work (IARC Monographs, 2020), and two thirds experience social jetlag (Caliandro et al., 2021). This literature review takes two approaches to investigating the effects of circadian misalignment on cognition. First, it will research the effects of misalignment through the zeitgebers of shift work, jet lag, and light. There is a lack of research investigating the overall effects of circadian misalignment on its most vulnerable populations. Thus, this study will also examine research on misalignment in populations whose lifestyles make them inclined to experience desynchrony, such as adolescents, aging and elderly persons, and patients with mild cognitive impairment and Alzheimer's disease. These findings have important implications for the lives and health of many often overlooked workers and populations.

Keywords: Circadian misalignment, shift work, jet lag, artificial light, cognition, cognitive function, memory, adolescents, elderly, mild cognitive impairment, Alzheimer's disease

Introduction

Organisms developed 24-hour internal timekeeping systems known as circadian clocks to synchronize biological functions to the Earth's light-dark cycle and environmental cues. These endogenous rhythms regulate various physical and behavioral processes, such as the sleep-wake cycle, reproduction, and metabolic processes, and persist under constant conditions. The principal cellular clock in mammals is located in the central circadian pacemaker (CCP) in the suprachiasmatic nucleus (SCN) of the hypothalamus. Circadian rhythms are maintained by a molecular clock system which is present in almost every cell of the body. It operates through a transcription-translation negative feedback loop and involves the core clock genes Brain and muscle arnt-like protein-1 (BMAL1) and its binding partner Circadian locomotor output cycles kaput (CLOCK). The BMAL1 and CLOCK proteins bind to specific deoxyribonucleic acid (DNA) sequences to produce several genes, including Period (Per1,2,3) and Cryptochrome (Cry1,2) which produce PER and CRY proteins that inhibit the activity of CLOCK and BMAL1 in a feedback loop (Cajochen & Schmidt, 2025).

Cognitive processes including memory, attention, mood, and reaction time also show circadian rhythms (Fisk et al., 2018). Cognition varies over the 24 hour day. Levels are low upon awakening but rapidly improve and reach highs 2-4 h after wake, which are maintained for the first 8 h awake. This is often followed by midday dip before returning to relatively high levels until habitual bedtime. Cognition is impaired when wakefulness is extended beyond its usual pattern. Additionally, the misalignment of the sleep-wake cycle with internal circadian time can lead to worsened performance (Wright et al., 2006).

Circadian misalignment occurs when an individual's behavioral (sleep/wake, activity/rest, etc) or environmental cycles (light/dark) are misaligned with circadian rhythms. Common circadian disrupters include shift work, jet lag, irregular sleep patterns, and exposure to artificial light at night (ALAN). Circadian misalignment can cause a variety of pathological consequences, such as weight gain and metabolic harm, as well as decreased cognitive performance, and worsened memory (Schrader et al., 2024). Approximately 20% of the workforce, including essential healthcare and emergency workers, participate in shift work. Thus, this topic is important to study as it impacts the lives and health of many often overlooked workers.

Additionally, research suggests that exposure to circadian disrupters can lead to misalignment in the biological systems and feedback loops meant to regulate homeostasis, causing dampened expression of core clock genes (Schrader et al., 2024). These genes, which play a crucial role in circadian rhythm, may also have a more widespread role in cognition, mood, and reward-related behaviors (Charrier et al., 2017).

This study will specifically examine the effects of different types of circadian misalignment caused by shift work, jetlag, and light, and how misalignment is associated with cognitive impairment. This review aims to better understand the impacts of circadian misalignment on behavior and cognition in vulnerable populations including adolescents, older people, and mild cognitive impairment patients.

Methodology

This paper used a literature review approach to examine the effects of circadian misalignment on cognitive function. It synthesized the results of 20 animal and human studies published between 2000 and 2025, with the majority of studies being from the last decade. Relevant research articles were selected using keywords such as “circadian misalignment,” “cognition,” “cognitive functioning,” and “desynchrony.” Specific topics of interest included shift work, jet lag, artificial light, effects on adolescent behavior and performance, and correlation with cognitive impairment and dementia.

Body

Shift Work

Globally, an estimated 20% of workers engage in regular night shift work, including those that work in transportation, health care, and emergency services (IARC Monographs, 2020), and that percentage will continue to rise. Since shift work is associated with increased workplace accidents, studies in chronic shift workers have examined the effects of circadian misalignment on cognitive performance (IARC Monographs, 2020).

One within-subject, randomized crossover study (n = 9) simulated two separate 3-day trials of both day (circadian alignment) and night shift (circadian misalignment) work conditions (Chellappa et al., 2019). Participants were then assessed using a variety of cognitive tests, including Psychomotor Vigilance Task (PVT), visual serial addition task (ADD), Digit Symbol Substitution Task (DSST), and probed recall memory (PRM) test. The researchers found that the night shift workers (exposed to circadian misalignment) showed slower sustained attention (PVT) and information processing speed (DSST) and increased lapses in the visual-motor task (TKT), whereas ADD and PRM accuracy was the same between aligned and misaligned groups. Participants who slept during the day (misalignment) also experienced lower sleep efficiency and reported higher levels of subjective sleepiness, which was correlated with the impaired sustained attention and visual-motor performance above.

Another study of a real-world work scenario looked at circadian misalignment in 30 hospital shift work nurses, 15 of whom had been working night-shifts for at least three weeks (Molzof et al., 2019). After completing three 12-hour shifts, the nurses were assessed using the PVT, the

Two-Digit Addition Test (ADD), and a medication calculation fluency test (DRUG). Night-shift nurses correctly completed fewer addition problems and took longer to complete each problem compared to day-shift nurses. Night-shift workers also took significantly longer to complete the drug calculation test, though both groups answered the same number of problems correctly.

Jet Lag

Jet lag is another instance when one's circadian system may become misaligned. When rapidly changing environmental conditions or traveling across time zones, shifts in the light-dark cycle can desynchronize the SCN and its downstream oscillatory networks (Vosko et al., 2010). Thus, exposure to light at the wrong time can disturb the circadian system and its regulated behaviors, such as sleep and memory (Boutrin et al., 2025).

One study (n = 62) followed flight attendants who had over 8 hours of jet lag per week and had 2-4 days of rest in between each flight (Cho et al., 2000). Three hours into their work, they were given delayed match-to-sample tasks to test memory performance. Researchers found that there was no significant difference in performance in flight attendants who had <3 years of service compared to the control group. However, flight attendants with 4 years of service had a significantly slower reaction time and lower number of correct responses compared to a control that also had 4 years of service. On the other hand, it was found that other flight attendants who had more than 14 days of rest between each flight answered more than 85% of questions correctly and showed no memory deficits.

Another study in which hamsters (n = 61) were exposed to experimental jet lag conditions found that jet lag suppressed hippocampal cell proliferation and reduced neurogenesis by >50% (Gibson et al., 2010). Jet-lagged hamsters also showed deficits in learning and memory that persisted even after the hamsters re-synchronized their circadian rhythms to the environment.

In addition, there is a phenomenon known as “social jetlag,” in which the body’s circadian rhythm and social schedule are misaligned. The body’s internal clock is constantly readjusting to different sleep cycles. This typically occurs when people sleep for later and longer on weekends in order to make up for earlier and shorter sleep on weekdays (Fischer & Hilditch, 2022). Similar to night-shift work, misalignment of the circadian system results in increased accident rates, risk for performance errors, and worsened cognitive abilities (Krishnan & Lyons, 2015).

Approximately half of adolescents experience social jetlag due to differences in sleep schedules on school days and weekends (Yang et al., 2023). Yang and colleagues studied 6335 adolescents and measured behavior, cognition, mental health and looked at school grades and MRI scans. At the second follow-up, it was found that high sleep-corrected jet lag (SJLsc, > 1 hour difference in sleep onset timing on school day versus free day) significantly affected 26 out of 39 behavioral measurements and had the greatest effect size on picture-vocabulary, oral reading recognition, positive urgency, grades, and number of yes’s on the Prodromal Psychosis Scale. Additionally, 33 out of 306 unique brain network connections significantly differed in high SJLsc and low SJLsc.

Light

External cues are constantly synchronizing the body's biological rhythms to the environment. Light is the main zeitgeber for circadian rhythms. Exposure before bed delays the onset of melatonin, a hormone that regulates sleep-wake cycles and re-entrains the CCP, whereas morning light exposure advances circadian rhythms (Gooley et al., 2011).

Disrupting cyclic light conditions has a variety of effects on cognition. In a study where mice were exposed to continuous light (LL) to desynchronize circadian rhythms from the environment, mice showed a significant reduction in hippocampal neurogenesis and impaired performance in a spatial awareness task (Fujioka et al., 2010). In another study (n = 24), mice increased depressive-like behavioral responses after three weeks of LL (Fonken et al., 2009). However, other rat studies showed no effect of LL on neurogenesis (Mueller et al., 2011).

As technology continues to advance, society is increasingly affected by inappropriate light exposure such as light emission from devices and artificial light at night (ALAN).
Extended exposure to these stimuli disrupts circadian rhythms by altering the environment's natural light-dark cycle. When healthy young adults (n = 12) were given an electronic book to read on a light-emitting device before bedtime, participants took longer time to fall asleep and experienced altered sleep quality, circadian phase delay, and lowered alertness the next day (Chang et al., 2014). Shao et al. (2025) found that outdoor ALAN exposure was associated with later sleep timing and impaired executive function in depressed patients (n = 701). Other studies have shown that outdoor light at night is correlated with a higher risk of mild cognitive impairment (Chen et al., 2022) and prevalence of Alzheimer's disease (Voigt, 2025), as mice

exposed to dim light showed increased interleukin-1β, a pro-inflammatory cytokine associated with Alzheimer's disease.

Additionally, artificial light exposure may affect brain function, including memory and learning. Hui et al. (2023) studied brain region activation and changes in genes in zebra finches (n = 13) exposed to ALAN. Compared to the control group, ALAN-exposed birds had significantly different immediate early gene (IEG) expression in visual and motor pathways, pain processing, hormone regulation, and parts of the brain involved in associative learning and spatial and object recognition.

A nationally representative cross-sectional study of teenagers in the US found that those living in areas with the highest levels of outdoor light slept 29 minutes later and got 11 fewer minutes of sleep compared to teenagers in areas with the lowest ALAN levels. Associations were also found between ALAN and mood and anxiety disorder, specific phobias, and major depressive disorder (Merikangas, 2020).

Adolescents

Insufficient sleep and circadian misalignment are prevalent among adolescents due to societal influences such as early school start times and late night activities and screen times (Adornetti et al., 2025). Circadian misalignment may impact executive function, risk-taking, and related behaviors such as alcohol involvement in adolescents. Adolescents (n = 29) underwent a 20-day sleep manipulation protocol. Executive function and risk-taking were assessed through the Trail Making Task, Iowa Gambling Task, and the Behavioral Inhibition and Behavioral Activation

System, which was a subjective measure of executive function and risk-taking. The study found that the adolescents with misaligned sleep patterns who took the gambling task significantly increased risk-taking compared to the aligned group. Misaligned adolescents also scored higher scores on the behavioral assessment and self-reported to have increasingly sensitive and nervous reactions to aversive outcomes and expected punishment (Mills et al., 2024, A6).

In another study (n = 31) of late adolescents (18-22 years) who consumed alcohol weekly, those with greater circadian misalignment had lower responses to anticipated monetary reward in the striatum and medial prefrontal cortex, which correlated with more baseline binge-drinking episodes but not alcohol drinking in the post-scan weekend (Hasler et al., 2022).

Additionally, research done on college undergraduates (n = 61) aged 18+ found a significant difference in grade point average in students with irregular sleep patterns (and thus circadian misalignment) compared to students with sleep regularity (Phillips et al., 2017).

Older People

Circadian rhythms change as people age. Older people experience advancement in timing of sleep, increased number of awakenings, and reductions in sleep efficiency and slow wave sleep (Duffy et al., 2016). A study (n = 1022) of patients with a mean age of over 80 years found that decreased circadian rhythm strength, smaller amplitude, increased variation, and reduced stability were associated with increased risk of incident frailty and faster deterioration of frailty over time (Cai et al., 2023).

Additionally, aging is a known risk factor for dementia, and the prevalence of cognitive impairment and dementia in older adults is steadily increasing. Approximately one-third of adults 65 years and older have mild cognitive impairment (MCI) or dementia, and from 1996 to 2014, cases of cognitive impairment increased from 18 to 21% in men over 50 (Manly et al., 2022, Hale et al., 2020). In a nationally representative sample of older (> 60 years) American men and women (n = 2710, 2772, and 2786), researchers found that a lower phasor magnitude (decreased strength of circadian alignment coupling) was associated with lower scores on the Digit Symbol Substitution Test, a cognitive measure for processing speed and attention (Leahy et al., 2024). There were also associations with lower verbal fluency scores, although this result was not significant after adjusting for other confounding factors.

In another study of healthy older adults (n = 1401), participants were tested annually for cognition and motor abilities (Li et al., 2020). Circadian amplitude, acrophase, and interdaily stability progressively decreased over time and these aging effects were doubled or more than doubled after a MCI diagnosis and doubled again after Alzheimer's diagnosis.

Furthermore, the expression of clock genes changes with age. Aging was shown to decrease the expression of *Bmal1* in hamsters in the SCN, and decreased *Bmal1* combined with aging potentially leads to greater risk of developing metabolic disorders and accelerates age-associated impaired memory and deficits in spatial and non-spatial learning (Iweka et al., 2023).

Mild Cognitive Impairment and Alzheimer's Disease

Circadian disturbances are common in people with mild cognitive impairment (MCI) and Alzheimer's disease (Li et al., 2020; Naismith et al., 2014). The results after 30 MCI patients underwent medical, psychiatric, neuropsychological, and memory tests showed advanced secretion timing of melatonin, the hormone that regulates circadian rhythm, greater wake after sleep onset, which is indicative of fragmented sleep, and increased rapid eye movement sleep latency, a key indicator of sleep quality. In MCI patients, dim light melatonin onset was also associated with poorer memory (Naismith et al., 2014).

Alzheimer's disease (AD) patients show altered synchronization in circadian rhythms. Compared to controls, there were noticeable differences in phase clock gene expression and phase relationships between genes in AD patients (Cermakian et al., 2011). Additionally, targeted deletion of core clock gene *Bmal1* in mice is linked to neurodegeneration, oxidative stress, and circadian rhythm dysfunction (Ahmad et al., 2022). *Bmal1* deletion may cause fluctuation of amyloid-beta (Aβ) in the hippocampal interstitial fluid and speed up the accumulation of amyloid plaque, a key characterization of AD.

Discussion

Evidence from both human and animal studies show that circadian misalignment, whether induced through jetlag, shiftwork, or artificial light, has serious consequences for cognition, neurogenesis, and overall brain health and function. However, it is important to evaluate the validity and shortcomings of these studies, as well as the trends they imply.

Short-term circadian misalignment caused by simulated shift work and jet lag conditions shows immediate deficits in attention, memory, information processing speed, and sleep efficiency. Though adequate rest may provide time needed for circadian rhythms to reentrain to environmental surroundings, hamster studies show that learning and memory deficits persisted even after their circadian rhythms were synchronized, suggesting the brain's sensitivity to misalignment and the potential long-lasting negative effects of disruption. When workers experience chronic forms of misalignment such as working night shifts or flying across multiple timezones with little breaks in between, performance is significantly slower and less accurate. This points to a pattern in which brief disruptions cause lasting damage and chronic misalignment creates constant physiological strain that lead to serious cognitive impairment.

Exposure to artificial light highlights the importance of synchronizing internal cues to the environment. Light exposure at different times of day can advance or delay the circadian rhythm, causing desynchrony. In rodent studies, continuous light exposure reduced hippocampal neurogenesis, impaired spatial awareness, and increased depressive-like behavior. However, the generalizability of these findings is limited due to contradictory results, although research varied in experiment duration, rodent species, and techniques used to study sleep deprivation, spatial learning, and behavior. Nevertheless, human studies support that artificial light exposure at night or before bedtime is associated with altered sleep quality, circadian phase delay, mood disorders, and a higher risk for mild cognitive impairment.

Fujioka and Fonken's studies about continuous light conditions in mice showed reduction in hippocampal neurogenesis, impaired performance in a spatial awareness task, and depressive-like behavior, although other studies showed no effect of LL on neurogenesis. It is possible that constant light exposure is a stable disruption compared to jet lag, which results in repeated mismatches between internal clocks and environmental cues. This would explain why jet lag studies show more consistently negative effects in both humans and animals despite the fact that both LL and jet lag are circadian disruptions.

Several age groups are particularly vulnerable to circadian misalignment due to societal demands and aging. Adolescents are prone to experiencing "social jetlag" and are often forced into waking early due to school start times and experiencing catch up sleep over the weekend. Misalignment in adolescents may impact executive function, risk-taking, and academic performance and is associated with the development of anxiety and depressive disorders. It was correlated with more baseline binge-drinking episodes in late adolescents who regularly consumed alcohol. Shift work is associated with increased workplace accidents. Adults who work shift jobs are prone to slower sustained attention and lower sleep efficiency. Throughout aging, circadian rhythms become less robust. Decreased circadian rhythm strength is associated with increased risk of frailty, lower processing speed and attention, and decreased expression of *Bmal1*, which accelerates age-associated impaired memory and deficits in spatial and non-spatial learning. This suggests that disturbed circadian rhythms in elderly people may be a risk factor or warning sign for frailty and cognitive impairment. Circadian disturbances are present in patients with mild cognitive impairment and Alzheimer's disease. Evidence suggests that *Bmal1* deletion causes neurodegeneration and circadian rhythm dysfunction and is linked to the progression of amyloid plaque accumulation, which points to a potential link between the progression of circadian dysregulation and Alzheimer's disease. Overall, circadian misalignment has been shown to affect learning, memory, and psychological wellbeing in adolescents, attention and performance in adults, and neurodegeneration in older populations.

It is important to consider limitations in the literature. Human studies that rely on data may be limited by missing data and the COVID-19 pandemic. Other studies, which are cross-sectional or short-term, limit causal inference. Many studies were limited by a relatively small sample size. Though animal studies provide important insights, they often rely on artificial environments such as the forced swim test which does not represent human environments. Studies assessing cognitive proficiency also could have been improved upon by assessing other cognitive functions that are necessary in a workplace environment, such as decision making and multitasking abilities. Future studies should study if reductions in neurogenesis are still prevalent after several months of jet lag recovery in humans and how ALAN is related to Alzheimer's incidence.

Maintaining aligned circadian rhythms is critical for cognitive health and overall wellbeing. Promising interventions include minimizing social jetlag by sticking to a consistent sleep schedule and minimizing screen time, blue light exposure, and artificial light at night at least one hour before bed (Yeom et al., 2024) to avoid further delaying the circadian rhythm. Light therapy through light boxes or natural sunlight may be another effective treatment, as exposing individuals to bright light shortly after waking can help reset the body's internal clock and advance the sleep-wake cycle. Sitting in front of a light intensity of 10,000 lux for at least 30 minutes is recommended by experts (Sloane & King, 2013). Melatonin supplements taken 1-2 hours before bedtime may be used to advance the sleep phase. Melatonin may also be a therapeutic aid for AD, as it shows protective effects against neurodegeneration, reduces oxidative stress, and enhances cognitive effects (Ahmad et al., 2022). Occupation-related efforts such as delaying school start times and reordering shift schedules to allow adequate recovery time may enhance productivity and efficiency. Public health efforts may raise awareness about circadian health and educate the community on how best to take care of their biological, psychological, and social health.

Conclusion

Circadian misalignment and factors that induce it (shift work, jetlag, light) are associated with worsened cognitive abilities. These include slower sustained attention, information processing speed, impaired executive function, heightened risk-taking behavior, and lower grades. Misaligned subjects showed significant learning impairment in comparison to synchronized groups, who improved cognitive performance. Misalignment is also associated with mood, anxiety and depressive disorders in teenagers and has been shown to reduce neurogenesis in animal studies. Circadian misalignment is prevalent in people with mild cognitive impairment and Alzheimer's disease. Due to its widespread nature and negative associations with cognition and behavior across all ages, it is important to maintain a healthy circadian rhythm for overall health and well-being. Consistent sleep schedules, light therapy, and melatonin supplements are lifestyle habits that can help individuals mitigate and avoid circadian disruption.

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