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The Impact of Modern Lifestyle on Circadian Rhythms: Implications for Mental and Physical Health

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Abstract

Introduction and purpose: Circadian rhythms are internal processes that regulate the sleep-wake cycle and repeat roughly every 24 hours. These rhythms are driven by a biological clock, primarily located in the suprachiasmatic nucleus (SCN) of the brain. Synchronized with environmental cues such as light and darkness, they play a crucial role in regulating sleep-wake patterns, hormone secretion, metabolism, and other physiological functions. Disruptions in circadian rhythms can have wide-ranging effects on health. This review aims to synthesize the current state of knowledge on how lifestyle factors affect circadian rhythms and explore the subsequent implications for both mental and physical health.
Description of the state of knowledge: Modern lifestyles factors characterized by artificial lighting, shift work, noise pollution, excessive caffeine use, worldwide traveling and irregular eating habits can significantly disrupt natural circadian rhythms. Such disruptions are associated with a spectrum of pathologies, such as sleep dysregulation, mood disorders (e.g., depression and bipolar disorder), metabolic impairments, and suboptimal immune responses.

Summary: This review synthesizes current research findings on the impacts of lifestyle-induced circadian misalignment, highlighting the complex interactions between modern life and circadian biology. Maintaining circadian rhythm integrity is crucial not just for enhancing overall well-being but also as a preventive strategy against a wide range of diseases. Integrating this understanding into health practices is essential for addressing the pervasive impact of circadian disruptions in modern society.

Keywords: Circadian rhythm, sleep, mental health, physical health

1. Introduction

1.1 Background

The term circadian rhythm was originally invented by Halberg to indicate the near-24-hour (h) endogenous oscillations of biological processes in organisms associated with the earth's daily rotation cycle [1]. It originated from the Latin words: "circa" means "around" and "dies" means "day". The circadian rhythm, also referred to as the near-24-hour rhythm, is perhaps the best characterized biological oscillator and they exist in virtually all light-sensitive organisms. In mammals, it influences nearly all aspects of physiology and behavior, including sleep-wake cycles, cardiovascular activity, endocrinology, body temperature, renal activity, physiology of the gastro-intestinal tract and hepatic metabolism [2].

The central circadian pacemaker is located in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus. Its major tract, the retinohypothalamic tract (RHT), ensures synchronization of day-night cycles. After exposure to light detected by the retina, non-visual melanopsin-containing retinal ganglionic cells transmit photic signals to the SCN through the RHT. The SCN clock projects to various brain centers, many of which contain local circadian clocks that direct behavioral (for example, feeding–fasting and sleep–wakefulness), autonomic and neuroendocrine circadian rhythms [3]. Notably, in the brain, beside the master clock in SCN operating as self-sustaining clocks, other functional nuclei have been found to act as semiautonomous clocks (i.e. olfactory bulb, dorsomedial hypothalamus, arcuate nucleus, habenula) or as slave oscillators (i.e. bed nucleus of the stria terminalis, amygdala, preoptic area, paraventricular nucleus, nucleus accumbens), both coordinated by the SCN [4]. While the SCN coordinates overall circadian rhythm, peripheral clocks in organs like the liver, heart, and lungs operate somewhat independently, driven by local cues and systemic signals from the SCN [4]. For example, feeding times can reset liver clocks, demonstrating how peripheral clocks adapt to both central cues and environmental factors.

At the core of the circadian system are clock genes that drive the cyclical expression patterns fundamental to the circadian rhythm. These genes include CLOCK, BMAL1, PER (Period), CRY (Cryptochrome), REV-ERB, and ROR, which produce proteins that interact to create rhythmic patterns lasting about 24 hours [5]. These interactions typically involve positive and negative feedback loops:

Positive Feedback: Proteins CLOCK and BMAL1 pair up to enhance the expression of PER and CRY genes [4]. Negative Feedback: As the levels of PER and CRY proteins increase, they interact to form a complex that inhibits their own expression by suppressing the CLOCK-BMAL1 activity, thus creating a self-regulating cycle [4]. This genetic and protein interaction network is critical for the sustained and autonomous oscillations observed in circadian rhythms across different organisms.

1.2 Problem Statement

In today's modern society, advancements in technology, changes in work patterns, and the widespread availability of artificial lighting have led to significant disruptions in circadian rhythms. Many factors such as chronic and acute jet lag, night meals, shift work, and extended shifts, contribute to circadian dysfunction, which can lead to sleep disorders, metabolic syndrome, decreased physical performance, cardiovascular and inflammatory diseases, neuropsychiatric illnesses, and cancer [6-7].

1.3 Objective

This review aims to explore the impact of modern lifestyle factors on circadian rhythms and the subsequent effects on mental and physical health. It seeks to synthesize research findings to present a clear picture of how lifestyle-induced circadian misalignment occurs and how its disruption affects overall health.

2. Impact of Modern Lifestyle on Circadian Rhythms

2.1 Artificial lighting

Artificial lighting has become an integral part of modern life, extending productive hours well beyond sunset and affecting our natural circadian rhythms. The widespread use of energy-efficient lighting and electronic devices such as smartphones, tablets, and computers emit significant amounts of blue light. This type of light is particularly impactful on melatonin production, a key hormone secreted by the pineal gland that signals nighttime to the body. The specific wavelengths of blue light emitted by electronic screens can inhibit the release of melatonin more powerfully than other light forms [8-9]. This suppression occurs because blue light is especially effective at stimulating photoreceptive cells in the retina called melanopsin-containing retinal ganglion cells, which directly communicate with the brain's circadian regulator, the suprachiasmatic nucleus (SCN) [9]. When melatonin release is delayed, it can shift the entire sleep-wake cycle, leading to later sleep onset and potentially shortened sleep duration [10].

2.2 Shift Work and Irregular Working Hours

Shift work and irregular working hours are prevalent in many modern industries, from healthcare to manufacturing and services. Approximately 10–20% of the workforce of industrialized nations participates in shift work [11]. In individuals with normal work hours, and regular sleep patterns, daytime alertness is governed by the circadian clock, which controls circadian rhythmicity leading to heightened alertness in the day and reduced alertness at night [12]. This biological process is counteracted by a sleep-promoting homeostatic pressure that accumulates throughout waking hours [13-14]. When working during daytime hours, these two processes align with the environmental light/dark cycle to maintain alertness while awake at work, while allowing for consolidated sleep during the night. Shift work, especially night shifts, forces workers to be awake during the night and sleep during the day, directly opposing the natural biological rhythm. This misalignment between the body's internal circadian clock and external environment leads to a disrupted circadian sleep-wake cycle.

2.3 Sound and Noise Pollution

Noise from modern technology is an increasingly prevalent issue as more devices and machinery become integral to daily life. It has been recognized as a significant environmental stressor that affects both physical and mental health [15-18]. Devices such as smartphones, tablets, and laptops often have notification sounds that can be disruptive, especially when multiple devices are in use simultaneously. Additionally, the sound output from personal entertainment systems can contribute significantly to the noise level in residential areas. Modern home appliances, including washing machines, dishwashers, air conditioners, and refrigerators, are designed to be more efficient but can still contribute to background noise levels. While individually they might not be overly loud, collectively, their operation can create a constant hum or buzz that can be disturbing. That noise can affect circadian rhythms primarily through its impact on sleep patterns. Sudden or continuous noise can cause sleep fragmentation, delay sleep onset, and alter sleep architecture, impacting the quality and quantity of sleep [15-17]. Furthermore, exposure to noise at night can shift the phase of circadian rhythms, leading to misalignment between internal biological clocks and the external environment [15,17]. During the sleep phase, noise activates the inflammatory response and alters endothelial function. This oxidative stress damages vital organs' vasculature and leads to various other clinical conditions [15].

2.4 Rapid travel across time zones (jet lag)

In our globalized world, rapid long-distance travel is both a privilege and a norm for many, enabling unprecedented personal and professional opportunities. Jet lag occurs when long travel by airplane quickly puts a person in another time zone. It is formally described as circadian desynchrony, or a mismatch between the timing of the internal circadian clock(s) and the external environment [19]. When traveling across time zones, the SCN receives light cues at unexpected times, leading to confusion and misalignment. If the light exposure occurs earlier or later than the SCN expects based on the previous environmental conditions, it attempts to reset the body's internal clock accordingly. This shift, however, does not happen instantly and usually requires several cycles of light and darkness to fully adjust [20]. Depending on the direction of travel, the phase of the circadian rhythm shifts. Traveling east typically causes a phase advance (needing to sleep and wake earlier than usual), while traveling west causes a phase delay (needing to sleep and wake later than usual) [21]. These shifts require the SCN to recalibrate its control over melatonin secretion and other circadian signals. The process of resetting the circadian genes to a new time zone involves complex transcriptional and translational feedback loops. Light perceived by the SCN during new daytime hours triggers signaling pathways that alter the expression of these core clock genes, gradually shifting their peak activity to align with local time [22].

2.5 Irregular Eating Patterns

Irregular eating patterns are common in modern lifestyles due to long work hours and social engagements. Eating times have a substantial impact on circadian rhythms. Besides the central circadian clock in the brain, peripheral clocks exist in almost all tissues and organs, including the liver, pancreas, and adipose tissue [23]. These clocks are primarily synchronized by the central clock in the SCN, which responds to light cues. However, peripheral clocks are also strongly influenced by timing cues from eating [23]. Food acts as a powerful zeitgeber (time-giver) for peripheral clocks [24]. Regular feeding schedules reinforce the alignment of these clocks to the central circadian rhythm. Irregular eating disrupts this alignment, leading to circadian dysregulation and metabolic processes disruption [24].

2.6 Excessive Caffeine use

Caffeine use is a significant modern lifestyle factor that impacts circadian rhythms, particularly because of its widespread consumption to counteract sleepiness and enhance alertness. Caffeine delays the human circadian clock and affects cellular timekeeping through an adenosine receptor–dependent mechanism [25]. Caffeine has been shown to delay the human circadian melatonin rhythm, affecting the body's internal clock by about 40 minutes, similar to the impact of exposure to bright light before bedtime [25]. Although further research is needed to investigate the exact role of Caffeine on circadian rhythm disruption.

3. Implications of disrupted circadian rhythm on health

3.1 Sleep disorders

Sleep is a critical biological function that rejuvenates the body and mind, influencing nearly all systems within the human body. The synchronization of sleep with the circadian rhythm, or the body’s internal clock, is crucial for optimal health. Disruptions in the circadian rhythm can lead to significant sleep disorders also called Circadian Rhythm Sleep-Wake Disorders (CRSWDs). The essential feature of CRSWDs is a persistent or recurrent pattern of sleep disturbance due primarily to alterations in the circadian timekeeping system or a misalignment between the endogenous circadian rhythm and exogenous factors that affect the timing or duration of sleep [26]. The American Academy of Sleep Medicine released in 2014 The International Classification of Sleep Disorders (ICSD-3). According to the ICSD-3 classification criteria, CRSWDs can be roughly divided into two categories: endogenous caused by alterations in the circadian rhythm system resulting from chronic changes in the regulation or capture mechanism of the biological clock and exogenous which results from a mismatch between the sleep-wake time and the internal circadian rhythm attributable to environmental changes [26]. The symptoms vary depending on the specific type of CRSWD but typically revolve around the inability to sleep, excessive daytime sleepiness and Insomnia [27]. If not addressed, the symptoms of CRSWDs can lead to broader health and lifestyle issues.

3.2 Depression

A growing body of evidence suggests a strong link between the misalignment of circadian rhythms and the development of depressive disorders. The most direct manifestation of circadian rhythm disruption is seen in sleep patterns. Individuals with depressive disorders frequently experience insomnia or hypersomnia, both of which are indicative of a misaligned circadian clock. Research has shown that these sleep disturbances often precede the onset of depressive episodes, suggesting a causative role in the development of the disorder [28]. In addition, a cross-sectional study of 91 105 participants from the UK Biobank, have shown that lower amplitude in circadian activity cycles correlates with higher rates of depressive symptoms, illustrating how diminished circadian signaling can affect mood [29]. Furthermore, molecular study from 2010 which examined 209 single-nucleotide polymorphisms (SNPs) covering 19 circadian genes in a sample of 534 patients (335 with unipolar major mood depression (MDD) have revealed associations between certain circadian genes and mood disorders [30-31].

3.3 Bipolar disorder

Bipolar disorder (BD) is a complex mood disorder characterized by significant fluctuations in mood, energy, and activity levels. Research has demonstrated that individuals with bipolar disorder often exhibit significant disruptions in their circadian rhythms, including altered sleep patterns and hormonal imbalances [32]. These disruptions are not only symptoms of the disorder but may also contribute to its development [32]. For instance, genetic studies have identified mutations in various circadian-related genes that are associated with an increased risk of bipolar disorder, highlighting a potential genetic link between circadian rhythm regulation and mood dysregulation [32-33]. Although future research is needed to clarify the associations between circadian rhythm disturbances and BD.

3.4 Schizophrenia

Schizophrenia is a complex psychiatric disorder characterized by symptoms such as delusions, hallucinations, disorganized thinking, and significant social or occupational dysfunction. Sleep and circadian rhythm disruption (SCRD) is a common feature of schizophrenia, and is associated with symptom severity and patient quality of life. It is commonly manifested as disturbances to the sleep/wake cycle, with sleep abnormalities occurring in up to 80% of patients, making it one of the most common symptoms of this disorder [34]. Dopamine, a key neurotransmitter involved in schizophrenia, is influenced by circadian processes [35]. Abnormalities in circadian rhythms can lead to dysregulation of dopamine pathways, which are central to the psychotic manifestations of schizophrenia. This dysregulation is not limited to increased levels but also involves the timing and synchronization of dopamine release, which is critical for normal cognitive and emotional processing [34].

3.5 Metabolic dysfunction

The circadian system coordinates the timing of essential metabolic hormones such as insulin, glucagon, and cortisol. Insulin regulates glucose levels in the blood, facilitating its uptake by cells for energy production. Disruptions in circadian rhythms can lead to irregular insulin release, increasing the risk of metabolic disorders such as diabetes [36]. Similarly, cortisol, which helps regulate metabolism and response to stress, follows a circadian pattern. Altered cortisol rhythms can lead to increased appetite and fat deposition, contributing to obesity [36]. Circadian disruption affects lipid metabolism, influencing cholesterol synthesis and storage. Studies have shown that a misaligned circadian rhythm can increase the production of triglycerides, leading to hyperlipidemia and associated cardiovascular risks [36].

3.6 Dysregulation of the Immune system

The circadian clock influences multiple aspects of the immune system, such as the trafficking of immune cells, the ability to recognize pathogens, the phagocytic capacity, and the secretion of inflammatory cytokines, chemokines, and complement factors [37]. Disruption of the circadian clock can lead to a dysregulated immune response, which may contribute to chronic inflammation, tissue damage, and endotoxin shock [38]. Such chronic inflammation is often seen in conditions like type 2 diabetes, obesity, and various neurodegenerative and neuropsychiatric diseases [38]. Moreover, the timing of infections can affect the severity of outcomes, as the immune system's effectiveness varies across the circadian cycle. The innate immune system, which serves as the first line of defense against pathogens, is also strongly influenced by circadian rhythms. Components such as macrophages and natural killer cells display circadian variations in both number and function. For instance, macrophages contain intrinsic circadian clocks that regulate their response to signals that trigger inflammation and pathogen recognition [39]. Disruption of these clocks can lead to an inappropriate inflammatory response, potentially leading to chronic inflammation or failing to respond adequately to pathogens [39].

4. Conclusions

This review emphasizes that maintaining and restoring circadian rhythm integrity is not merely beneficial but essential for health and well-being in a modern, interconnected world. Latest technologies and lifestyle choices play significant roles in disturbing circadian rhythms. Disruptions in these rhythms have been closely linked with numerous health challenges, including sleep disorders, metabolic dysregulation and mood disorders like depression and bipolar disorder. Awareness and appropriate management of circadian rhythms could lead to significant improvements in global health outcomes, highlighting the critical interplay between our biological clocks and the environments we inhabit. Future research should focus on defining the most effective interventions for circadian realignment and exploring the genetic basis of circadian sensitivity to further tailor personalized medicine approaches.

Disclosure

Author's contribution
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References:

1. Halberg F. Chronobiology. Annu Rev Physiol. 1969;31:675-725. doi:10.1146/annurev.ph.31.030169.003331

2. Gachon F, Nagoshi E, Brown SA, Ripperger J, Schibler U. The mammalian circadian timing system: from gene expression to physiology. *Chromosoma*. 2004;113(3):103-112. doi:10.1007/s00412-004-0296-2

3. Hastings MH, Maywood ES, Brancaccio M. Generation of circadian rhythms in the suprachiasmatic nucleus. *Nat Rev Neurosci*. 2018;19(8):453-469. doi:10.1038/s41583-018-0026-z

4. Fagiani F, Di Marino D, Romagnoli A, et al. Molecular regulations of circadian rhythm and implications for physiology and diseases. *Signal Transduct Target Ther*. 2022;7(1):41. Published 2022 Feb 8. doi:10.1038/s41392-022-00899-y

5. Dierickx, P. et al. (2016). Circadian Rhythms in Stem Cell Biology and Function. In: Madonna, R. (eds) Stem Cells and Cardiac Regeneration. Stem Cell Biology and Regenerative Medicine. Springer, Cham. https://doi.org/10.1007/978-3-319-25427-2_5

6. Dibner C. The importance of being rhythmic: Living in harmony with your body clocks. Acta Physiol (Oxf). 2020;228(1):e13281. doi:10.1111/apha.13281

7. Ruan, W., Yuan, X., & Eltzschig, H. K. (2021). Circadian rhythm as a therapeutic target. In Nature Reviews Drug Discovery (Vol. 20, Issue 4, pp. 287–307). Nature Research. https://doi.org/10.1038/s41573-020-00109-w

8. Wood, B., Rea, M. S., Plitnick, B., & Figueiro, M. G. (2013). Light level and duration of exposure determine the impact of self-luminous tablets on melatonin suppression. Applied Ergonomics, 44(2), 237–240. https://doi.org/10.1016/j.apergo.2012.07.008

9. West, K. E., Jablonski, M. R., Warfield, B., Cecil, K. S., James, M., Ayers, M. A., Maida, J., Bowen, C., Sliney, D. H., Rollag, M. D., Hanifin, J. P., & Brainard, G. C. (2011). Blue light from light-emitting diodes elicits a dose-dependent suppression of melatonin in humans. Journal of Applied Physiology, 110(3), 619–626. https://doi.org/10.1152/japplphysiol.01413.2009

10. Giudice, A., Crispo, A., Grimaldi, M., Polo, A., Bimonte, S., Capunzo, M., Amore, A., Arena, G. D., Cerino, P., Budillon, A., Botti, G., Costantini, S., & Montella, M. (2018). The effect of light exposure at night (LAN) on carcinogenesis via decreased nocturnal melatonin synthesis. In Molecules (Vol. 23, Issue 6). MDPI AG. https://doi.org/10.3390/molecules23061308

11. Sachdeva, A., Goldstein, C. (2020). Shift Work Sleep Disorder. In: Auger, R. (eds) Circadian Rhythm Sleep-Wake Disorders. Springer, Cham. https://doi.org/10.1007/978-3-030-43803-6_11

12. Dijk DJ, Czeisler CA. Paradoxical timing of the circadian rhythm of sleep propensity serves to consolidate sleep and wakefulness in humans. *Neurosci Lett*. 1994;166(1):63-68. doi:10.1016/0304-3940(94)90841-9

13. Borbély AA. A two process model of sleep regulation. *Hum Neurobiol*. 1982;1(3):195-204.

14. Daan S, Beersma DG, Borbély AA. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am J Physiol*. 1984;246(2 Pt 2):R161-R183. doi:10.1152/ajpregu.1984.246.2.R161

15. Pal, Jagriti1,2; Taywade, Manish3,; Pal, Rajni1; Sethi, Divya1,4. Noise Pollution in Intensive Care Unit: A Hidden Enemy affecting the Physical and Mental Health of Patients and Caregivers. Noise and Health 24(114):p 130-136, Jul–Sep 2022. | DOI: 10.4103/nah.nah_79_21

16. Jariwala, Hiral & Syed, Huma & Pandya, Minarva & Gajera, Yogesh. (2017). " Noise Pollution & Human Health: A Review ".

17. Passchier-Vermeer W, Passchier WF. Noise exposure and public health. *Environ Health Perspect*. 2000;108 Suppl 1(Suppl 1):123-131. doi:10.1289/ehp.00108s1123

18. Firdaus G, Ahmad A. Noise Pollution and Human Health: A Case Study of Municipal Corporation of Delhi. *Indoor and Built Environment*. 2010;19(6):648-656. doi:10.1177/1420326X10370532

19. Giudice, A., Crispo, A., Grimaldi, M., Polo, A., Bimonte, S., Capunzo, M., Amore, A., Arena, G. D., Cerino, P., Budillon, A., Botti, G., Costantini, S., & Montella, M. (2018). The effect of light exposure at night (LAN) on carcinogenesis via decreased nocturnal melatonin synthesis. In Molecules (Vol. 23, Issue 6). MDPI AG. https://doi.org/10.3390/molecules23061308

20. Arendt, J. Approaches to the Pharmacological Management of Jet Lag. *Drugs* **78**, 1419–1431 (2018). https://doi.org/10.1007/s40265-018-0973-8

21. Roach, G. D., & Sargent, C. (2019). Interventions to minimize jet lag after westward and eastward flight. In Frontiers in Physiology (Vol. 10, Issue JUL). Frontiers Media S.A. https://doi.org/10.3389/fphys.2019.00927

22. Ramkisoensing A, Meijer JH. Synchronization of Biological Clock Neurons by Light and Peripheral Feedback Systems Promotes Circadian Rhythms and Health. *Front Neurol*. 2015;6:128. Published 2015 Jun 5. doi:10.3389/fneur.2015.00128

23. Johnston JD, Ordovás JM, Scheer FA, Turek FW. Circadian Rhythms, Metabolism, and Chrononutrition in Rodents and Humans. *Adv Nutr*. 2016;7(2):399-406. Published 2016 Mar 15. doi:10.3945/an.115.010777

24. Challet E, Caldelas I, Graff C, Pévet P. Synchronization of the molecular clockwork by light- and food-related cues in mammals. *Biol Chem*. 2003;384(5):711-719. doi:10.1515/BC.2003.079

25. Burke, T., Markwald, R., McHill, A., Chinoy, E., Snider, J., Bessman, S., Jung, C., O'Neill, J., & Wright, K. (2015). Effects of caffeine on the human circadian clock in vivo and in vitro. *Science Translational Medicine*, 7, 305ra146 - 305ra146. https://doi.org/10.1126/scitranslmed.aac5125.

26. Sack RL, Auckley D, Auger RR, et al. Circadian rhythm sleep disorders: part I, basic principles, shift work and jet lag disorders. An American Academy of Sleep Medicine review. Sleep. 2007;30(11):1460-1483. doi:10.1093/sleep/30.11.1460

27. Auger RR, Burgess HJ, Emens JS, Deriy LV, Thomas SM, Sharkey KM. Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders: Advanced Sleep-Wake Phase Disorder (ASWPD), Delayed Sleep-Wake Phase Disorder (DSWPD), Non-24-Hour Sleep-Wake Rhythm Disorder (N24SWD), and Irregular Sleep-Wake Rhythm Disorder (ISWRD). An Update for 2015: An American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med*. 2015;11(10):1199-1236. Published 2015 Oct 15. doi:10.5664/jcsm.5100

28. Nutt D, Wilson S, Paterson L. Sleep disorders as core symptoms of depression. *Dialogues Clin Neurosci*. 2008;10(3):329-336. doi:10.31887/DCNS.2008.10.3/dnutt

29. Lyall, L., Wyse, C., Graham, N., Ferguson, A., Lyall, D., Cullen, B., Morales, C., Biello, S., Mackay, D., Ward, J., Strawbridge, R., Gill, J., Bailey, M., Pell, J., & Smith, D. (2018). Association of disrupted circadian rhythmicity with mood disorders, subjective wellbeing, and cognitive function: a cross-sectional study of 91 105 participants from the UK Biobank.. *The lancet. Psychiatry*, 5 6, 507-514 . https://doi.org/10.1016/S2215-0366(18)30139-1.

30. Soria, V., Martínez-Amorós, E., Escaramís, G., Valero, J., Pérez-Egea, R., Garcia, C., Gutiérrez-Zotes, A., Puigdemont, D., Bayés, M., Crespo, J., Martorell, L., Vilella, E., Labad, A., Vallejo, J., Pérez, V., Menchón, J., Estivill, X., Gratacós, M., & Urretavizcaya, M. (2010). Differential Association of Circadian Genes with Mood Disorders: CRY1 and NPAS2 are Associated with Unipolar Major Depression and CLOCK and VIP with Bipolar Disorder. *Neuropsychopharmacology*, 35, 1279-1289. https://doi.org/10.1038/npp.2009.230.

31. Bergen, S., Pålsson, E., Isgren, A., Song, J., Jakobsson, J., & Landen, M. (2017). Genetic Influences On Inflammatory Biomarkers In Bipolar Disorder. European Neuropsychopharmacology, 27, S483–S484. https://doi.org/10.1016/j.euroneuro.2016.09.572

32. Melo MCA, Abreu RLC, Linhares Neto VB, de Bruin PFC, de Bruin VMS. Chronotype and circadian rhythm in bipolar disorder: A systematic review. *Sleep Med Rev*. 2017;34:46-58. doi:10.1016/j.smrv.2016.06.007

33. Bellivier F, Geoffroy PA, Etain B, Scott J. Sleep- and circadian rhythm-associated pathways as therapeutic targets in bipolar disorder. *Expert Opin Ther Targets*. 2015;19(6):747-763. doi:10.1517/14728222.2015.1018822

34. Ashton, A., & Jagannath, A. (2020). Disrupted Sleep and Circadian Rhythms in Schizophrenia and Their Interaction With Dopamine Signaling. *Frontiers in Neuroscience*, 14. https://doi.org/10.3389/fnins.2020.00636.

35. Verwey M, Dhir S, Amir S. Circadian influences on dopamine circuits of the brain: regulation of striatal rhythms of clock gene expression and implications for psychopathology and disease. *F1000Res*. 2016;5:F1000 Faculty Rev-2062. Published 2016 Aug 24. doi:10.12688/f1000research.9180.1

36. Marcheva B, Ramsey KM, Peek CB, Affinati A, Maury E, Bass J. Circadian clocks and metabolism. *Handb Exp Pharmacol*. 2013;(217):127-155. doi:10.1007/978-3-642-25950-0_6

37. Haspel JA, Anafi R, Brown MK, et al. Perfect timing: circadian rhythms, sleep, and immunity - an NIH workshop summary. *JCI Insight*. 2020;5(1):e131487. Published 2020 Jan 16. doi:10.1172/jci.insight.131487

38. Wang, X. L., & Li, L. (2021). Circadian Clock Regulates Inflammation and the Development of Neurodegeneration. In Frontiers in Cellular and Infection Microbiology (Vol. 11). Frontiers Media S.A. https://doi.org/10.3389/fcimb.2021.696554

39. Curtis AM, Bellet MM, Sassone-Corsi P, O'Neill LA. Circadian clock proteins and immunity. *Immunity*. 2014;40(2):178-186. doi:10.1016/j.immuni.2014.02.002