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# *The Influence of Circadian Rhythm on the Aging Process*

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***Abstract:*** Aging is a complex process that affects all parts of the body, and it happens in almost all living organisms. It is characterized by systemic functional deterioration that elevates risks for neurodegenerative, metabolic, and cardiovascular pathologies. The circadian rhythms are regulated by the suprachiasmatic nucleus (SCN) and peripheral clocks, and they play a crucial role in maintaining sleep quality, metabolism, immune function, and cognition. However, aging disrupts circadian rhythms, resulting in advanced sleep phases, reduced melatonin secretion, and desynchronization of peripheral clocks in elderly people. These disruptions would contribute to various problems, like oxidative stress, mitochondrial dysfunction, inflammation, and metabolic dysregulation, exacerbating age-related diseases, including type 2 diabetes, Alzheimer's and Parkinson's disease, and cancer. Conversely, circadian misalignment accelerates aging processes by impairing cell repair and toxin cleaning and irregular hormone secretion. This creates a bidirectional relationship. Emerging therapeutic strategies, including chronotherapy, melatonin supplementation, and time-restricted feeding, show promise in restoring circadian rhythms and mitigating age-related pathologies. This review highlights the critical interplay between circadian biology and aging processes, while exploring the therapeutic potential of circadian-targeted interventions for enhancing healthy longevity and mitigating age-related pathologies.

***Keywords:*** Circadian rhythm, Aging, Suprachiasmatic nucleus

## 1. Introduction

Aging represents a time-dependent deterioration of physiological integrity, characterized by hallmark molecular processes including cellular senescence, genomic instability, mitochondrial dysfunction, and epigenetic remodeling, collectively impairing organismal fitness and survival capacity. As a result, aging is often associated with an increased risk of developing various chronic diseases, including neurodegeneration, metabolic disorders, and cardiovascular diseases, such as Alzheimer's disease (AD), type 2 diabetes, and hypertension. The data has shown that there is one individual who has AD in every ten people aged 65 and above; the percentage is growing as the age increases [1]. The circadian rhythm represents an endogenous ~24-hour biological timing system that orchestrates fundamental physiological processes across organisms, including sleep-wake regulation, metabolic homeostasis, immune modulation, and neurocognitive function. Most of the control over this rhythm comes from the suprachiasmatic nucleus (SCN), a small area in the hypothalamus, working with clocks in different tissues. To regulate the circadian rhythm, photoreceptive retinal ganglion cells (pRGCs) in the retina detect light and transmit signals to the SCN. In response, the SCN modulates the production of melatonin, a hormone essential for sleep. Circadian regulation is mediated by an

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autoregulatory transcription-translation feedback loop, wherein the CLOCK-BMAL1 heterodimer binds E-box enhancers in SCN neurons, driving the expression of core clock genes—Per* (Period) and Cry (Cryptochrome). The resulting CRY and PER proteins accumulate in the cytoplasm, form inhibitory complexes, and suppress the activity of CLOCK and BMAL1, thereby downregulating their own production. As CRY and PER degrade over time, the inhibition lifts, allowing CLOCK and BMAL1 expression to resume, thus maintaining an approximately 24-hour cycle. Meanwhile, the peripheral clock in different tissues also runs a similar cycle. But unlike the SCN central clock, which is only affected by light, the peripheral clock may be influenced by other external factors, such as temperature.

However, the effects of circadian rhythm and aging is bidirectional. On the one hand, external effectors that cause the disruption of circadian rhythm could have serious effect on organisms' physical and mental health, especially in aging populations. Disrupted circadian rhythm may escalate the risk of cardiovascular disease, diabetes, cognitive impairment, and neurodegenerative diseases like Alzheimer's. On the other hand, aging also has negative effects on circadian rhythms. Studies indicate that aging is associated with an advanced circadian phase. A decline in the amplitude of circadian rhythm and an abnormal response to light, which will lead to disturbance in sleep and metabolism [2].In addition, the studies also mentioned that the sensitivity of the circadian clock to the environment is reduced through the aging process, which will cause the inconsistency of the internal clock and external time [2]. As age-related diseases become more common and highly regarded, there is a potential to reduce the risk of these age-related diseases by restoring the circadian function in aging. More specifically, by increasing light exposure during the day, decreasing it during the night, taking melatonin supplements, and modifying patients' behaviors [2]. The principal goals of this review are to summarize the current studies on aging and circadian rhythms and to provide an insight into future research and the development of therapeutic implications in this field.

## 2. Age-associated changes in circadian rhythms

### 2.1. Alterations in sleep-wake cycles

The most pronounced age-related sleep alterations emerging after age 60 include progressive deterioration in: (1) sleep phase timing, (2) sleep continuity maintenance, and (3) sigma (12-16 Hz) power during NREM sleep [3]. In a study conducted by Bryce A. Mander et al., tt is clearly shown that the sleep fragmentation among elderly people is much higher. The data indicates that there are only 2 wakes during sleeping (23:00 to 8:00) in young adults, but in older adults, there are 11 wakes during the same period [4]. The study also suggests that daytime sleepiness increases in later life in terms of the frequency of diurnal naps: As the age range rises from 55-64 to 75-84, the percentage of people who have daytime naps increases from 10% to 25% [4]. More directly, roughly 25% of older adults who join in this study report serious sleepiness in the daytime [4]. Moreover, there is usually a reduction in slow-wave sleep (SWS) and REM sleep duration among the elderly. In Daneault et al.'s study, the EEG data plots indicate that, compared to young individuals, there are no significant differences in the time spent in NREM1 and NREM2 of older individuals, but the time in NREM3 is much shorter in older individuals [5]. The data from 4157 individuals whose ages ranged from 20 to 92 years old show the percentage of REM sleep also decreases dramatically along the life span [6]. Additionally, it is evident that there is an Advanced sleep phase syndrome (ASPS) in elderly people. In Didikoglu et al.'s study, using data from 6000 participants aged 35.5, the researchers found that the phase shifts earlier for about 30 minutes in total from 40 to 90 years old and above, and the sleep midpoint advanced at a speed of 6 minutes per decade [4].

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### 2.2. Decline in suprachiasmatic nucleus (SCN) function

The SCN is an important part of the circadian rhythm. It will not have a distinct change in molecular clock level, but significant changes may occur at the neuron level as age increases. Experiments show that the elderly rats have fewer vasopressinergic cells compared to younger ones; this would affect downstream signaling. Additionally, elderly rats show decreased responsiveness to zeitgebers, which are external factors like light. As a person ages, the lens becomes yellow and thicker. The yellowing effect preferentially attenuates shorter wavelength light, which is predominantly detected by intrinsically photosensitive retinal ganglion cells (ipRGCs) - the specialized photoreceptors responsible for photic entrainment of the suprachiasmatic nucleus (SCN) [7]. Then there will be an expected 1% reduction in light passage through the retina per year [7]. Furthermore, aging will also lead to impaired regulation of core body temperature rhythms. In Suzanne Hood and Shimon Amir's research, these 2 researchers witnessed that the amplitude of temperature rhythm in older adults (60s to 80s) is decreased by 20% to 40% compare to that of younger adults (20s and 30s), and the phase of the rhythm is advanced by 1-2 hours in older adults [7].

### 2.3. Melatonin and cortisol dysregulation

Melatonin is a hormone that can directly regulate the circadian rhythm in various ways, such as the core body temperature and sleepiness. Throughout a person's life span, total melatonin secretion decreases, beginning more noticeably in their 30s [7]. The loss of melatonin would cause SCN dysfunction, which will lead to internal circadian misalignment. This process ultimately leads to disruptions in sleep patterns. On the other hand, cortisol rhythms operate in opposition to those of melatonin. The alteration of cortisol circadian rhythms due to aging can increase blood glucose levels, vasoconstriction, and cardiac output. It can trigger inflammation by activating immune cell receptors and cytokine production and preparing the body for a "fight or flight" response to acute stress at a high level of cortisol.

### 2.4. Peripheral clock dysregulation

The decline in SCN function always accompanies the peripheral clock dysregulation. The decline in neuronal electrical rhythms may indicate a loss of synchronization in firing patterns among SCN cells in aging animals, ultimately resulting in phase desynchronization [8]. This, in turn, can lead to a desynchronization between the central and peripheral clocks in aging organs. For instance, in Nygård et al. and Farajnia et al.'s study, the clusters of cells may exhibit antiphase activation during the night, while the number of silent cells during the day increases with advancing age [8]. Furthermore, the circadian clock regulates many genes that exhibit rhythmic expression. As a result, the dysregulation of the central and peripheral clocks would cause a loss of the rhythmic gene expression in organs and tissues, like the liver, muscle, and immune system. Finally, it leads to a huge negative impact on metabolism and immune function. For example, disruption of core circadian clock genes (e.g., Bmal1, Clock, Per, Cry) contributes to hepatic pathophysiology, promoting steatosis, hepatocellular carcinoma, inflammatory responses, viral hepatitis progression, and cholestasis.

## 3. Molecular and cellular mechanisms linking circadian rhythm to aging

### 3.1. Oxidative stress and mitochondrial dysfunction

Mitochondria serve as the primary site of ATP production through the process of oxidative phosphorylation. Side products of this oxidation reaction are reactive oxygen species (ROS). However, the elevated ROS level can be harmful to the organism itself. Hence, the detoxification of

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ROS is needed, and it is made by the antioxidant defense mechanisms, which are formed by antioxidant enzymes and regulated by various systems, including the circadian rhythm. The core circadian transcription factors BMAL1/CLOCK and their downstream clock-controlled regulators directly modulate the expression of antioxidant defense genes through canonical E-box and other cis-regulatory elements. In several animal models with circadian deficiency, reduced mitochondrial volume, decreased respiration rate, and increased oxidative damage are observed [9]. It also shows the relation between the circadian clock, the antioxidant defense mechanism, and the mitochondria function. Moreover, the decline in mitochondria bioenergetics and ATP production is correlated to aging. In Amorim JA et al.'s study, the longevity signaling pathways indicate that age and mitochondrial bioenergetics are inversely related [9]. Subsequent experimental evidence indicates that BMAL1 plays a crucial role in mitochondrial health and longevity. It is evident that hepatic Bmal1 can regulate rhythmic mitochondrial dynamics and improve metabolic fitness. Vice versa, the decline in Bmal1 also leads to mitochondrial dysfunction and increased oxidative damage [10]. The lack of Bmal1 not only would result in loss of circadian rhythm and acceleration of aging but also cause a reduced life span in mice [10].

### 3.2. Genomic instability and epigenetic modifications

DNA repair capacity exhibits circadian oscillation, with peak efficiency coinciding with the active phase in humans (daylight hours) and diminished activity during the rest phase, reflecting circadian regulation of repair pathway components [11]. As people get older, their chromatin remodeling and histone modifications change. These changes include loss of global histones, changes to histone modifications, and reorganization of chromatin structure. Moreover, aging is linked to decreased histone H3-H4 acetylation, increased H3K27me3, and shifts from H3K9me2 to H3K9me3, leading to heterochromatin loss and lamina-associated domain (LAD) detachment from the nuclear lamina. These changes reduce the chromatin accessibility and transcriptional stability [12].

### 3.3. Inflammation and immune dysregulation

Circadian clock genes play a crucial role in various diseases associated with inflammation or triggered by inflammatory processes [13]. Genetic ablation of core clock genes in macrophages or brain-resident cells elevates production of pro-inflammatory cytokines (e.g., TNFα, IL-1β) and chemokines. These inflammatory mediators further disrupt circadian rhythms by directly inhibiting CLOCK/BMAL1 heterodimer activity, which is essential for E-box-mediated transcriptional activation of clock-controlled genes. Experimental evidence confirms that TNFα and IL-1β suppress CLOCK/BMAL1 binding to E-box elements, creating a feed-forward loop of circadian dysfunction and inflammation [13]. Recently, inflammation has become a new hallmark of aging, especially the low-grade chronic type without overt infection (also known as "inflammaging"). The core genes, including BMAL1 and CLOCK, act as positive transcription factors in circadian rhythms and play a role in regulating immune cell function. Additionally, circadian rhythms can impact immune cell activity and responses by influencing specific genes, thereby shaping the balance and overall functionality of the immune system. Therefore, the disrupted circadian rhythms can impair and decrease the immune cell function and immune surveillance.

### 3.4. Metabolic dysregulation

Disrupted circadian rhythm is linked to obesity and related metabolic disorders, such as type 2 diabetes. This is because the circadian clock affects the function of the liver, pancreas, and adipocytes, which controls insulin sensitivity, lipid metabolism, and glucose homeostasis. From the perspective of aging, the increased fat and decreased muscle composition in the elderly body lead to a rising risk

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of type 2 diabetes in this age group [14]. Several studies shows that the mitochondrial dysfunction that is mentioned above in aging can induce the age-related metabolic diseases [9]. As a result of the prevalence of type 2 diabetes and metabolic syndromes among aging and even younger populations nowadays, a method called time-restricted feeding appeared to restore the metabolic rhythm. By reducing the eating time from 12 hours starting at 8 am to only 6 hours beginning at the same time and extending the fasting time from 12 to 18 hours, there is an improvement in insulin sensitivity and β cell function and a decline in blood pressure and oxidative stress that can trigger type 2 diabetes in the prediabetic men [15].

## 4. Circadian rhythm disruptions and aging-related diseases

### 4.1. Neurodegenerative diseases

In Parkinson's disease (PD) patients, there are always some problems associated with the circadian rhythm disorder, such as insomnia, daytime sleepiness, and parasomnias. The circadian rhythm's amplitude in these patients generally flattens without a distinct phase shift. Furthermore, more evidence shows that circadian dysfunction can directly or indirectly contribute to cognitive impairment in PD. Previous studies suggested that circadian dysfunctions would make neurodegeneration worse in people with Alzheimer's disease (AD) by causing problems with cholinergic signals, melatonin loss, and neuron loss in the SCN. Studies on both animals and people showed that during SWS, the brain was better able to get rid of metabolic waste and amyloid-β (Aβ), a type of toxic protein that is also a cause of AD [16]. Several pieces of evidence indicate that increased neuronal firing that is usually declined in SWS relative to wakefulness or REM sleep could stimulate Aβ production [16]. The experiment on 23 individuals who have chronic insomnia revealed that CSF Aβ42 levels dramatically increased in these insomniac patients [16]. Moreover, Aβ levels correlated with the Pittsburgh Sleep Quality Index (PSQI) scores, a measurement of sleep quality [16]. Thus, sleep disruption can lead to impaired clearance of toxic proteins, such as Aβ, p-tau, and α-synuclein that are the cause of AD and PD. However, photobiomodulation (PBM) is a kind of light therapy that recently has been shown to be effective in reducing the symptoms of preclinical models of AD, TBI, stroke, ALS, and MS, giving neuroprotection and regenerating neurons. Furthermore, a number of studies and clinical trials ensure the neuroprotective potential of melatonin, indicating that melatonin can promote TFEB-mediated mitophagy, clear damaged mitochondria, and reduce inflammatory responses to improve cognitive function in Alzheimer's disease models.

### 4.2. Cardiovascular diseases

Evidence shows that PER, a repressor protein that is involved in the transcription-translation loop of the circadian clock, can regulate blood pressure and handle sodium, but light exposure stimulates the expression of PER in SCN. Hence, when the light stimulates the circadian clock gene expression, the Per increases, and the blood pressure and heart rate increase. A clinical study shows that the circadian rhythm has a significant influence on the blood pressure. The blood pressure and heart rate will dramatically increase in an irregular time (e.g., reverse dipper at night, morning surge) if there is a circadian misalignment due to aging, finally causing hypertension, arrhythmia, and other heart diseases [17]. There is increased attention on a method named chronotherapy, which includes the personalized timing of medication doses to fit into the daily rhythm and behavioral pattern of the body [18], and numerous studies show that moving one or more antihypertensives from daytime to bedtime can significantly decrease the morning blood pressure surge and nocturnal blood pressure without increasing adverse effects [18].

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### 4.3. Cancer and cellular senescence

The circadian clock exerts temporal control over cell cycle progression and apoptotic pathways through the transcriptional activity of the BMAL1/CLOCK heterodimer, which rhythmically regulates key cell cycle checkpoints and apoptosis-related genes. The downregulation of core circadian transcription factors BMAL1 and CLOCK (which normally suppress apoptotic pathways) leads to dysregulation of key cell-cycle regulators, including the G2/M checkpoint kinase Wee1 and the cyclin-dependent kinase inhibitor p21, disrupting normal cell cycle control. A reduction in Wee1 leads to apoptosis activation, and an increase in p21 can halt the cell cycle at the G2/M phase. Therefore, both of these regulations can result in tumor cell death [19]. Moreover, other components in the transcription-translation loop also control the cell cycle and apoptosis. For example, PER2 improves cancer cell sensitivity to the radiation-induced apoptosis, and the absence of PER1 can alter the antiapoptotic and proapoptotic gene expression, which induces apoptosis. Due to this, age-related circadian disruption that causes the irregular expression of BMAL1 and CLOCK may increase the cancer risk. Multiple hallmarks of aging - including accumulated genomic instability and progressive cellular senescence - exhibit mechanistic overlap with oncogenic pathways, establishing a biological foundation for the well-documented association between advancing age and elevated cancer incidence. Chronotherapy plays an important role in curing cancer with minimized adverse effects. The distinct circadian properties of malignant versus normal cells enable chronotherapeutic optimization - timing treatments to coincide with peak vulnerability in cancer cells while minimizing toxicity to healthy tissues during their repair-active phases.

### 4.4. Metabolic and endocrine disorders

Several studies have indicated that there is a straightforward link between obesity and circadian rhythm disturbance [19]. Furthermore, in the BMAL1-deficient mice model, the mice usually have metabolic defects, including high serum triglycerides, low circulating insulin, and high insulin sensitivity that may lead to obesity, insulin resistance, and diabetes [19]. It has been proved that the growth hormone's synthesis and secretion are decreased as age increases in all mammals. In Anne R. Cappola et al.'s study, the production of thyroxine (T3) and triiodothyronine (T4) in the elderly is reduced from 30 and 80 to 20 and 60μg respectively while the half-life increases from 7 to 9 days through the increase in age [20]. Studies suggest that exercise and dietary interventions have a therapeutic potential for metabolic and endocrine diseases. For example, data has indicated that supervised, combined physical activity and a Mediterranean diet lead to the greatest improvements in subjects with metabolic diseases.

## 5. Conclusion

In conclusion, this review highlights the bidirectional relationship between circadian rhythms and aging. It highlights how circadian disturbance contributes to age-related diseases and how aging leads to clock-related dysfunctions, including altered sleep-wake cycles, reduced SCN function, melatonin and cortisol dysregulation, and peripheral clock desynchronization. These disruptions exacerbate metabolic, immune, and cognitive decline. Key molecular mechanisms that are relevant include oxidative stress, mitochondrial dysfunction, genomic instability, epigenetic modifications, inflammation, and metabolic dysregulation. Circadian misalignment is strongly associated with neurodegenerative diseases, cardiovascular diseases, cancer, and diseases of metabolic disorders. Therefore, future research should focus on developing novel therapeutic strategies to restore circadian rhythms and reduce age-related diseases, as well as the potential of personalized medicine tailored to one's circadian variations, which could improve treatment efficacy and minimize adverse effects. It is essential for healthy aging to maintain circadian health by optimizing light exposure, regulating

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sleep patterns, and utilizing time-restricted feeding. Integrating personalized medication with chronotherapy offers an innovative approach to managing these prevalent age-related disorders.

## References


[1] Hou, Y., Dan, X., Babbar, M., Wei, Y., Hasselbalch, S. G., Croteau, D. L., & Bohr, V. A. (2019). Ageing as a risk factor for neurodegenerative disease. Nature Reviews. Neurology, 15(10), 565–581. https://doi.org/10.1038/s41582-019-0244-7

[2] Duffy, J. F., Zitting, K.-M., & Chinoy, E. D. (2015). Aging and Circadian Rhythms. Sleep Medicine Clinics, 10(4), 423–434. https://doi.org/10.1016/j.jsmc.2015.08.002

[3] Taillard, J., Gronfier, C., Bioulac, S., Philip, P., & Sagaspe, P. (2021). Sleep in Normal Aging, Homeostatic and Circadian Regulation and Vulnerability to Sleep Deprivation. Brain Sciences, 11(8), 1003. https://doi.org/10.3390/brainsci11081003.

[4] Mander, B. A., Winer, J. R., & Walker, M. P. (2017). Sleep and Human Aging. Neuron, 94(1), 19–36. https://doi.org/10.1016/j.neuron.2017.02.004

[5] Daneault, V., Orban, P., Martin, N., Dansereau, C., Godbout, J., Pouliot, P., Dickinson, P., Gosselin, N., Vandewalle, G., Maquet, P., Lina, J.-M., Doyon, J., Bellec, P., & Carrier, J. (2021). Cerebral functional networks during sleep in young and older individuals. Scientific Reports, 11, 4905. https://doi.org/10.1038/s41598-021-84417-0

[6] Floyd, J. A., Janisse, J. J., Jenuwine, E. S., & Ager, J. W. (2007). Changes in REM-Sleep Percentage Over the Adult Lifespan. Sleep, 30(7), 829–836. https://doi.org/10.1093/sleep/30.7.829

[7] Hood, S., & Amir, S. (2017). The aging clock: circadian rhythms and later life. Journal of Clinical Investigation, 127(2), 437–446. https://doi.org/10.1172/jci90328

[8] Zhao, J., Warman, G. R., & Cheeseman, J. F. (2019). The functional changes of the circadian system organization in aging. Ageing Research Reviews, 52, 64–71. https://doi.org/10.1016/j.arr.2019.04.006

[9] Amorim, J. A., Coppotelli, G., Rolo, A. P., Palmeira, C. M., Ross, J. M., & Sinclair, D. A. (2022). Mitochondrial and metabolic dysfunction in ageing and age-related diseases. Nature Reviews Endocrinology, 18. https://doi.org/10.1038/s41574-021-00626-7

[10] Yang, G., Chen, L., Grant, G. R., Paschos, G., Song, W.-L., Musiek, E. S., Lee, V., McLoughlin, S. C., Grosser, T., Cotsarelis, G., & FitzGerald, G. A. (2016). Timing of expression of the core clock gene Bmal1 influences its effects on aging and survival. Science Translational Medicine, 8(324), 324ra16–324ra16. https://doi.org/10.1126/scitranslmed.aad3305

[11] Su, Z., Hu, Q., Li, X., Wang, Z., & Xie, Y. (2024). The Influence of Circadian Rhythms on DNA Damage Repair in Skin Photoaging. International Journal of Molecular Sciences, 25(20), 10926–10926. https://doi.org/10.3390/ijms252010926

[12] Wang, K., Liu, H., Hu, Q., Wang, L., Liu, J., Zheng, Z., Zhang, W., Ren, J., Zhu, F., & Liu, G.-H. (2022). Epigenetic regulation of aging: implications for interventions of aging and diseases. Signal Transduction and Targeted Therapy, 7(1), 1–22. https://doi.org/10.1038/s41392-022-01211-8

[13] Vieira, E., Mirizio, G. G., Barin, G. R., de Andrade, R. V., Nimer, N. F. S., & La Sala, L. (2020). Clock Genes, Inflammation and the Immune System—Implications for Diabetes, Obesity and Neurodegenerative Diseases. International Journal of Molecular Sciences, 21(24), 9743. https://doi.org/10.3390/ijms21249743

[14] Al-Sofiani, M. E., Ganji, S. S., & Kalyani, R. R. (2019). Body composition changes in diabetes and aging. Journal of Diabetes and Its Complications, 33(6), 451–459. https://doi.org/10.1016/j.jdiacomp.2019.03.007

[15] Sutton, E. F., Beyl, R., Early, K. S., Cefalu, W. T., Ravussin, E., & Peterson, C. M. (2018). Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. Cell Metabolism, 27(6), 1212-1221.e3. https://doi.org/10.1016/j.cmet.2018.04.010

[16] Cordone, S., Annarumma, L., Rossini, P. M., & De Gennaro, L. (2019). Sleep and β-Amyloid Deposition in Alzheimer Disease: Insights on Mechanisms and Possible Innovative Treatments. Frontiers in Pharmacology, 10(695). https://doi.org/10.3389/fphar.2019.00695

[17] Faraci, F. M., & Frank A.J.L. Scheer. (2024). Hypertension: Causes and Consequences of Circadian Rhythms in Blood Pressure. Circulation Research, 134(6), 810–832. https://doi.org/10.1161/circresaha.124.323515

[18] Xie, Z., Zhang, J., Wang, C., & Yan, X. (2021). Chronotherapy for morning blood pressure surge in hypertensive patients: a systematic review and meta-analysis. BMC Cardiovascular Disorders, 21(1). https://doi.org/10.1186/s12872-021-02081-8

[19] Qu, M., Zhang, G., Qu, H., Vu, A., Wu, R., Tsukamoto, H., Jia, Z., Huang, W., Lenz, H.-J., Rich, J., & Kay, S. A. (2023). Circadian regulator BMAL1::CLOCK promotes cell proliferation in hepatocellular carcinoma by controlling apoptosis and cell cycle. Proceedings of the National Academy of Sciences of the United States of America, 120(2). https://doi.org/10.1073/pnas.2214829120

DOI: 10.54254/2753-8818/110/2025.AU22985

*[20] Cappola, A. R., Auchus, R. J., El-Hajj Fuleihan, G., Handelsman, D. J., Kalyani, R. R., McClung, M., Stuenkel, C. A., Thorner, M. O., & Verbalis, J. G. (2023). Hormones and Aging: An Endocrine Society Scientific Statement. The Journal of clinical endocrinology and metabolism, 108(8), 1835–1874. https://doi.org/10.1210/clinem/dgad225.*