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Late chronotype and associated health problems

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Abstract:

Introduction: Chronotype reflects an individual's preference for activity and rest within a 24-hour period, governed by the internal circadian clock system located in the suprachiasmatic nuclei of the hypothalamus. There are three chronotypes: Morning, Evening, and Intermediate. The evening type is also called “night owls” or late chronotype. Night owls prefer to be active in the evening and sleep and wake up late. The misalignment between the sleep patterns in late chronotype and the social schedules puts the night owls in danger of physical and mental health issues.

Purpose of work: The primary aim of this review is to provide a comprehensive overview of current knowledge on the impact of late chronotype on health.

Methods and materials: A review of the literature available in the PubMed database, the following keywords and their combinations were searched: "chronotype", “mental health", "cancer", “late chronotype”, “circadian rhythm”, “type 2 diabetes”, “depression”.
State of knowledge: Studies have confirmed that late chronotype is associated with a higher risk of type 2 diabetes, obesity, cancer, alcohol and cigarette addiction, and unhealthy eating habits. Furthermore, the evening chronotype is an independent risk factor for depression. It is also linked with anxiety, bipolar disorder, and schizophrenia.
Summary: In this review, we have summarized the latest research on late chronotype, circadian misalignment, and their potential consequences on human health. Most studies on evening chronotype and related health issues are cross-sectional. Further longitudinal or experimental research is needed to examine the potential cause-and-effect relationships on this cause.

Keywords: "chronotype"; “mental health"; "cancer"; “late chronotype”; “type 2 diabetes”; “depression”.

Introduction

Chronotype is the behavioral expression of the internal circadian clock system, indicating an individual's preference for activity and rest within a 24-hour period. The suprachiasmatic nuclei in the hypothalamus oversee circadian rhythms, governing the daily patterns of sleep and wakefulness. There are three main chronotypes: morning, evening, and intermediate. Morning chronotypes, or "larks," prefer early wake and activity times, while evening chronotypes, or "owls," prefer later wake and activity times. Intermediate chronotypes fall between these two extremes. Chronotype is generally stable throughout an individual life. Genetics and age are the major factors determining the chronotypes, but sociocultural influences and environmental cues, such as sunlight exposure and seasonal changes also play a role. Adolescents tend to have the latest sleep schedules compared to other age groups, with puberty associated with up to a 2-hour delay in the sleep cycle. This delayed pattern typically persists until early adulthood, after which sleep times gradually shift back and become earlier with age [1,2]. Approximately 40% of adults fall into either the morning or evening chronotype category, while the remaining

60% do not fit clearly into either morning or evening types [3]. The misalignment of sleep timing in late chronotype and social schedules (work and school) puts the owls at a higher risk of physical and mental health issues as well as a higher mortality rate [4,5]. In recent years, several studies have suggested a correlation between evening chronotype and various diseases including diabetes mellitus, obesity, breast cancer, and mental health disorders. In this research paper, we have compiled the latest insights into the potential health consequences associated with an evening chronotype.

Cancer

Evening chronotype may lead to circadian misalignment when the work and social behaviors misalign with the chronotype of the individual and consequently contribute to the development of cancer [6]. Evening chronotype is also associated with lower levels of physical activity and unhealthy eating habits, which may also contribute to an increased risk of malignancy [7]. Those claims are supported by the observed association between evening chronotype and increased cancer risk [8]. A retrospective case-control study nested within the California Teachers Study revealed that individuals with a definite evening chronotype exhibited an increased risk of breast cancer. It was also suggested that an evening chronotype may be an independent risk factor for breast cancer among women who have not engaged in significant night shift work [4]. A prospective cohort analysis with a 6.5-year follow-up time on the same group of women observed a modestly elevated postmenopausal breast cancer risk associated with an evening chronotype, consistent with previous findings [9]. On the other hand, multivariable regression analysis of UK Biobank data on breast cancer incidence revealed a protective effect of morning preference on breast cancer risk [10]. Morning chronotype is also a protective factor against the development of chemotherapy-induced peripheral neuropathy among women with breast cancer who were treated with docetaxel[11]. Moreover, a late chronotype following a breast cancer diagnosis was correlated with increased symptoms of fatigue, depression, insomnia, and chemotherapy-induced nausea and vomiting[12,13]. The same cohort from the California Teachers Study was also assessed for incident cases of endometrial cancer. It was confirmed that postmenopausal women with evening chronotypes may be at an increased risk of endometrial cancer, particularly among those in the highest BMI category of 30 or more [14]. Xie et al. demonstrated that an evening chronotype is associated with an increased risk of lung cancer, particularly among individuals with low to moderate genetic susceptibility [6]. Peeri et al. revealed a significant association between late chronotype

and lung cancer risk [15]. Papantoniou et al. showed an elevated risk of prostate cancer among people with a history of night shift work and an evening chronotype [16]. Furthermore, the Older Finnish Twin Cohort study, which included 11,370 twins, found that participants with an evening chronotype had an increased risk of prostate cancer compared to those with a morning chronotype [17]. On the other side, a Mendelian randomization study by Sun et al., utilizing data from the UK Biobank and the PRACTICAL Consortium, reported that a morning preference is associated with a reduced risk of developing prostate cancer [18]. Barrea et al. conducted a study on the role of chronotype in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs), revealing that patients, particularly those with metastatic (grade G2) and progressive disease, exhibited an unhealthy metabolic profile and more commonly presented with an evening chronotype [19].

Cardiometabolic health

Numerous studies have investigated the relationship between late chronotype and cardiometabolic risk. It is claimed that an evening chronotype is associated with a higher risk of type 2 diabetes (T2D) and with deteriorated glycemic control estimated by glycated hemoglobin levels. In the conducted studies night owls had a higher percentage of total daily calories consumed at dinners, often skipped breakfast, and tended to eat later than individuals with morning chronotype. Glucose tolerance fluctuates throughout the day, reaching its peak during daylight hours when food is typically consumed, and dipping at night when fasting usually takes place. Therefore, if night owls delay their eating to later in the day compared to morning larks, they may experience poor glycemic control and an increased risk of type 2 diabetes. What is more, the study conducted by Reutrakul et al. reports, that each hour delay in mid-sleep time on free days (MSF) was associated with a significantly higher HbA_{1c} of 2.5% of its original value [5,20,21]. Additionally, researchers have discovered that individuals with a late chronotype are more likely to be overweight or obese. Several explanations have been proposed for the link between an evening chronotype and metabolic disorders. One hypothesis suggests that an unhealthy lifestyle may be to blame, as evening chronotypes tend to participate less in sports, eat later, smoke more, and consume more alcohol. Another explanation is that the difference in sleep timing between workdays and free days can lead to circadian misalignment and chronic sleep insufficiency, both of which are associated with health problems. Circadian misalignment can contribute to obesity, which in turn causes adipose tissue to secrete various active compounds that may negatively impact cardiometabolic health.

Baldanzi et al. performed a cross-sectional study and found out that the evening chronotype is associated with circulating cardiometabolic proteins. They preselected 242 proteins and found that 17 of them were simultaneously associated with a late chronotype, hypertension, diabetes, and obesity. Among these, three adipokines were identified: FABP4, Leptin, and RARRES2. FABP4, secreted by adipocytes, stimulates hepatocyte glucose production, and is associated with obesity and insulin resistance. Leptin, a well-known appetite regulator produced by adipose tissue, is found at higher levels in obese individuals, who are also more resistant to its anorexigenic effect. Lastly, RARRES2 is involved in adipogenesis, inflammation regulation, and metabolism, and is considered a potential link between obesity and the development of insulin resistance [22]. Furthermore, it has been reported in numerous studies that individuals with late chronotype had higher levels of triglycerides, LDL cholesterol, fasting blood glucose and HbA1c, compared with lower HDL cholesterol [8,23,24]. Overall, the studies emphasize the role of circadian regulation in glycemic control and report that individuals with late chronotype are at higher risk of developing type 2 diabetes, and obesity and have worse metabolic profiles.

Mental Health

Multiple studies showed a correlation between chronotypes and mental health, identifying late chronotype as an independent risk factor for depression [25]. This statement has been confirmed by studies conducted across diverse age groups and in different countries [26,27,28,29]. Additionally, people with a late chronotype perceived lower social support, suggesting that an evening chronotype may be associated with social isolation and decreased opportunities for interactions with friends [27]. There is also an association between late chronotype and suicidality, which is fully mediated by depressive symptoms [30,31]. Evening chronotype has also been associated with bipolar disease [32]. The study by Melo et al. indicated that an evening chronotype predicts a poor prognostic for patients with bipolar disease due to its association with greater anxiety, lower functioning, and more mood episodes [33]. Furthermore, individuals with bipolar disorder who identify as late chronotypes are more likely to have mild to more severe depressive symptoms and self-harm [34,35]. Eveningness has also been linked to increased anxiety [36]. In addition, people with schizophrenia tend to be more evening-oriented compared to healthy controls and exhibit a chronotype similar to people with bipolar disease. An evening chronotype may serve as an indicator or potential risk factor for a range of mental health disorders [37]. Moreover, late chronotype appears to be a risk factor for substance use disorders, including the abuse of alcohol, tobacco, stimulants, and marijuana.

Chronotherapy, which helps establish regular daily activities, may be beneficial for patients with substance use disorders [25].

Conclusions

Circadian rhythms are cyclical endogenous processes that last approximately 24 hours, playing a crucial role in regulating sleep/wake cycles, metabolism, hormonal secretions, and immune function. Their stability is essential in maintaining human health.

Humans living in modern industrialized societies risk engaging in activities and behaviors that are misaligned with their chronotype. The 24-hour access to light, irregular eating patterns, and social rhythms imposed by work and school schedules can lead to a timing mismatch, known as "circadian misalignment". In our review, we have summarized the latest knowledge about the potential health consequences of late chronotype and circadian misalignment. Numerous studies have shown that this disparity can interfere with the natural rhythms of physiological processes, such as blood pressure regulation and glycemic and lipid metabolism, leading to a higher risk of chronic diseases, obesity, and cancer. While the pathogenesis of most psychiatric disorders remains unclear, emerging evidence indicates a link between evening chronotype and mental health issues. Due to sleep deprivation and desynchronization of circadian rhythms, night owls can suffer from potentially worse mental health problems over time. Additionally, evening chronotype may influence the treatment and prognosis of specific mental disorders. The identification of chronotypes can help develop targeted and personalized treatments for psychiatric conditions. It is significant to better understand the connection between chronotype, the circadian clock, and health, and to develop a chronobiological approach for the prevention and treatment of cardiometabolic, mental, and chronic disorders. The majority of performed studies on evening chronotype and associated health issues are cross-sectional, although they are valuable for identifying associations, they cannot establish causality or analyze behavior over time. Therefore, additional longitudinal or experimental studies are required to better investigate the potential cause-and-effect relationship on this issue.

Author's contribution:

Conceptualization, JJ, AK; methodology, EW, AK, TSz; software, KC; check, KC, AMK, AK and KB; formal analysis, EO; investigation, EW; resources, OS, KC, EW, TSz; data curation,

OŁ, KS, AMK, KC, AK, JJ, OS, EO, EW, KB; writing – rough preparation, OŁ, KS, EW, AK, JJ, TSz; writing – review and editing, OŁ, KS, AMK, KC, AK, JJ, OS, EO, EW, KB; visualization, JJ and AMK; supervision, OŁ and KS; project administration, OŁ, KS, AK, OS, JJ;

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