

Beyond Sleep: A Multidimensional Model of Chronotype

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ABSTRACT

Chronotype can be defined as an expression or proxy for circadian rhythms of varied mechanisms, for example in body temperature, cortisol secretion, cognitive functions, eating and sleeping patterns. It is influenced by a range of internal (e.g., genetics) and external factors (e.g., light exposure), and has implications for health and well-being. Here, we present a critical review and synthesis of existing models of chronotype. Our observations reveal that most existing models and, as a consequence, associated measures of chronotype have focused solely or primarily on the sleep dimension, and typically have not incorporated social and environmental influences on chronotype. We propose a multidimensional model of chronotype, integrating individual (biological and psychological), environmental and social factors that appear to interact to determine an individual's true chronotype with potential feedback loops between these factors. This model could be beneficial not only from a basic science perspective but also in the context of understanding health and clinical implications of certain chronotypes as well as designing preventive and therapeutic approaches for related illnesses.

Keywords: chronotype, circadian preference, multidimensional model, genetics, environment, social factors

1. Introduction

Biologically, like many other mammals, humans are diurnal. This means they are typically active during the day and asleep at night. However, the timing, preference, environment, and various constraints surrounding sleep-wake behaviour across modern-day human societies began to change rapidly with industrialisation which led to a) the availability of, and overexposure to, artificial light at night (Aulsebrook et al., 2018), b) television, smartphones, and similar technologies, c) irregular lifestyles, including shift work (Juda et al., 2013), d) novel dietary habits (Pot, 2017), and e) increasing use of caffeine and other stimulants in many societies across the globe (Siudej & Malinowska-Borowska, 2021). These social and occupational factors have placed immense pressure on individuals to attempt to adjust their sleep patterns to better fit with modern-day lifestyles and practices, and, for many people (e.g., warehouse workers, lorry drivers, and nurses), this creates a conflict between professional duties and the need, as well as the desire to sleep, leading us toward a 'sleep sick society'.

Taillard and colleagues (2021) suggested that depending upon an individual's day-to-day social life, their sleep timings may be in or out of phase with internal circadian timings, which are determined by the circadian clock. They further argued that social factors might impact an individual's sleep timings and preferences. These sleep timings or preferences going out of phase with the biological time are called circadian disruptions. In addition, sleep or diurnal preference varies across individuals (Parsons et al., 2014). In recent decades, there has been a growing interest in the role of diurnal preference and chronotype, and how its disruption by social factors not only has an impact on our internal time (Duffy & Czeisler, 2009) but also has striking comorbidity with psychiatric illnesses (Tesler et al., 2013), neurodevelopmental disorders (Kotagal, 2015), cognitive dysfunction, and aberrant emotional processing (Pilcher and Huffcutt 1996; Gobin et al., 2015).

A timely question in this context is whether, and to what extent, there might be an interaction between an individual's chronotype and their need or desire to sleep that influences various physical and mental health outcomes, including brain structure and function. However, before attempting to answer this question, it is prudent to establish the most comprehensive and useful model and measures of chronotype that can be utilised in a global research context.

1.1 Circadian Rhythms (CRs)

Humans have a range of predictable biological rhythms, which refer to any endogenous or exogenous cyclic change in the level of bodily chemicals or functions (Aschoff, 2013). Some biological rhythms occur many times a day (e.g., ultradian rhythms such as appetite), some once every 24 hours (e.g., circadian and diurnal rhythms), and some take weeks to complete (e.g., infradian rhythms such as the menstrual cycle in women). These diverse rhythms can be found at different complex and structural levels, from single cells to social behaviour (Aschoff, 2013). Moreover, nearly all physiological and psychological functions vary in periodicity.

Circadian rhythms (CRs) refer to the internal processes that oscillate for 24 hours (e.g., biochemical, physiological, behavioural rhythms) (Fuller & Fuller, 2002). The word 'circadian' has been derived from two Latin words, 'circa' meaning 'about' and 'diem' meaning 'day or 24 hours cycle'. These CRs are generated by the body's internal biological clock or an endogenous pacemaker, and are regulated by external and environmental cues, such as exposure to darkness/light (Aschoff, 1967; Aschoff & Wever, 1976; Wever, 1986). The main internal biological clock is found in the suprachiasmatic nucleus (SCN) of the hypothalamus (Moore & Eichler, 1972); it influences the sleep-wake cycle in close association and interaction with the pineal gland (Moore et al., 2002; Leon Llamas et al., 2021) (see 1.2.1

Circadian Circuits in Humans for more details). Peripheral clocks or circadian oscillators occur throughout the brain and other body cells (Nováková et al., 2013); these are synchronised by the suprachiasmatic nucleus and genetically programmed to generate CRs (Hastings et al., 2003; Novakova et al., 2013). In humans, the endogenous CRs oscillate with some periodic variation in length (Czeisler & Gooley, 2007), causing considerable intra-individual variations.

1.1.1 Circadian Circuits in Humans

Like many photoperiodic organisms, humans possess a complex mechanism for registering day/night length that is vital for synchronised expression of physiological processes, such as body temperature and cortisol levels (Hastings, 1991). Interest in understanding this mechanism can be traced back to 1662 when Descartes (1662) put forward the idea of a pathway connecting the human eye and the pineal gland. Supporting this 17th century notion, there is evidence of a multi-synaptic pathway connecting the SCN of the hypothalamus to the pineal gland (Hastings, 1991; Larsen et al., 1998; Koller et al., 2020), and showing that the SCN plays a vital role in regulating different endocrine, physiological, and behavioural CRs (Hofman & Swaab, 1983). Specifically, natural or artificial light signals detected by intrinsic photosensitive retinal ganglion cells are transduced and conveyed to the SCN. This information is then transmitted via the paraventricular nucleus to the intermediolateral column of the thoracic spinal cord (via the lateral medulla), where first-order sympathetic neurons project down to the superior cervical ganglion and the second-order sympathetic fibres from the superior cervical ganglion project to the pineal gland via the tentorium cerebelli (Clark, 1940), terminating at the apex of the pineal gland (Kappers, 1960) as single nervus conarius. These nerve fibres release norepinephrine from their terminals (Iraldi & Robertis, 1961). As a result of this norepinephrine release, synapses are formed on the surface of pinealocytes (main cells

within the pineal gland containing a high concentration of serotonin) and serotonin is converted into melatonin (Alarma-Estrany & Pintor, 2007), helping individuals to fall asleep (Figure 1).

*****Figure 1 about here*****

1.1.2 Disrupted CRs and Associated Illnesses

We use the term ‘disrupted CRs’ as an unspecified umbrella term to outline any disturbance or dysregulation that interferes with circadian functions such as hormone secretion, heart rate, or sleep-wake cycle in 24 hours. Many factors including lifestyle, jetlag, exposure to light before bed-time, shift work, and stimulant intake contribute to disrupting functions of the circadian clock. Of note, misalignment or disruption of sleep-wake cycle and hormone secretion have severe repercussions for an individual’s physical and mental health. Recent evidence suggests that disrupted CRs, increase the risk for the development and greater severity of various illnesses, including neurodegenerative disorders (Musiek et al., 2016; Leng et al., 2020), neurodevelopmental disorders (Smith et al., 2019), and psychiatric illnesses including schizophrenia and mood disorders (Jones & Benca, 2015; Logan & McClung, 2019; Walker et al., 2020). A consistent relationship between disrupted CRs, poor sleep quality, and a compromised human immune system is well established (Spiegel et al., 2002; Cuesta et al., 2016). SARS-CoV-2 offered one of the best examples of this relationship between an individual’s health and disrupted CRs in immunology, with misaligned CRs seemingly increasing the risk of being infected with the SARS-CoV-2 virus (Silva et al., 2019; Fatima et al., 2021). It has also been speculated that this virus dampens melatonin rhythm and alters the timing of clock gene expression, which then results in misalignment and upregulation of the damaging inflammatory cytokine expression (Haspel et al., 2021).

In healthy individuals, this endogenous rhythm of the sleep-wake cycle is well synchronised with the alterations of the day and night cycle as well as other factors, including daily routines and the timing of meals (Zerón-Ruggerio et al., 2020). Such synchronisation is essential to maintain healthy sleep and wake patterns as disruptions or misalignment may lead to diverse cognitive, emotional, and sleep-related problems.

1.2 The Historical View of Chronotype

Research on individual differences in CRs and the self-report questionnaires designed to determine them can be traced back to, respectively, the early 1870s and 1900. Jundell (1904) confirmed that the sleep-wake cycle is responsible for the periodic rise and fall of body temperature. This viewpoint was shared by others, for example, Marsh (1906), who further confirmed individual differences in CRs and categorised his sample into morning and evening workers. However, a better understanding of the Morningness-Eveningness phenomenon emerged with the work of Wuth (1931), who categorised people into two types: a) individuals tired in the evening, sleeping, and reaching their maximum sleep depth early, and b) individuals performing their best in the evening, sleeping, and reaching their maximum sleep depth comparatively later. Winterstein (1932) also suggested that morning and evening sleepers respond differently to any factors preventing them from falling asleep, with the latter type finding it harder to tolerate sleep deprivation.

Freeman and Hovland (1934), based on their review of 135 studies for performance/work output and associated physiological processes, proposed a categorical division of CRs: a) continuous rise, b) continuous fall, c) morning rise-afternoon fall, and d) morning fall-afternoon rise. Kleitman (1939), however, criticised Freeman and Hovland's (1934) categorial division of CRs as it was based on the findings of small sample studies, predominantly

comprising of either morning or evening types. Instead, Kleitman broadly classified individuals into ‘morning types’ i.e., individuals whose temperature and performance peaks early in the day, and ‘evening types’ i.e., those who peak much later. He also noted another category called an ‘intermediate type’. A resurgence in this ‘Morningness-Eveningness’ classification became evident with Oquist’s (1970) ‘Morningness-Eveningness questionnaire’ (MEQ), which was designed to distinguish between morning and evening circadian preferences. Ostberg (1973) adapted and modified the MEQ to investigate CRs of food intake and oral temperature in the morning and evening types and concluded that the MEQ could potentially differentiate between these types in the context of food intake and oral temperature patterns. Thus, this classification of morningness-eveningness became the first widely accepted conceptualisation of diurnal preferences in scientific research. Interestingly, a great deal of research has used the word ‘chronotype’ and ‘diurnal preference’ interchangeably, assuming them to be the same, which is a fallacy.

1.3 The Construct of Chronotype

The term chronotype refers to a multimodal construct that can be defined as an expression of various CRs. Adan and colleagues (2012) describe chronotype as an individual’s activity-rest preference over a 24-hour period. Chronotype can also be referred to as rhythms of varied mechanisms ranging from body temperature, hormone or metabolic levels, cognitive functions, and eating to sleeping (Kasukawa et al., 2012; Levandovski et al., 2013). These processes can have a normal distribution in the general population, regardless of the geographical regions and cultural aspects of the instruments used to assess the phenotype (Horne & Ostberg, 1976; Kerkhof, 1985; Benedito-Silva et al., 1998; Adan & Natale, 2002; Roenneberg et al., 2007).

Over the past few decades, the study of chronotype has received much attention. However, this construct may not have been fully incorporated in some models (and related measures of chronotype) or consistently assessed in many previous studies (see 1.4.1 *Commonly Used Self-Report Scales*). Not surprisingly, while reviewing the literature on this topic, Kerkhof (1985) argued that the results from different studies could not be compared directly because of marked inconsistency in the chronotype questionnaires and analysis methods employed. Furthermore, non-sleep-related rhythms are not assessed directly by any of the commonly used self-report measures of chronotype, as most of these provide estimates of an individual's sleep rhythm while ignoring socially-driven or external influences (Levandovski et al., 2013), as we discuss in the next section.

1.3.1 Commonly Used Self-Report Scales

1.3.1.1 Morningness-Eveningness Questionnaire (MEQ)

The MEQ (Horne & Ostberg, 1976) was the first validated self-report questionnaire to assess 'Morningness-Eveningness' dimensions. It estimates 'phase preference' to categorise individuals into 'morning type' (individuals who prefer sleeping and waking up early as well as planning their activities early), 'evening type' (individuals who prefer sleeping and waking up late as well as planning their activities later in the day) (see Figure 2), or 'intermediate type' (individuals who are neither morning nor evening type and show considerable flexibility). The MEQ consists of 14 multiple-choice questions and five open questions framed in a preferential manner with Likert-type responses (e.g., what time would you get up if you were entirely free to plan your day?). These questions focus on preferred timings for sleep-wake cycles, physical and mental activity as well as subjective alertness. MEQ scores range from 16 to 86, with lower score (16-41) indicating evening preference, higher scores (59-86) indicating morning

preference, and scores between 42-58 indicating neither morning nor evening preference (intermediate type).

*****Figure 2 about here*****

In the first validation study of the MEQ (Horne & Ostberg, 1976) that was conducted in a student sample (18-32 years), body temperature was found to peak significantly earlier for morning types than evening types, whilst intermediate types had their body temperatures peak between those of the morning and evening types. Horne and Ostberg's (1976) sample included 62.1% 'morning types' who woke up an average of 114 minutes earlier than evening types, 36.6% 'intermediate types', and 2.2% 'evening types' who went to bed 99 minutes later than 'morning types'. Taillard and colleagues (2004), however, suggested revised cut-off scores for the MEQ based on their study of middle-aged French workers (N=566) which suggested that the bedtime of 11:30 pm in a student sample may reflect 'morningness', but this would indicate 'eveningness' in individuals aged 40-50 years. They proposed that scores 16-53 indicate evening preference, scores 64-86 indicate morning preference, and scores 54-63 indicate no preference. Applying these parameters, they classified 20.2% of their sample as evening types, 28.15% of the sample as morning types, and 51.7% as intermediate types. However, studies have consistently reported the MEQ to be reliable (coefficient range between 0.77 to 0.86) across different countries (Larsen, 1985; Adan & Natale, 2002; Caci et al., 2009; Lie et al., 2011) with strong split-half reliability (0.80; Adan & Natale, 2002) and test-retest reliability (coefficient range, 0.80 to 0.95; Larsen, 1985; Griefan et al., 2001).

A number of studies have also included objective circadian phase markers, such as body temperature (Andrade et al., 1992; Baehr et al., 2000), melatonin, and cortisol levels (Bailey & Heitkemper, 2001; Duffy et al., 2001), and these generally correspond well with MEQ scores.

Overall, the MEQ has been demonstrated to have high internal consistency (Cronbach $\alpha = 0.83$; Paine et al., 2006), with medium-to-large sized correlations, in the expected direction, between MEQ scores and circadian phase markers (Sack et al., 2007).

1.3.1.2 The Reduced MEQ (rMEQ)

Adan and Almirall (1991) reduced the original 19-item MEQ to a five-item self-report questionnaire. Of these five items, the first three ask individuals to indicate the time of the day when they a) feel at their best, b) prefer to get up, and c) prefer to go to bed. The fourth item is related to the degree of tiredness perceived in the first half hour of waking up. Finally, the last item asks individuals to indicate their morningness and eveningness preferences. The rMEQ has been demonstrated to be a quick and reliable instrument with good convergent validity (Caci et al., 2009), although inter-item correlations are poor (Cronbach α range: 0.08 to 0.46; Danielsson et al., 2019).

1.3.1.3 The Composite Scale of Morningness (CSM)

The CSM (Smith et al., 1989) is a popular 13-item self-report scale to assess an individual's preference for various activities, including sleep-wake preferences. Smith and colleagues (1989) created this scale by selecting the best items, using factor analysis, from the MEQ (Horne & Ostberg, 1976), and the Circadian Type Questionnaire (Folkard et al., 1979). Notably, 9 of the CSM items are from the MEQ. The scores range from 13 to 55, with lower scores indicating evening type (≤ 22), higher scores indicating morning type (≥ 44), and intermediate falling between 23 and 43. The scale was found to be reliable (Adan et al., 2005) with high internal consistency ($\alpha = 0.87$) and psychometric properties comparable to those of the MEQ and the DTS. The original factor structure of the CSM, however, could not be

replicated in a later study (Smith et al., 2002) and further studies have suggested one, two or three-factors solution (Caci et al., 2000; Bohle et al., 2001; Adan et al., 2005; Randler, 2008).

1.3.1.4 The Munich Chronotype Questionnaire (MCTQ)

The MCTQ (Roenneberg et al., 2003) is another self-report questionnaire that consists of different questions carefully differentiating between an individual's sleep and wake times on both work and free days, making this the best characteristic of the MCTQ. To assess chronotype, it uses the midpoint between sleep onset and offset, which is corrected for oversleeping due to sleep deficit that individuals aggregate during their working week (Roenneberg et al., 2015). Roenneberg and colleagues (2004) argued that except for those classified as 'early chronotypes' according to the MCTQ, all individuals show greater sleep timing differences between work and free days, with most individuals accumulating sleep deficits during their workdays. They further suggested that the MCTQ quantitatively measures an individual's chronotype based on sleep behaviours rather than sleep preferences and provides population-specific distribution of scores for 'early' and 'late' chronotypes. MCTQ scores also correlate meaningfully with biochemical markers such as melatonin (Kantermann et al., 2015), cortisol (Facer-Childs et al., 2019), and behavioural measures, including actimetry and sleep logs (Santisteban et al., 2018; Kuhnle, 2006). Further versions of the MCTQ have also been developed such as MCTQ core (Roenneberg et al., 2015) and MCTQ shift work (Juda et al., 2013), which now include additional items, for example, concerning substance use.

1.3.2 Methodological Limitations

Many of the self-report measures of chronotype are well researched and widely used questionnaires (see Figure 3) with high reliability and validity. Some of them have been

considered the gold standard assessment of chronotype (e.g., MEQ and MCTQ). However, they still have notable limitations, as we discuss further.

*****Figure 3 about here*****

1.3.2.1 The MEQ and CSM

As about two-thirds of the CSM items are taken from the MEQ, it may suffer from some of the same limitations that apply to the MEQ.

a) Psychometric issues: The scoring of the MEQ is not consistent across studies. This maybe because Horne and Ostberg (1976) did not clarify the rationale behind weighing item 11 as 6, 4, 2, 0 while the values for item 12 (i.e., if you got into bed at 11 pm, how tired would you be?) are 0, 2, 3, 5 (Caci et al., 2009). Furthermore, many studies have questioned the low inter-item correlation range for the MEQ items (0.20-0.40; Larsen, 1985; Adan & Natale, 2002) and have suggested two, three, and four-factor solutions (Adan & Natale, 2002; Hätönen et al., 2008; Li et al., 2011), challenging the assumption of the MEQ to be unidimensional. The CSM has been reported to have high convergent and construct validity against the MEQ, perhaps not surprisingly given that the CSM and MEQ have 9 common items. However, the MEQ or CSM's predictive validity has seldom been tested.

b) Inappropriate cut-offs: The cut-off points provided for the original MEQ (Horne and Ostberg, 1976) were based on a student sample (18-32 years). Later studies, however, showed that the cut-offs vary between different age groups and cultures (Taillard et al., 2004; Paine et al., 2006). Furthermore, morning types were found to predominate when the Morningness-

Eveningness frequency was compared using Horne and Ostberg's (1976) MEQ scores (Paine et al., 2006).

c) *Social and work schedules not considered:* Individuals tend to change their sleep preferences depending upon their work schedule. Unfortunately, the MEQ does not take this into account. Additionally, because the CSM is based on the MEQ, psychometric adequacy comes into question. As argued earlier by Roenneberg and colleagues (2003), the MEQ does not explicitly assess work and free days separately, and none of the MEQ items ask for actual sleep times (Putilov, 2000) or exposure to outdoor light.

d) *Influence of demographic and socio-cultural aspects ignored:* Neither the MEQ nor the CSM consider the masking effects of geographical location, different sleeping norms and patterns, as well as cultural differences on chronotype. Of note, afternoon naps are still prevalent in East Asian, Mediterranean, and South American countries, whereas they are much less common in the Western world (Borbely & Borbely, 1986). Not surprisingly, various Western societies differ from developing countries or small-scale societies on the grounds of having a climate/temperature-controlled environment preference for sleeping alone in a quiet and dark environment, which directly affect an individual's sleep phase. These inevitable differences may potentially influence the overall MEQ score distribution across regions. For instance, Spanish students were found more likely to be morning type than Italian students (Natale et al., 2009). The geographical location of the studied sample may not differ significantly; however, the samples differed in terms of culture, habits, norms, and lifestyles. Similarly, Randler and colleagues (2014) compared sleep-wake behaviour in German, Slovakian, and Indian students, and reported Indian students to be more frequently morning type than German and Slovakian students. Park and colleagues (1998) also reported

significantly different mean scores in two east Asian countries, i.e., Japan (56.2) and Korea (49.1). Different climatic and cultural conditions could explain these effects. Also, factors such as age (Duffy & Czeisler, 2002; Taillard et al., 2004; Randler et al., 2017), sex (Adan et al., 2005; Tonetti et al., 2008), and eating habits (Pot, 2017) have often not been considered (though often included as covariates), when examining the influence of demographic and socio-cultural aspects in the MEQ; and these may also impact the MEQ score distribution. This highlights the need for more cross-cultural studies and understanding the construct of chronotype from a multidimensional perspective.

1.3.2.2 The MCTQ

The MCTQ was developed to address the limitations of the MEQ and is largely used in genetic and epidemiological studies. However, although the MCTQ assesses one of the most important variables related to chronotype, i.e., sleep-wake patterns or sleep phase on both free and workdays, it still has some limitations. Firstly, it does not incorporate other temporal behaviours (e.g., mealtimes or social habits). Secondly, the calculation or scoring of the MCTQ relies solely on structured work schedules, which hinders its use in a population with more flexible schedules or uncertain work times (e.g., freelancers and content creators). Thirdly, it might not be ideal to use this questionnaire in a population whose culture and language do not rely on the metric-based concept of time (e.g., indigenous tribes across the globe) (Sinha et al., 2011; Silva Sinha, 2019). Lastly, sleep timing is not only controlled by circadian oscillations but also regulated by homeostatic oscillators (Borbély, 1982). Unlike the MEQ, which includes facets concerning sleep homeostasis (e.g., slow build-up of sleep pressure; Taillard et al., 2003; Mongrain et al., 2006), the MCTQ has not considered this.

1.3.3 Refining the Measurement of Chronotype

There are many different views on the construct of chronotype and how to best measure it. As previously mentioned, chronotype refers to an individual's rest-activity preference that occurs within a 24-hour cycle (Adan et al., 2013). However, this definition is rather broad, and the wide range of processes included has allowed researchers to select some processes (over others) that best fit their models. For example, Horne and Ostberg (1976) conceptualised chronotype as a 'psychological construct'. On the other hand, Levandovski and colleagues (2013) define chronotype as an 'attribute' of an individual reflecting their circadian phase. Roenneberg and colleagues (2019) argued that it should be viewed as a 'biological construct', which agrees with the initially used term 'an organism's temporal behaviour' or 'temporal phenotype' (Ehret, 1974; Samis, 1978). In the previous literature, chronotype has also been described as a 'dichotomous human trait' (Roenneberg et al., 2015), 'behavioural manifestation' and an 'inherited trait' (Kalmbach et al., 2017).

There are clearly multiple models and definitions of chronotype that are not fully aligned, and this problem gets amplified when applied to methodological approaches and measures of chronotype. For example, as discussed earlier, the MEQ measures psychological preference for behaviour (i.e., diurnal preference), while the MCTQ primarily focuses on sleep timings and categorises chronotypes into the morning, evening, and intermediate types. Various other existing self-report questionnaire measures of chronotype (e.g., MEQ, MCTQ core, rMEQ, CSM) predominantly assess only one dimension (i.e., sleep), do not incorporate any physiological indicators of chronotype, and overlook various factors that might influence, or can be related to, circadian manifestation and lead to a mismatch between an individual's measured and real chronotype as discussed in further sections.

2. Physiological Indicators of Chronotype

2.2.1 Melatonin Secretion

Melatonin onset is the most reliable marker of the endogenous circadian clock (Benloucif et al., 2005). On average, melatonin levels in humans increase 2-3 hours before sleep onset (Burgess & Fogg, 2008). However, this onset can easily be suppressed by structural constraints (e.g., nightlife, constant exposure to artificial light, and shift work), delaying melatonin secretion at night, with long-term detrimental consequences (e.g., circadian rhythm disorders, depression, and poor wellbeing).

In a noncontrolled environment, studies using blood and salivary measurements in healthy participants have reported that melatonin onset (highest secretion level) and its offset appear approximately 3 hours earlier in morning types than in evening types (Gibertini et al., 1999; Griefahn et al., 2002; Liu et al., 2000). Similar results were reported by Mongrain and colleagues (2004, 2005, N=34, age range=16-34). In an experimental study, Taillard and colleagues (2011, N=18) collected salivary melatonin hourly between the 12th and 26th hour of extended wakefulness (36 hours) of their participants. They observed that both salivary melatonin and dim light melatonin onset peaked earlier in individuals with morning orientation than in those with evening orientation.

Among adults, decreased melatonin levels have been associated with a range of neurodegenerative and psychiatric illnesses (Srinivasan et al., 2005; Pandi-Perumal et al., 2013). Studies have also suggested a potential relationship between melatonin onset and higher anxiety in school students (Diaz-Morales, 2015). Furthermore, Robillard and colleagues (2013, N=32, age range=15-30 years) reported reduced level and delayed onset of evening melatonin in individuals with mood disorders. In addition, Nagane and colleagues (2011, N=15, age

range=21-22 years) suggested that delayed melatonin secretion, growth hormone, and asynchronicity may reflect evening orientation in individuals.

2.2.2 Cortisol Secretion

Studies have shown that the cortisol awakening response is characterised by a marked increase (within the range of 60-150%) in cortisol secretion into the bloodstream after waking up and reaching its maximum approximately 30 minutes later (Clow et al., 2004). Not surprisingly, cortisol awakening response varies across populations, mostly in adults, students, and adolescents, because of sex and age differences as well as health status, perceived stress, and light exposure (Pruessner et al., 1997; Wust et al., 2000; Edwards et al., 2001). Like most rhythms, the cortisol awakening response appears to be tightly linked with the circadian clock and differs between morning and evening types, with morning types showing relatively higher cortisol levels in the first hour after awakening than evening types (Clow et al., 2004; Kudielka et al., 2006). There is also evidence that cortisol levels peak earlier in the day in morning types than in evening types. For example, Bailey and Heitkemper (1991) showed a delayed early-morning peak of salivary cortisol in evening types, relative to morning types; and Bailey and Heitkemper (2001) reported that plasma cortisol levels peaked 55 minutes earlier in morning types than in evening types. Some studies, however, have reported a complex relationship between cortisol awakening response or cortisol secretion curve and circadian preferences (Griefahn & Robens, 2008; Oginska et al., 2010; Dockray & Steptoe, 2011). The reasons for this may include other factors that also influence cortisol levels, for example, sleep loss (Oginska et al., 201), a prolonged exposure to environmental stressors (Lenaert et al., 2016), or presence or psychological and physical conditions associated with cortisol abnormalities (Geiss et al., 1997) in their samples.

2.2.3 Body Temperature

Body temperature has long been a popular physiological marker to measure an individual's endogenous CRs. It has a stable diurnal rhythm (Wever, 2013) and a complex feedback mechanism (Hammel & Pierce, 1968), which maintains an equilibrium between heat gain and loss. A direct relationship between body temperature (rectal, oral, skin) and circadian preference has been reported on several occasions (Pati & Gupta, 1994; Mongrain et al., 2004). In one study conducted in a noncontrolled environment (Martinez-Nicolas et al., 2013), it was found that body temperature drops significantly immediately after waking up, then starts to increase, peaking in early morning hours until it reaches its maximum (36°C), and then decreases until it reaches the lowest point (31°C) during the evening. Demonstrating the influence of Morningness-Eveningness, Baehr and colleagues (2000, N=172) reported that on average, minimum temperature occurred at 3:50 AM for morning types, at 6:01 AM for evening types, and at 5:02 AM for intermediate type individuals. This can potentially explain why evening type individuals have a higher tolerance for shift work, are often exhausted in the morning, and are alert during standard bedtime (9-10 pm). Additionally, an advanced circadian temperature phase, measured via rectal and oral temperature, has been reported more often in morning than evening types (Pati & Gupta, 1994; Duffy et al., 1999).

3. Factors Influencing Chronotype

3.1 Genetics

As mentioned earlier, circadian rhythmicity is also found in cells throughout the central nervous system and other body cells (Novakova et al., 2013). These peripheral clock components are defined as genes whose proteins are vital for generating and regulating CRs

within individual cells (Takahashi, 2004), as well as being synchronised by the central SCN to generate CRs (Hastings et al., 2003). Since circadian and sleep systems interact to determine a circadian preference, genetic variations can be expected to play a role in determining this preference. This notion has been supported by studies conducted in the UK, Scandinavia, and Brazil, showing that 50% of individuals' circadian preferences could be determined by genetics (Vink et al., 2001; Barclay et al., 2010), whereas studies in ethnic groups, of note, Hutterites and Amazonians, reported significantly lower heritability rates ranging between 14 and 23% (De Souza Aguiar et al., 1991; Klei et al., 2005).

The most studied human gene variants involved in circadian preference are CLOCK (Katzenberg et al., 1998), PER1 (Carpen et al., 2006), PER2 (Lee et al., 2011), PER3 (Archer et al., 2010; Lazar et al., 2012) though there are also studies which failed to replicate some of these associations, including CLOCK (Pedrazzoli et al., 2007; Robilliard et al., 2002) and PER3 (Barclay et al., 2011; Osland et al., 2011). These failures may be explained by varying sample sizes, age, sex, phenotyping methods or other as-yet unknown factors. Moreover, genome-wide association studies have identified 351 independent loci and independently supported the relationships between chronotype and genes, including PER2, RGS16, FBXL13, and AK5 (Hu et al., 2016; Lane et al., 2016; Jones et al., 2016).

3.2 Individual Factors

3.2.1 Developmental Influences

Over the past few decades, age has been identified as one of the most significant factors influencing chronotype. Several studies provided evidence of a constant shift in Morningness-Eveningness preference during an individual's lifespan (Ronneberg et al., 2007; Borisenkov, 2011; Merikanto et al., 2012), suggesting that children are more likely to be morning types,

with adolescents being continuously evening types until the age of 20 and 21, and a shift from evening type to morning type with increasing age (Randler et al., 2011). Paine and colleagues (2006) also reported that individuals between 30 and 34 years are more likely to be evening types, while those between 45 and 49 years are more likely to be morning types. Interestingly, most of the population in these samples was classified as intermediate type followed by evening type and morning type (Adan & Natale, 2001; Paine et al., 2006; Randler et al., 2011). However, this trend has not been observed in individuals above 60 years, suggesting older people likely have higher morning preferences with minimal or no sex differences (Roenneberg et al., 2007). This shift from morningness to eveningness and vice-versa across an individual's lifespan has been supported by later studies with larger samples and more comprehensive age ranges [e.g., Merikanto et al. (2012), N=6858, age range: 26-72 years; Duarte et al., (2014), N=16,650, age range 20-60 years; Tonetti et al., (2008), N=8972, age range: 10-87 years].

This constant shift from morningness to eveningness has been reported in studies on toddlers and pre or early-schoolers. For example, Zimmermann (2016) reported decreased morningness right from the beginning in toddlers (N=529; age range: 2-4 years). Wada and colleagues (2009), in a comparative study (N=697 Japanese and 627 Czech children, age range: 0-8 years), also reported that infants in Japan and the Czech Republic became more evening oriented with age. A similar shift has been reported in adolescents (Roenneberg et al., 2004; Randler et al., 2017). Furthermore, as these adolescents reach early adulthood (20/21 years), the morningness increases again and stabilises when they reach middle adulthood (Roenneberg et al., 2004; Adan et al., 2012). These studies suggest that chronotype is not a fixed trait for life but changes as individuals age.

3.2.2 Sex Differences

The possibility of sex differences influencing human chronotypes is well documented (Randler, 2007; Fabbian et al., 2016; Kim et al., 2020). However, these studies are scarce, and the findings remain inconsistent due to a) large age effects masking sex differences, especially when males and females are of unequal age (see Natale & Danesi, 2002; Caci et al., 2005), b) different instruments used to assess circadian typology (Mecacci et al., 1991; Chelminski et al., 1997; Zimmermann, 2016), and c) insufficient sample sizes to produce reliable findings. For instance, some studies in children (Simpkin et al., 2014, N=48, age range: 2.5-3 years; Zimmermann 2016, N=529, age range: 2-4 years) found no sex differences. The first large-scale (N=25,000) study to describe sex differences was conducted by Roenneberg and colleagues (2004), who reported women to be more morning type than men during most of adulthood. However, this difference appears to be reduced after middle age (50 years and above). Tonetti and colleagues (2008, N=8,972) also reported the absence of chronotype differences between the two sexes beyond the age of 55. Furthermore, Randler (2011, N=7,480) reported that the shift from late to early chronotypes from adolescence to early adulthood is more apparent in females than males. These findings are also supported by physiological data showing that melatonin peaked later in males than in females (Gibertini et al., 1999; Baehr et al., 2000). Overall, it seems that sex differences in chronotype are most apparent during the reproductive years for women versus age-matched men but not, or less apparent, during childhood or post-menopause.

3.2.3 Personality Traits

Several studies have examined possible associations between Morningness-Eveningness and personality traits using the 'Big Five' model of personality (Costa & McCrae, 1992). Of the

Big Five personality dimensions, *conscientiousness* has been considered the best predictor of morningness, with a medium-sized correlation seen between *conscientiousness* and morningness (Randler, 2008, $r = 0.336$; Tsaousis, 2010, $r = 0.33$). A relationship between *agreeableness* and morningness was found, with a small effect size, in some studies (DeYoung et al., 2007; Hogben et al., 2007; Randler, 2008; Tsaousis, 2010) but not in others (Jackson & Gerard, 1996; Tonetti et al., 2009). The relationships between circadian preference and other *Big Five* dimensions, namely *openness*, *extraversion*, and *neuroticism* appear to be either weak or absent. For example, in a meta-analysis (Tsaousis, 2010), *extraversion* ($r = 0.02$) was related to morningness, while *openness* ($r = -0.02$) and *neuroticism* ($r = -0.05$) were related to eveningness with negligible effect sizes.

In the context of Eysenck's model of personality (1967), some studies using the *Eysenck Personality Inventory*' (Eysenck & Eysenck, 1965) suggested that evening types score higher on *extraversion* than morning types (Horne & Ostberg, 1977; Adams et al., 1986; Neubauer, 1992; Mitchell & Redman, 1993; Tankova et al., 1994; Langford & Glendon, 2002). However, other studies did not find this (Mura & Levy, 1986; Mecacci & Rocchetti, 1998), or reported this relationship only in females (Matthews, 1998). In a comprehensive review, Adan and colleagues (2012) indicated a stable relationship between eveningness and extraversion using the Eysenck Personality Inventory. However, the results for *neuroticism* are less consistent. Some studies reported that evening types score higher on *neuroticism* than morning types (Mecacci & Rocchetti, 1998; Tankova et al., 1994), while several others did not (Mitchell & Redman, 1993; Tankova et al., 1994; Langford & Glendon, 2002). Inconsistent results may be explained by varying sample characteristics (e.g., age, sex, student versus non-student population). Evening types have also been reported to score higher than morning types on

psychosis-proneness (Mitchell & Redman, 1993; Tankova et al., 1994) as measured by the Psychoticism scale of the Eysenck Personality Questionnaire (Eysenck & Eysenck, 1976).

There are also studies examining temperament and character profiles, as conceptualised in Cloninger's model of personality (Cloninger et al., 1993). Lee and colleagues (2017, N=2857) found eveningness to be associated with higher *novelty seeking* (found to correlate positively with *extraversion* in Big Five; and with *psychoticism* in Eysenck's model; De Fruyt, et al., 2000) and *harm avoidance* (positive correlations with *neuroticism* in both Big Five and Eysenck's models, e.g. Corr et al., 1995; Kumari et al., 1996; De Fruyt, et al., 2000), while morningness was associated with *persistence*, *self-directedness*, and *cooperativeness*. Lastly, there is evidence that morning types may be more empathetic (Wilson, 1990) and less hostile (Zelenski et al., 2003) than evening types.

Overall, individuals who are evening types appear to be extroverted, open-minded, and to score higher on psychoticism, whereas morning types appear to be more introverted, conscientious, agreeable, and emotionally stable. These relationships, however, were present mostly with very small effect sizes, and not found in all studies. Many researchers (Randler, 2008; Tsaousis, 2010) have argued that the chronotype-personality relationship might be dependent on specific theoretical models and associated measures used to assess specific personality traits, rather than different measures used to assess Morningness-Eveningness (DiMilia et al., 2008).

3.3 Environmental Factors

3.3.1 Season of Birth

The season of birth could be an essential proxy for environmental factors in relation to an individual's circadian preference (Takao et al., 2009; Natale et al., 2009, 2011; Harada et al.,

2011; Tonetti et al., 2011). However, the evidence is obscured due to various methodological issues (e.g., questionnaire used to define morningness, sample size, and geographical location). For instance, in Japan, one study (Takao et al., 2009, N=1156) reported no association between the season of birth and chronotypes in individuals between 18-30 years old while another study (Harada et al., 2011, N=9740) reported a relationship between the season of birth and chronotype in 2-12 years old children. This finding is supported by previous research done in the northern hemisphere on Italian adolescents (Tonetti et al., 2011) as well as Italian, Spanish (Natale et al., 2009), and Canadian adults (Mongrain et al., 2006). In general, these various studies reported individuals who were born in spring and summer tend to have evening orientation or late chronotype, while those born in autumn and winter tended to have morning orientation. Also, this pattern was seen more in males than females (Natale & Adan, 1999; Tonetti et al., 2011), possibly due to other biological and cultural influences or sex-specific rhythms. For instance, menstrual cycle related fluctuations in females may make their chronotype more variable across the female population in particular geographical locations (Natale & Adan, 1999).

Variations in daylight during the early stages of development (prenatally) may influence the formation of the neurohormonal system in the hypothalamic nuclei (Sivan et al., 2001; Kenneway, 2002). In humans, this period may correspond to the first three months and is highly crucial for the ontogenesis of the sleep-wake cycles (Fukuda & Ishihara, 1997). In addition, the photoperiod hypothesis also points towards that the season of birth could potentially mediate environmental factors for developing Morningness-Eveningness preference, suggesting individuals born in spring or summer (long photoperiod) may prefer eveningness and those born in autumn or winter may prefer morningness (Natale et al., 2011). Natale and colleagues (2011) further explored a possible association between the season of birth and

circadian preference in the northern (e.g., Italy) and southern hemispheres (e.g., Australia). Despite the seasons being reversed between hemispheres, their findings were in line with the previous literature (Mongrain et al., 2006; Natale et al., 2009; Tonetti et al., 2011).

3.3.2 Altitude and Longitude

Altitude and longitude may also impact the circadian preference of an individual. Randler (2008) investigated this possible relationship in German adolescents residing in 17 different countries with different time zones, differing in temperature and hours of sunlight received and found the individuals in the subtropics prefer evening orientation while those in tropic zones prefer morning orientation. There was also a significant relationship between circadian preference and longitude as well as latitude within the time zone of central Europe. Adolescents were found to be more morning oriented towards the east and north.

Furthermore, Borisenkov and colleagues (2012) investigated this relationship in 11-18-year-olds in northern Russia (latitude ranging between 59.5° North - 67.6° North) and reported that each 8° increment in latitude results in the midpoint of sleep being delayed by an hour. Recently, Leocadio-Miguel and colleagues (2017) investigated this relationship in a larger sample (N=12884, age range 18-75 years) in Brazil (latitude ranging between 0° South -32°33 South and longitude range from 34°50 West - 57°05 West). They reported that the further away individuals are from the equator, the more significant is the shift of chronotype distribution towards late chronotype. These findings are in line with previous literature focusing on different hemispheres and circadian preference (Natale et al., 2011) and indicate that latitude and longitude coordinates influence an individual's circadian preference.

3.3.3 Seasonal Daylight-Saving Time (DLST)

Many northern sphere countries (e.g., France, Norway, and the UK) have adopted '*daylight-saving time*,' i.e., the social clock is adjusted by an hour which results in advancing the time in spring and delaying it in autumn. Kantermann and colleagues (2007) investigated the role of DLST in the disruption of the circadian clock in a larger sample (N=55,000) in seven different countries (e.g., Netherlands, Luxembourg, Slovakia, Switzerland). They reported chronotype-dependent differences in adjustments to DLST, especially after the springtime change when the social clock advances by an hour. Individuals classified as early chronotypes using the MCTQ adjusted more readily to the DLST than those classified as evening chronotypes. This suggests that individuals with morning orientation can re-entrain more quickly than individuals with evening orientation within a certain (3 weeks) phase of time transition.

A later study by Allebrandt and colleagues (2014, N=9765) also demonstrated disrupted seasonal adaption in individuals living in central Europe (Scotland, Estonia, Germany, and Croatia) during the annual transition to DLST. They assessed their sample during DLST and '*standard time zone*' and reported variation in chronotype throughout a year was primarily dependent on age, sex, and season of assessment, with the last factor having more significant influence. This implies that assessment during the DLST period may be less reliable than during the standard time zone.

3.4 Social Factors

3.4.1 Social Jetlag and Structural Constraints

Initially, Wittmann and colleagues (2006) computed social jetlag as an absolute difference between midsleep on both free and workdays (social jetlag = midsleep on free days - midsleep on workdays). However, Jankowski (2017) argued that social jetlag not necessarily results only

from different sleep timings on work and free days but also because of accumulated sleep debt during this period. Therefore, Jankowski proposed a correction to the original formula that corrects for sleep debt (social jetlag sleep corrected = sleep onset on free days - sleep onset on workdays). In a later study, they (Wittmann et al., 2009) found this social jetlag to be significantly greater in late chronotypes than in early chronotypes. A potential explanation of this finding may be that school/university/work timings are not often receptive to individual's late phases, which results in significantly greater social jetlag in these individuals; this social jetlag remains present until retirement and generally decreases with age (Roenneberg et al., 2019). Haraszti and colleagues (2014) reported that differences between weekends and schooldays in bedtime, rise time, and total nocturnal sleep were more significant for young people with evening orientation than those with morning orientation. They suggested that young people with evening orientation sleep more on weekends than on school days to cover this sleep debt accumulated during the week. Higher sleep-related issues in individuals with evening orientation can be understood as a more pronounced misalignment between their biological and social rhythms posed by school schedules and related social interactions and, as a result, they tend to complain frequently about daytime sleepiness (Haraszti et al., 2014).

Different sleep habits in adolescents with morning and evening orientation may be influenced by developmental endocrine factors (Randler et al., 2012). These differences could also be related to high academic and social demands, laidback parental restrictions, increased independence, and greater involvement in late-night activities (Randler et al., 2012). The findings aid the understanding that the onset of adolescence affects sleep and marks poor sleep duration (Gradisar et al., 2011) as well as increases sleep irregularity (Giannotti et al., 2005; Russo et al., 2007), resulting in the desynchronization of an individual's circadian rhythm.

*****Figure 4 about here*****

Social jetlag has also been reported in young adults who carry out shift work (Kang et al., 2020). Also, not all populations show similar results. For instance, Zhang and colleagues (2019) reported social jetlag less frequently among Chinese shift workers than in the European population. Also, it was not correlated with higher body mass index in Chinese workers as is typically seen in western societies.

3.4.2 Exposure to Artificial/Natural Light

Since antiquity, natural cycles of light and darkness have governed the timing of most aspects of our behaviour and physiology (Aulsebrook et al., 2018). However, these cycles have been disrupted by artificial light at night (Gaston et al., 2017). This light pollution is becoming a global phenomenon at an alarming rate (Falchi et al., 2016; Davies & Smyth, 2018), prompting severe threats to human sleep patterns. Previous literature has suggested that exposure to artificial light in the evening (before sleeping) delays the circadian phase, as assessed by subjective questionnaires (MEQ and CSM) (Martin et al., 2012; Vollmer et al., 2012), sleep timings (Koo et al., 2016), salivary melatonin levels (Benlucif et al., 2008; Cajochen et al., 2011), and body temperature (Krauchi et al., 1997). However, on the contrary, exposure to bright natural or artificial light in the morning advances the circadian phase of melatonin synthesis and release (Dijk et al., 1989; Revell et al., 2005). Furthermore, Vollmer and colleagues (2012) also reported that adolescents who live in urban areas and are exposed to artificial light at night tend to have an evening orientation more than those living in rural areas.

3.4.3 Dietary Patterns and Obesity

Emerging literature supports the potential relationship between chronotype and metabolic health (Yu et al., 2015), especially amongst individuals with evening orientation. These individuals are more susceptible to obesity (Sun et al., 2019), cardiovascular diseases, and type 2 diabetes (Merikanto et al., 2013). In addition, they adhere to various unhealthy behaviours such as a sedentary lifestyle (Mota et al., 2016), reduced healthy diet (Maukonen et al., 2016), delayed meal timings (Sato-Mito et al., 2011), skipping breakfasts (Reutrakul et al., 2014), preference for food and beverages having higher concentrated sugar (Wilson et al., 2016; Wright & Zelman, 2018), and lower consumption of nutritious food (Patterson et al., 2016). These harmful habits can possibly be explained by a lack of synchronisation of the biological and social clock (Munoz et al., 2016) and a tendency to eat later (Teixeira et al., 2019). Furthermore, a recent systematic review (Teixeira et al., 2022) concluded that individuals with evening orientation are more likely to show unhealthy eating habits, while those with morning orientation show healthy and protective habits (e.g., eating early and predominantly fresh as well as less processed food items). In addition, individuals falling in the intermediate category show similar patterns to those with morning orientation or evening orientation. They also concluded that individuals with evening orientation are more likely to present higher weight and body mass index.

3.4.4 Stimulants

The relationship between chronotypes and consumption of stimulants and other substances (e.g., caffeine, nicotine, alcohol) is well established (Singleton & Wolfson, 2009; Wittmann et al., 2009; Whittier et al., 2014; Patterson et al., 2016). Individuals with evening orientation are reported, on average, to consume more nicotine (Schneider et al., 2011) and alcohol (Prat & Adan, 2011) and lead an unhealthier lifestyle compared to those with morning orientation

(Taylor et al., 2011; Fabbian et al., 2016). Detrimental consequences ranging from health hazards to decreased psychological well-being in evening types have been found to be mediated by higher consumption of these stimulants (Wittmann et al., 2010). A study on Dutch students (Van Den Berg et al., 2018, N=742, age range=18-56 years) reported similar findings in showing a strong relationship between evening orientation and depressed mood as well as higher alcohol and nicotine consumption. A recent study (Siudej & Malinowska-Borowska, 2021) reported that morning type individuals consume stimulants less frequently than evening type individuals, especially those above 30 years.

4. Refining the Construct of Chronotype: Need for a Multidimensional Model

Mounting evidence suggests that the true chronotype not only differs between individuals but its expression is also influenced by a range of environmental, social, and individual factors. It is crucial not to underestimate such influencers, including lifestyle, geographical location, personality traits, drug consumption, type of work (freelancing, shift work, regular work, working remotely), dietary patterns and obesity to better understand an individual's true chronotype. We, therefore, propose a multidimensional model (depicted in Figure 5) and argue for refining the measures of chronotype where social, environmental, genetic, and individual factors are not studied in isolation but as a part of a holistic system in which they interact to determine an individual's true chronotype. We integrate these influencing factors into a cumulative model (Figure 5a), present their known or likely influence (on their own) to affect chronotypes by either delaying or advancing an individual's natural circadian phase in a consistent manner (Figure 5b), and outline various potential feedback loops between these factors (Figure 5c). We acknowledge that directionality in some of the loops we have proposed (Figure 5c) may vary over an individual's life span, and that some of these factors may have

additive or interactive effects, and thus propose ‘potential pathways’ (see Figure 5c). We hope that the model we have proposed here will stimulate empirical research to refine it further, and provide a solid foundation for developing multidimensional self-report measures of chronotype suitable for different age groups, societies and locations.

*****Figure 5a-c about here*****

5. Conclusions and Future Directions

Existing models of chronotype, self-report measures and empirical studies have significantly advanced our understanding of the importance of chronotype, especially disrupted CRs and their implications. However, it appears that much of the chronotype literature has employed a simplistic view of chronotype, with a disproportionate focus on aspects pertaining to sleep. Here, we have proposed a more fine-grained, multidimensional model of chronotype and disrupted CRs, incorporating age, health parameters including hormonal status, psychosocial and environmental factors, sleep-wake and meal patterns, and other daily life activities for developing preventive and therapeutic approaches to effectively address various psychological, cardiometabolic, biological, and neurodevelopmental diseases associated with the disrupted CRs. With this multidimensional view of chronotype and transdisciplinary approaches to allow a more comprehensive understanding than currently available of the construct and its implications for our physical and mental health (individually as well as at the societal level), we make a number of recommendations for the future scientific enquiry in this area.

First, there is a need for a more comprehensive and standardised measure of chronotype. The current self-report measures of chronotype predominantly focus on sleep habits and yet vary considerably in what exactly they measure. For example, the MEQ focuses on the phase

preference of sleep, and the MCTQ focuses mainly on the desynchronisation of sleep. Although these measures have contributed significantly to chronobiology, genetics, epidemiology, clinical, developmental, social and cultural studies, they could be usefully expanded to incorporate both sleep and non-sleep aspects (e.g., dietary habits) and consider social and cultural influences that are found to influence the chronotype in the rapidly changing human societies in different parts of the world.

Second, we need longitudinal studies capable of uncovering the utility of age-dependent changes in chronotype to predict mental and physical health outcomes (i.e., identifying early signs and symptoms of various illnesses), considering late chronotype (eveningness) has been associated with a range of adverse outcomes, including poor physical and mental health, lower academic achievement, poor athletic performance, poor cognitive function, emotion dysregulation, and overall poor well-being. An individual's chronotype, however, appears to fluctuate over the lifespan (Section 3.2.1), and it may also be amenable to targeted interventions. If predisposed or acquired morningness is indeed found to be a 'preventive factor', and eveningness a 'risk factor' for poor mental and physical health in longitudinal investigations, it has policy and practice implications for healthcare and well-being across the globe. The findings from such studies could have further societal implications; for example, city designs need to take care of not only factors such as noise pollution that impact our cognitive function and well-being health (review, Wright et al., 2014) but also urban lighting, given the known association between outdoor light at night and eveningness in adolescents (Vollmer et al., 2012).

Third, there is a need to pay greater attention to sex and hormonal status in chronotype studies. We need a better understanding of why and how individuals, especially males, gravitate

towards eveningness during adolescence, to what degree social factors affect their chronotype and how personality traits, especially neuroticism or psychosis-proneness, might be linked to chronotypes. These answers will allow us to uncover the critical mechanisms behind these relationships and their implications for various negative outcomes that have been linked to the late chronotype.

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Figure 1. The schematic representation of circadian circuits in humans according to the model proposed by Koller et al. (2020). Light signals (artificial or natural) are transduced by ipRGCs in the eye and transmitted to the following structures in order: the SCN (suprachiasmatic nucleus), the PVN (paraventricular nucleus), the intermediolateral column of the thoracic spinal cord, the SCG (superior cervical ganglion), and finally terminates in the pineal gland.

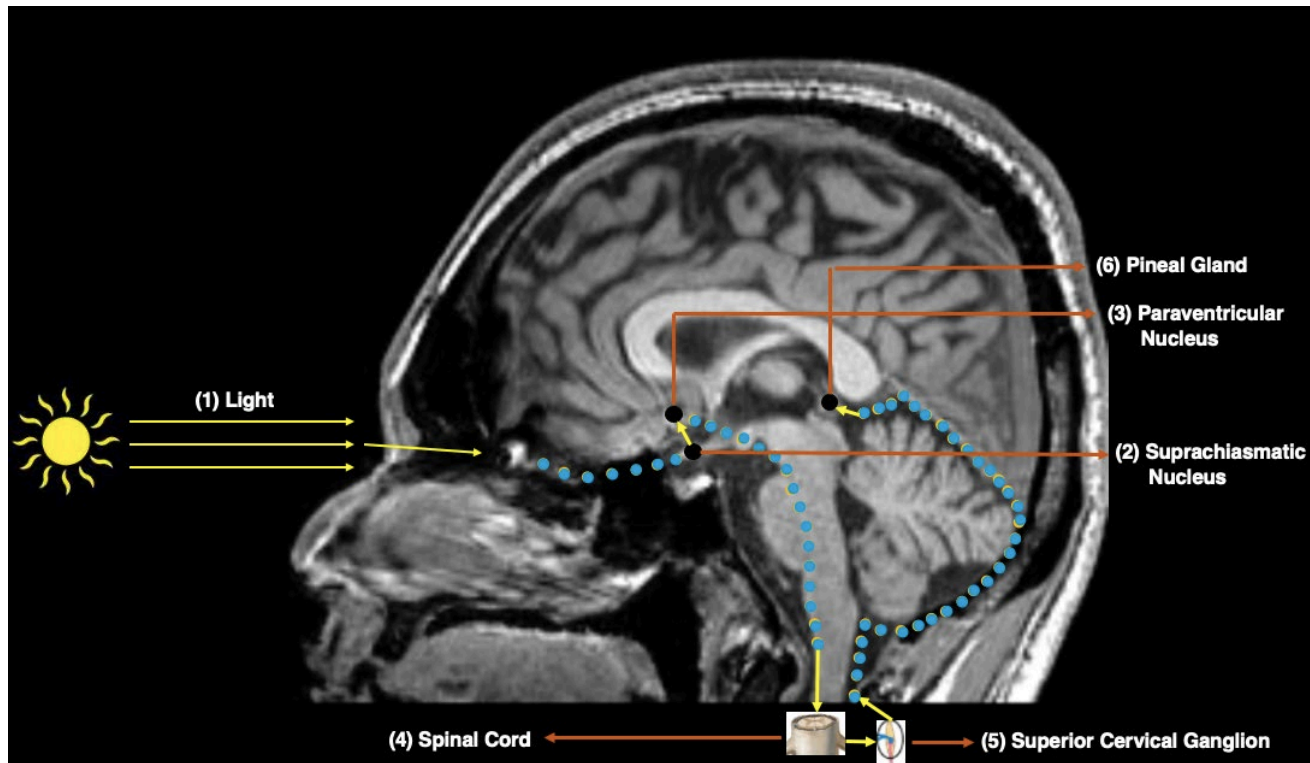


Figure 2. The schematic representation of sleep periods preferred by morning and evening types. These periods and timings are commonly found, on average, in most populations across the world.

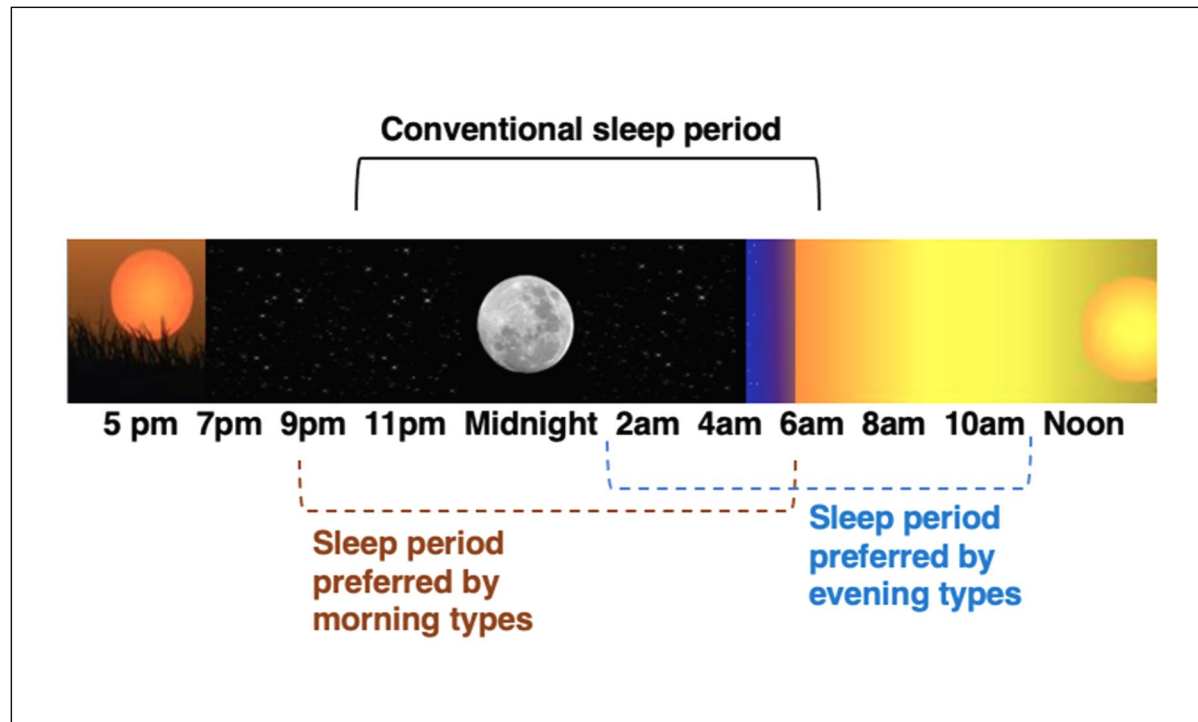


Figure 3. Graphical representation of commonly used self-report scales cited from 1976 to 2022 (highlighted in grey) and 2014 to 2022 (highlighted in black) based on Google scholar search conducted on 8th November 2022. Abbreviations: rMEQ, Reduced Morningness-Eveningness Questionnaire (1991); CSM, Composite Scale of Morningness (1989); MCTQ, Munich Chronotype Questionnaire (2003); MEQ, Morningness-Eveningness Questionnaire (1976).

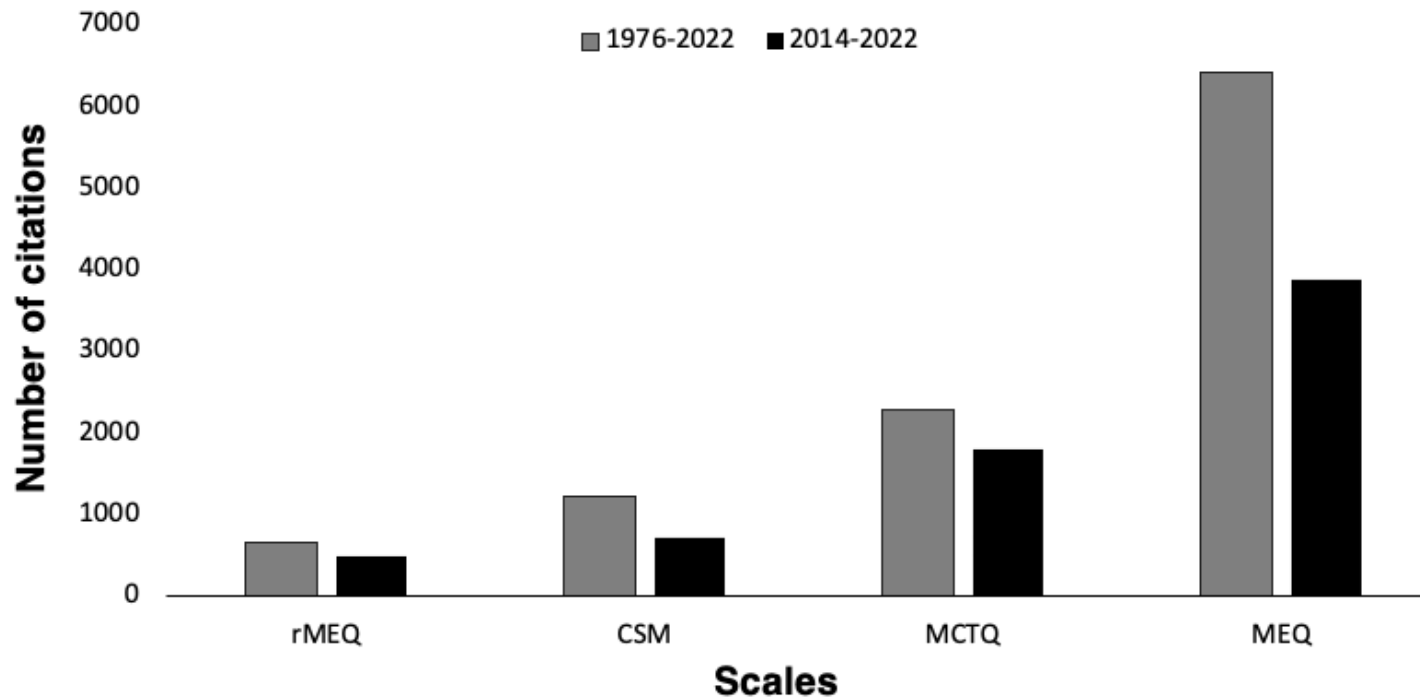


Figure 4. Example of social jetlag (adapted from Taillard et al., 2021). Light blue bar represents 'sleep timing on free-days', light yellow bar represents 'sleep timing on workdays', and the dotted black vertical line shows social jetlag of 2-3 hours.

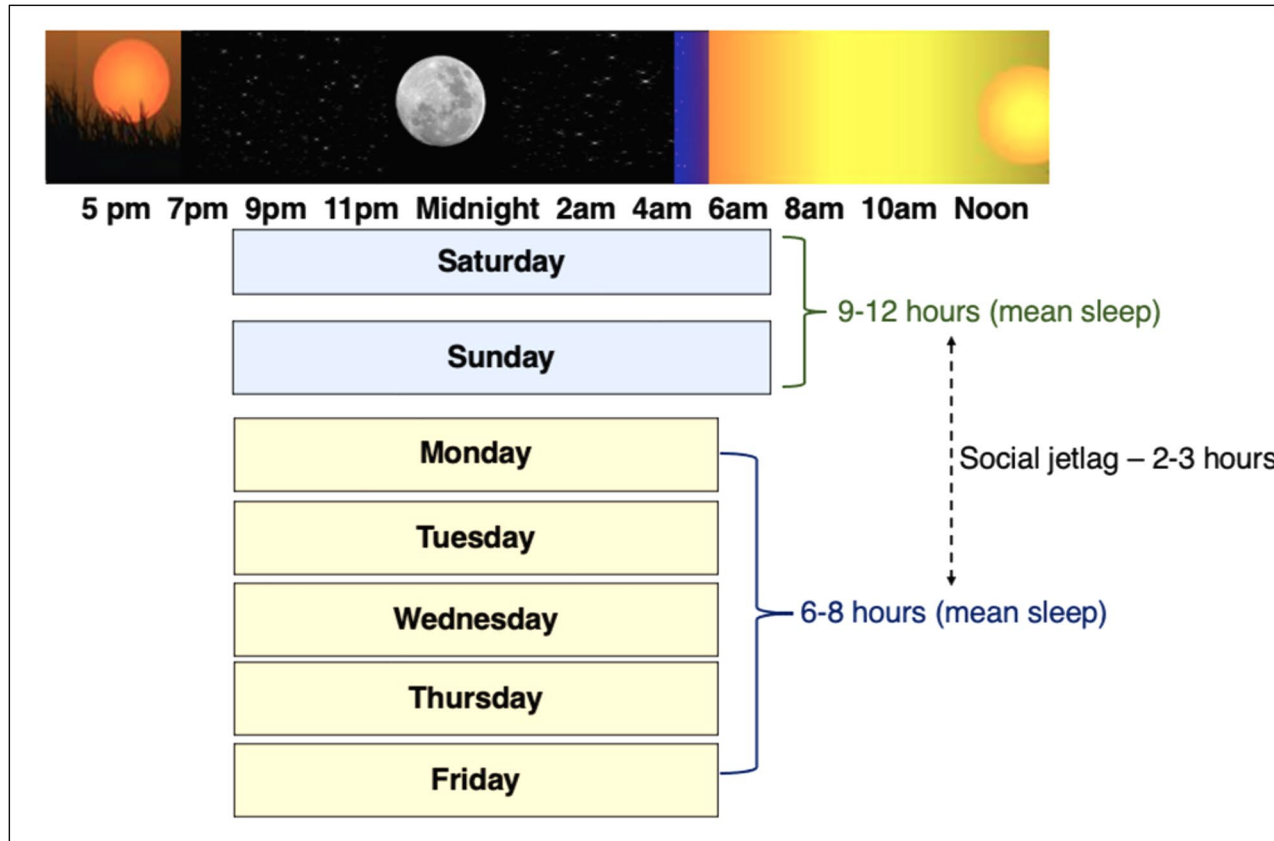
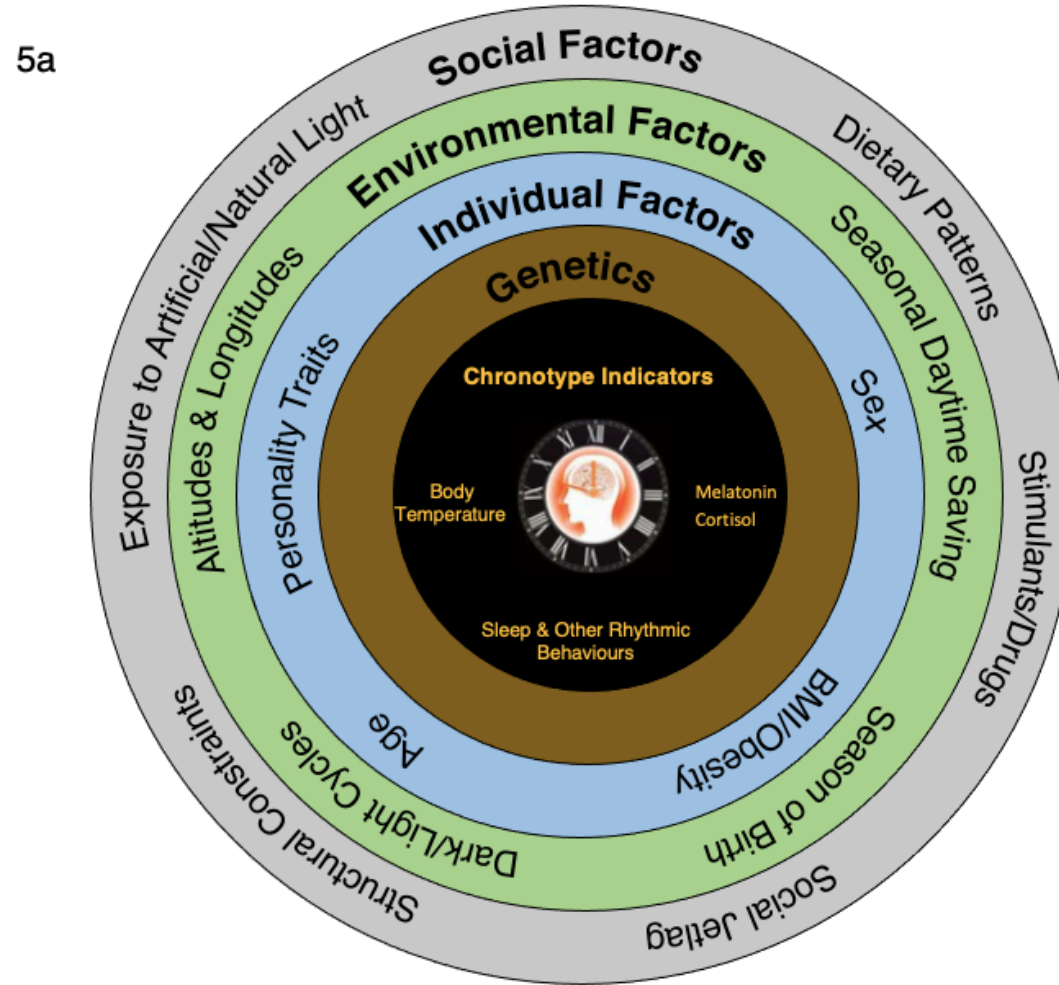


Figure 5. The schematic representation of (5a) the proposed multidimensional model of chronotype integrating various social, environmental and individual factors (5a; the clock in the centre represents an individual's circadian preference or chronotype, and each circle represents a factor), (5b) the known or likely association of these factors with morningness or eveningness, and (5c) proposed networks of inter-linked factors (colour-coded) capable of influencing chronotype (black-headed arrows connecting different variables reflect established relationships and dotted black-headed arrows connecting different variables show potential relationships).



5b

Factors	Known or Likely Influences and Associations
Nighttime Artificial Light	Delay circadian phase
Irregular Dietary Habits	Linked to evening chronotype
Stimulants/Drug Intake	Linked to evening chronotype
Social Jetlag	Linked to evening chronotype
Irregular Lifestyle	Linked to evening chronotype
Shiftwork/Irregular Work Hours	Delay or advance circadian phase
Altitudes and Longitudes	Higher morningness with higher coordinates
Timing of, Exposure to, Natural Light	Delay or advance circadian phase
Seasonal Daytime Saving	Morning chronotypes re-entrain faster
Season of Birth	Mixed findings
Sex	Increased morningness in females of reproductive age, with relatively weaker sex differences in old age
Age	Continuous shift from morningness to eveningness and vice-versa
Personality Traits	Extraversion, open-mindedness and schizotypy associated with eveningness and conscientiousness, agreeableness, and emotional stability associated with morningness - mixed findings with small effect sizes (for positive findings)
Higher Body Mass Index (BMI)	Linked to evening chronotype
Genetics	Mixed findings

5c

