Chronotype and Self-Reported Sleep Quality: Effects on Mental Health and Cognitive Functions

A Thesis Submitted for the Degree of Doctor of Philosophy

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Thesis Abstract

Chronotype is a multidimensional construct underlying circadian rhythms (CRs) of varied mechanisms, including sleep-wake cycles, body temperature, and alertness/arousal levels. It exists on a spectrum from morning (MCs; peak circadian arousal in the morning) to evening chronotypes (ECs; peak circadian arousal in the evening), with most individuals falling in the middle, known as intermediate chronotypes (ICs). Evening chronotype (EC) has been linked with sleep-related disturbances and psychopathology-related personality traits. EC has also been associated with adverse mental, physical and cognitive health outcomes but the roles of sleep-related disturbances and/or psychopathology-related personality traits in this association needs to be clarified.

This thesis addressed two broad questions: i) *Is chronotype linked to mental health and what is the role of sleep quality in this relationship?* To address this question, two psychometric studies were conducted to probe the chronotype-mental health relationship while also quantifying sleep quality and psychopathology-related personality traits (neuroticism, schizotypy, impulsivity) in young non-clinical adults residing in India (N=313), the UK (N=213), or Germany (N=247). ii) *Does chronobiological variables [i.e., chronotype, time of day (ToD), synchrony effect] influence neurocognitive functions?* First, a systematic review of the existing studies addressing the effects of chronotype, ToD or synchrony effects on cognitive performance was conducted. This was followed by two empirical studies: a) a behavioural study (N=63; age range: 18-40 years) to examine the effect of chronobiological variables and/or sleep quality on verbal learning and memory (immediate recall, recognition, delayed recall), and b) a psychophysiology study (N=45; age range: 18-40 years) to examine the effects of chronobiological variables and/or sleep quality on prepulse inhibition (PPI) of the acoustic startle response (an operational measure of sensorimotor gating function).

The findings of the investigations conducted in three independent samples (India, the UK, Germany) showed no direct association between chronotype and mental health in young non-clinical populations. Instead, sleep quality fully mediated chronotype-mental health relationship in these populations. The findings of the systematic review indicated (i) no main effect of chronotype on any cognitive function in most studies, and (ii) a synchrony effect in MCs and/or ECs, mainly but not exclusively in attention, inhibition and memory, in

approximately 45% of the studies involving adults aged 18-45 years, and in 80% of the studies involving older (50+ years) adults. The empirical studies conducted as part of this project showed no main effect of chronotype and showed a partial synchrony effect (only in MCs) on delayed recall (episodic memory) but not on PPI (sensorimotor gating) in healthy young adults, most of whom self-reported good sleep quality.

In conclusion, the findings show that chronotype does not directly affect mental health and may influence some cognitive functions in interaction with ToD. The findings provide strong support for the sleep hypothesis as a predisposing, precipitating, and perpetuating risk factor for poor mental health and reject the widely reported role of chronotype as an independent transdiagnostic risk factor for mental health problems. The findings also highlight the need for sleep-centred interventions in clinical practices and public health initiatives to improve mental health, and the importance of synchrony (chronotype x ToD) effects when assessing cognitive performance of older adults.

Declaration of Originality

I hereby declare that this thesis is my own work. Any material, including figure or text, sourced from various online databases has been properly referenced. Additionally, my own published and submitted work has been clearly stated.

Satyam Chauhan

To my mum - the strongest person I know,

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List of Abbreviations

A/D	Analog-to-Digit
AGFI	Adjusted Goodness of Fit Index
AK5	Adenylate Kinase 5
ANOVA	Analysis of Variance
BMI	Body Mass Index
C	Celsius
CFI	Comparative Fit Index
CLOCK	Clock Circadian Regulator
CRs	Circadian Rhythms
CSM	Composite Scale of Morningness
CTQ-SF	Childhood Trauma Questionnaire – short form
DASS-21	Depression Anxiety Stress Scale-21
DB	Decibel
DLMO	Dim Light Melatonin Onset
DLST	Daylight-Saving Time
EC	Evening Chronotype
ECs	Evening chronotypes
EMG	Electromyography
EPQR-S	Eysenck Personality Questionnaire – revised short form
EUR	Euro
FBXL13	F-box and Leucine Rich Repeat Protein 13
GBP	Pound Sterling
GFI	Goodness of Fit Index
HVLT	Hopkins Verbal Learning Test
HZ	Hertz
IBM	International Business Machines
IC	Intermediate chronotype
ICs	Intermediate chronotypes
MC	Morning chronotype
MCs	Morning chronotypes
MCTQ	Munich Chronotype Questionnaire
MEQ	Morningness-Eveningness Questionnaire

MS	Milliseconds
N	Number of Observations/Individuals
PER1	Period Circadian Regulator 1
PER2	Period Circadian Regulator 2
PER3	Period Circadian Regulator 3
PPI	Prepulse Inhibition
PSQI	Pittsburgh Sleep Quality Index
PVN	Paraventricular Nucleus
RAVLT	Rey Auditory Verbal Learning Test
RGS16	Regulator of G protein signalling 16
rMEQ	Reduced Morningness-Eveningness Questionnaire
RMSEA	Root Mean Square of Approximation
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SCG	Superior Cervical Ganglion
SCN	Suprachiasmatic Nucleus
SD	Sleep Deprivation
SEM	Structural Equation Modelling
SJL	Social Jetlag
SPSS	Statistical Package for the Social Sciences
SPSS AMOS	Statistical Package for the Social Sciences (Analysis of Moment Structures)
SR-lab	Startle-Response Lab
s-OLIFE	Oxford-Liverpool Inventory of Feelings and Experiences short version
S-UPPS-P	Impulsive Behaviour Scale short version
TLI	Tucker Lewis index
ToD	Time of day
UK	United Kingdom
USA	United States of America
µV	Microvolt
WMZ	Wakeful Maintenance Zone
a	Alpha
b	Beta
g+	Hedges g
ηp^2	Partial Eta Squared

Preface

While the roots of chronobiology research can be traced back to Jean Jacques De Mairan's (1729) work on CRs in plants, significant advances in this field were made mostly in the last 100 years. The evolutionary logic of why humans developed a circadian system that oscillates periodically to cause intra and interindividual differences in various rhythms, including sleep-wake cycles, stands compelling. The most frequently studied interindividual difference in humans is known as chronotype or diurnal preference.

For decades, a preference for morningness (i.e., MC) has been associated with good mental, physical and cognitive health, while a preference for eveningness (i.e., EC) has been considered as an independent risk factor for adverse mental health. Over the past few decades, we have also learnt that chronotype influences sleep behaviour and that sleep quality has strong associations with mental health and cognitive performance. This PhD thesis, therefore, focuses on adding insights to our understanding of the influence of chronotype, separate to that of sleep quality, on mental health and cognitive functions in young non-clinical adults.

This thesis is divided into three parts. Part I provides comprehensive literature reviews on chronotype, highlighting its history, concepts, theories and models, and influences on sleep, mental health, and cognition (Chapter 1-3); it ends with an overview of the aims and objectives of the empirical work reported in this thesis (Chapter 4). Part II (Chapters 5-8) presents four empirical investigations of how chronotype and sleep quality might affect mental health and cognitive performance in young, non-clinical adults while also considering psychopathology-related personality traits. Part III (Chapter 9) synthesises the findings of the empirical studies presented in Part 2, discusses various implications, strengths and limitations, and offers suggestions for future research.

PART I

Chapter 1: Chronotype: Theories, Models, and Assessments

Chapter 2: Chronotype-Mental Health Relationship: Making a Case for Sleep Quality as a Mediator

Chapter 3: Chronotype Influences in Neurocognitive Functions: A systematic Review

Chapter 4: Thesis Aims and Objectives

Chapter 1: Chronotype: Theories, Models, and Assessments

This chapter has been published in *Neuroscience and Biobehavioural Reviews* as:

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Abstract

Chronotype can be defined as an expression or proxy for CRs of varied mechanisms, for example 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. A comprehensive review was conducted to critically review and synthesise the existing models and theories of chronotype. These 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. 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, was proposed. 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.

1.1 Chapter Aims and Overview

This chapter contains observations from a comprehensive review, wherein the existing theories, models, assessments, indicators and influencers of chronotype were critically reviewed and synthesised. This chapter then progresses towards refining the construct of chronotype and propose a new approach/model, concluding with future directions for chronobiology research.

1.2 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 (Gobin et al., 2015; Pilcher and Huffcutt 1996).

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.

1.3 Circadian Rhythms (CRs)

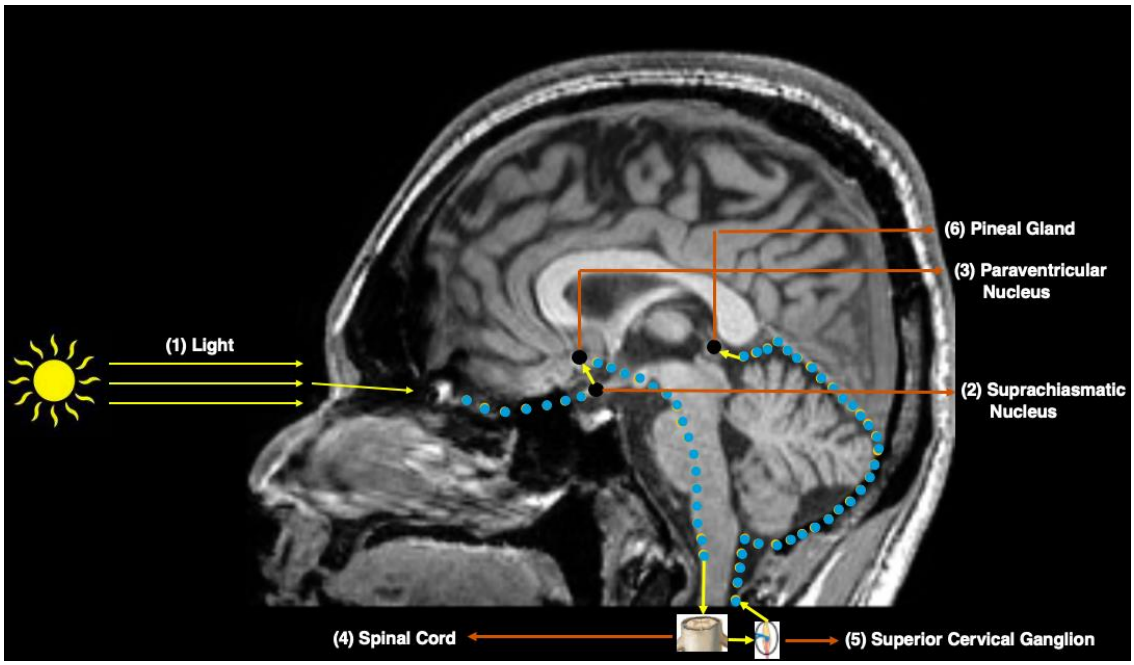
Humans have a range of predictable biological rhythms, which refer to any endogenous or exogenous cyclic change in the level of bodily chemicals or functions (Aschoff, 2013). Some biological rhythms occur many times a day (e.g., ultradian rhythms such as appetite), some once every 24 hours (e.g., circadian 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.

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 research on the mammalian circadian clock has long focused on the role of the suprachiasmatic nucleus (SCN) of the hypothalamus (Moore & Eichler, 1972) as a central pacemaker, which influences the sleep-wake cycle in close association and interaction with the pineal gland (Leon Llamas et al., 2021; Moore et al., 2002) (see 1.3.1 *Circadian Circuits in Humans* for more details). Previous research has suggested that circadian oscillators or peripheral clocks are genetically programmed to generate CRs (Novakova et al., 2013; Yoo et al., 2004). These circadian oscillators are intrinsic properties of the cells across various tissues in mammals and are found throughout the brain and other human body cells (Yoo et al., 2004) (see 1.7.1 *Genetics* for more details). The SCN synchronises the peripheral clocks to generate and regulate the CRs. (Hastings et al., 2003). In humans, the endogenous CRs oscillate with some periodic variation in length (Czeisler & Gooley, 2007), causing considerable intra-individual variations.

1.3.1 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; Koller et al., 2020; Larsen et al., 1998), 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 1.1).

Figure 1.1. *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.*



1.3.2 Disrupted CRs and Associated Illnesses

The term ‘disrupted CRs’ is used 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 (Leng et al., 2020; Musiek et al., 2016), 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 (Cuesta et al., 2016; Spiegel et al., 2002). 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 (Fatima et al., 2021; Silva et al., 2019). 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-Rugerio 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.

1.4 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 chronotypes (MCs) or evening chronotypes (ECs). Instead, Kleitman broadly classified individuals into 'MCs' i.e., individuals whose temperature and performance peaks early in the day, and 'ECs' i.e., individuals whose temperature and performance peaks much later in the day. He also noted another category called an 'intermediate chronotype' (ICs). 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 MCs and ECs 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.

1.5 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 (Adan & Natale, 2002; Benedito-Silva et al., 1998; Horne & Ostberg, 1976; Kerkhof, 1985; 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 1.5.1 *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 discussed in the next section.

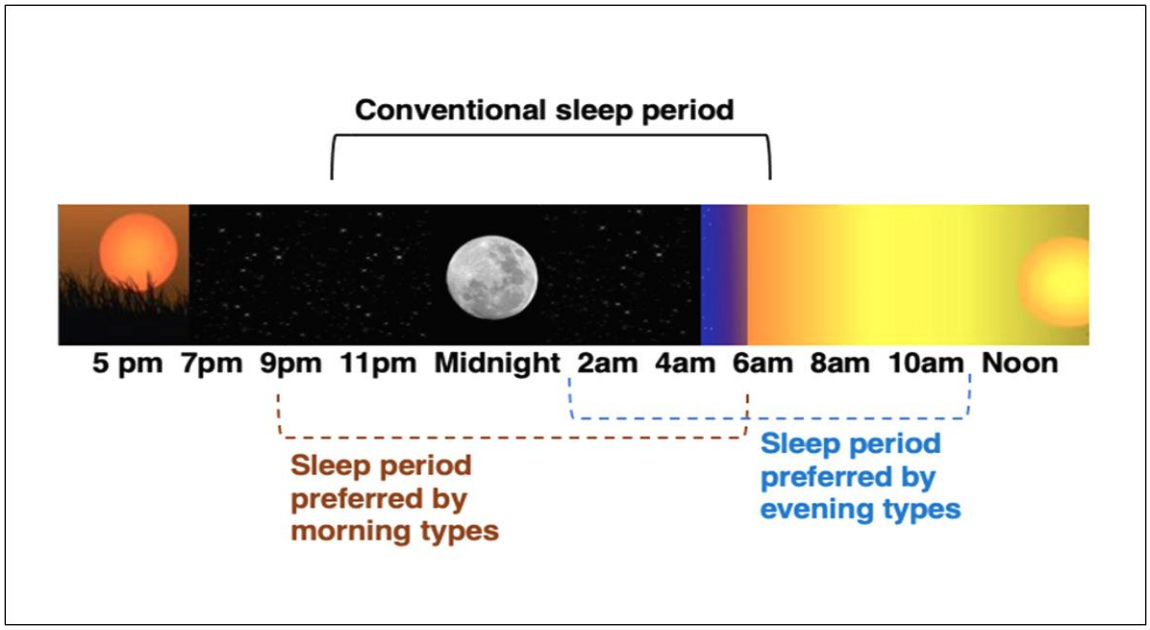
1.5.1 Commonly Used Self-Report Scales

1.5.1.1 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 MCs (individuals who prefer sleeping and waking up early as well as planning

their activities early), ECs (individuals who prefer sleeping and waking up late as well as planning their activities later in the day) (see Figure 1.2), or ICs (individuals who are neither MCs nor ECs 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 (ICs).

Figure 1.2 *The schematic representation of sleep periods preferred by MCs and ECs. These periods and timings are commonly found, on average, in most populations across the world.*



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 MCs than ECs, whilst ICs had their body temperatures peak between those of MCs and ECs. Horne and Ostberg's (1976) sample included 62.1% MCs who woke up an average of 114 minutes earlier than ECs, 36.6% ICs, and 2.2% ECs who went to bed 99 minutes later than MCs. 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 23:30 hour 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 ECs, 28.15% of the sample as MCs, and 51.7% as ICs. However, studies have consistently reported the MEQ to be reliable (coefficient range between 0.77 to 0.86) across different countries (Adan & Natale, 2002; Caci et al., 2009; Larsen, 1985; 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 α=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).

1.5.1.2 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 day (ToD) 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: 0.08-0.46; Danielsson et al., 2019).

1.5.1.3 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 EC ($\leq$22), higher scores indicating MC ($\geq$44), and ICs falling between 23 and

43. The scale was found to be reliable (Adan et al., 2005) with high internal consistency (α=0.87) and psychometric properties comparable to those of the MEQ and the Diurnal Type Scale. 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 (Adan et al., 2005; Bohle et al., 2001; Caci et al., 2000; Randler, 2008).

1.5.1.4 The Munich Chronotype Questionnaire (MCTQ)

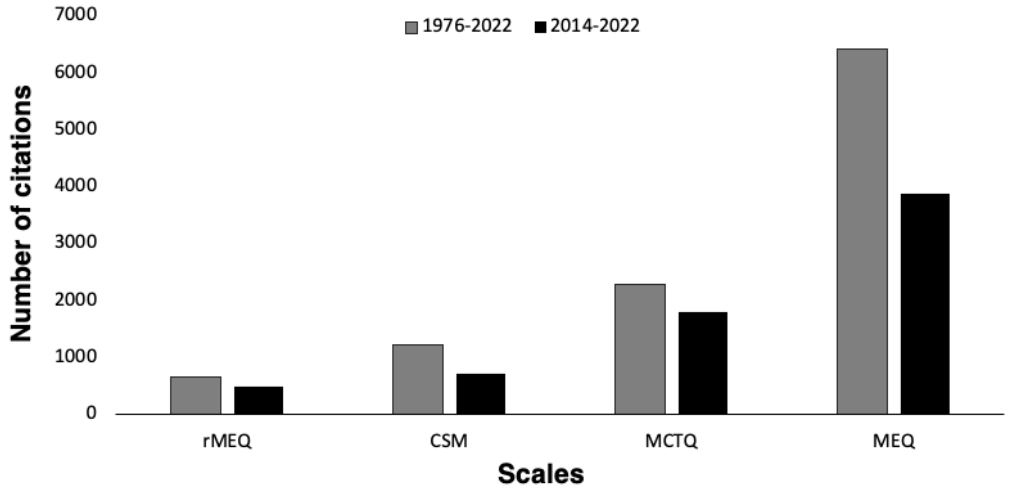
The MCTQ (Roenneberg et al., 2003) is another self-report questionnaire that consists of different questions carefully differentiating between an individual's sleep and wake times on both work and free days, making this the best characteristic of the MCTQ. To assess chronotype, it uses the midpoint between 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 MCs 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 MCs and ECs. 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 (Kuhnle, 2006; Santisteban et al., 2018). 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.

1.5.2 Methodological Limitations

Many of the self-report measures of chronotype are well researched and widely used questionnaires (see Figure 1.3) 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 discussed further.

Figure 1.3 *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).



1.5.2.1 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; Adan & Natale, 2002; Larsen, 1985) 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 (Paine et al., 2006; Taillard et

al., 2004). Furthermore, MCs 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 MCs 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 MCs 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; Randler et al., 2017; Taillard et al., 2004), 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.

1.5.2.2 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) (Silva Sinha, 2019; Sinha et al., 2011). 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; Mongrain et al., 2006; Taillard et al., 2003), the MCTQ has not considered this.

1.5.3 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 MCs, ECs, and ICs. 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.

1.6 Physiological Indicators of Chronotype

1.6.1 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), with considerable individual differences in the timings of peak melatonin levels (Burgess & Fogg, 2008). 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). Dim light melatonin onset (DLMO) has been widely recognised as a key marker in determining the circadian phase (Kennaway, 2023; Pandi-Perumal et al., 2006) due to its reliance on the SCN. Some studies have also shown an association between DLMO and sleep onset, offset and midpoint in healthy adults (Martin & Eastman, 2002; Reiter et al., 2020).

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 MCs than in ECs (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 12^{th} and 26^{th} hour of extended wakefulness (36 hours) of their participants. They observed that both salivary melatonin and dim light melatonin onset peaked earlier in MCs than ECs. A recent study by Cox and colleagues (2024) also showed that ECs tend to have a later DLMO offset, and the interval between their melatonin offset and wake-up time is positively larger than that of MCs. This suggests that ECs have a delayed melatonin rhythm or a longer circadian period (24 h 31 mins) than MCs (23 h 50 mins), making

them more susceptible to developing disrupted sleep patterns (Lazar et al., 2012). As previously described, Mongrain and colleagues (2004) also argued that a delayed circadian phase is associated with a shorter phase angle (i.e., reduced time difference between circadian events). This shorter phase may contribute to difficulty falling asleep (Lazar et al., 2012; Mongrain et al., 2004) and has been associated with delayed sleep-wake disorders (Chang et al., 2009).

Among adults, decreased melatonin levels have been associated with a range of neurodegenerative and psychiatric illnesses (Pandi-Perumal et al., 2013; Srinivasan et al., 2005). 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 ECs.

1.6.2 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 (Edwards et al., 2001; Pruessner et al., 1997; Wust et al., 2000). Like most rhythms, the cortisol awakening response appears to be tightly linked with the circadian clock and differs between MCs and ECs, with MCs showing relatively higher cortisol levels in the first hour after awakening than ECs (Clow et al., 2004; Kudielka et al., 2006). There is also evidence that cortisol levels peak earlier in the day in MCs than in ECs. For example, Bailey and Heitkemper (1991) showed a delayed early-morning peak of salivary cortisol in ECs, relative to MCs; and Bailey and Heitkemper (2001) reported that plasma cortisol levels peaked 55 minutes earlier in MCs than in ECs. Some studies, however, have reported a complex relationship between cortisol awakening response or cortisol secretion curve and circadian preferences (Dockray & Steptoe, 2011; Griefahn & Robens, 2008; Oginska et al., 2010). 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 abnormities (Geiss et al., 1997) in their samples.

1.6.3 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. Increased heat loss in the evening has been linked to an increased ability to fall asleep (review, Krauchi & Deboer, 2010). Melatonin secretion reduces core body temperature (Cagnacci et al., 1997) and helps promote sleepiness (Aschoff, 1971). Studies under controlled environments have shown that lying down enhances blood flow to the skin, facilitating blood cooling from the legs to the body's core (Harding et al., 2019; Tikuisis & Ducharme, 1996). This cooling occurs via convective heat exchange, transferring heat from the core to the cooler circulating blood, effectively reducing core body temperature (Tikuisis & Ducharme, 1996). Further evidence suggests that sleep propensity peaks when core body temperature is minimal (Dijk & Czeisler, 1995; Harding et al., 2019).

A direct relationship between body temperature (rectal, oral, skin) and circadian preference has been reported on several occasions (Mongrain et al., 2004; Pati & Gupta, 1994). 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 hour for MCs, at 6:01 hour for ECs, and at 5:02 hour for ICs. This can potentially explain why ECs have a higher tolerance for shift work, are often exhausted in the morning, and are alert during standard bedtime (21:00-22:00 hour). Additionally, an advanced circadian temperature phase, measured via rectal and oral temperature, has been reported more often in MCs than ECs (Duffy et al., 1999; Pati & Gupta, 1994).

1.7 Factors Influencing Chronotype

1.7.1 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 (Barclay et al., 2010; Vink et al., 2001), 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; Jones et al., 2016; Lane et al., 2016).

1.7.2 Individual Factors

1.7.2.1 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 (Borisenkov, 2011; Merikanto et al., 2012; Ronneberg et al., 2007), suggesting that children are more likely to be MCs, with adolescents being continuously ECs until the age of 20 and 21, and a shift from ECs to MCs 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 ECs, while those between 45 and 49

years are more likely to be MCs. Interestingly, most of the population in these samples was classified as ICs, followed by ECs, and MCs (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 (Randler et al., 2017; Roenneberg et al., 2004). Furthermore, as these adolescents reach early adulthood (20/21 years), the morningness increases again and stabilises when they reach middle adulthood (Adan et al., 2012; Roenneberg et al., 2004). These studies suggest that chronotype is not a fixed trait for life but changes as individuals age.

1.7.2.2 Sex Differences

The possibility of sex differences influencing human chronotypes is well documented (Fabbian et al., 2016; Kim et al., 2020; Randler, 2007). 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 Caci et al., 2005; Natale & Danesi, 2002), b) different instruments used to assess circadian typology (Chelminski et al., 1997; Mecacci et al., 1991; 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 MCs 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 ECs to MCs 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 (Baehr et al., 2000; Gibertini et al., 1999). 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.

1.7.2.3 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 ECs score higher on *extraversion* than MCs (Adams et al., 1986; Horne & Ostberg, 1977; Langford & Glendon, 2002; Mitchell & Redman, 1993; Neubauer, 1992; Tankova et al., 1994). However, other studies did not find this (Mecacci & Rocchetti, 1998; Mura & Levy, 1986), 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 ECs score higher on *neuroticism* than MCs (Mecacci & Rocchetti, 1998; Tankova et al., 1994), while several others did not (Langford & Glendon, 2002; Mitchell & Redman, 1993; Tankova et al., 1994). Inconsistent results may be explained by varying

sample characteristics (e.g., age, sex, student versus non-student population). ECs have also been reported to score higher than MCs 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 corelate 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; De Fruyt, et al., 2000; Kumari et al., 1996), while morningness was associated with *persistence, self-directedness*, and *cooperativeness*. Lastly, there is evidence that MCs may be more empathetic (Wilson, 1990) and less hostile (Zelenski et al., 2003) than ECs.

Overall, individuals who are ECs appear to be extroverted, open-minded, and to score higher on psychoticism, whereas MCs 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).

1.7.3 Environmental Factors

1.7.3.1 Season of Birth

The season of birth could be an essential proxy for environmental factors in relation to an individual's circadian preference (Harada et al., 2011; Natale et al., 2009, 2011; Takao et al., 2009; 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 be ECs, while those born in autumn and winter tend to be MCs. 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 (Kenneway, 2002; Sivan et al., 2001). 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).

1.7.3.2 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 ECs. 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.

1.7.3.3 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 MCs using the MCTQ adjusted more readily to the DLST than those classified as ECs. This suggests that MCs can re-entrain more quickly than ECs on 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.

1.7.4 Social Factors

1.7.4.1 Social Jetlag and Structural Constraints

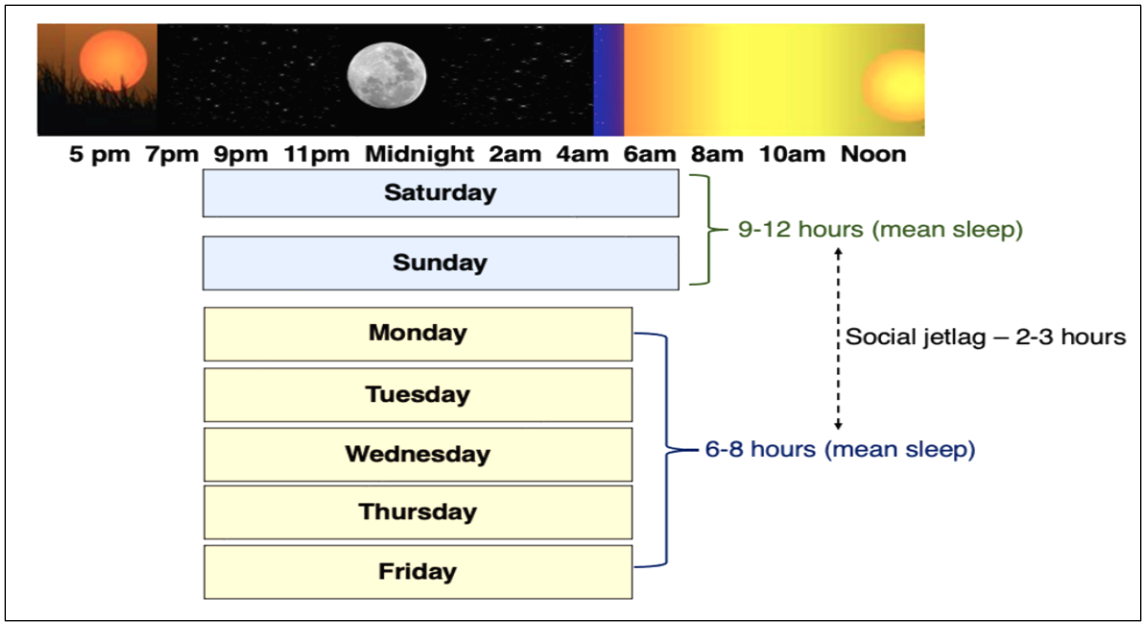
Initially, Wittmann and colleagues (2006) computed social jetlag (SJL) as an absolute difference between midsleep on both free and workdays (SJL=midsleep on free days - midsleep

on workdays). However, Jankowski (2017) argued that SJL 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 (SJL sleep corrected=sleep onset on free days - sleep onset on workdays). In a later study, they (Wittmann et al., 2009) found this SJL to is significantly greater in ECs than MCs. 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 SJL 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 desynchronisation of an individual's CR.

SJL 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 SJL 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.

Figure 1.4 *Example of SJL (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.*



1.7.4.2 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 (Davies & Smyth, 2018; Falchi et al., 2016), 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.

1.7.4.3 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 sedimentary 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 ECs show unhealthy eating habits, while MCs show healthy and protective habits (e.g., eating early and predominantly fresh as well as less processed food items). They also concluded that ECs are more likely to present higher weight and body mass index.

1.7.4.4 Stimulants

The relationship between chronotypes and consumption of stimulants and other substances (e.g., caffeine, nicotine, alcohol) is well established (Patterson et al., 2016; Singleton & Wolfson, 2009; Whittier et al., 2014; Wittmann et al., 2009). ECs are reported, on average, to consume more nicotine (Schneider et al., 2011) and alcohol (Prat & Adan, 2011) and lead an unhealthier lifestyle compared to MCs (Fabbian et al., 2016; Taylor et al., 2011). Detrimental consequences ranging from health hazards to decreased psychological well-being in ECs 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 ECs and depressed mood as well as higher alcohol and nicotine consumption. A recent study (Siudej & Malinowska-Borowska, 2021) reported that MCs consume stimulants less frequently than ECs, especially those above 30 years.

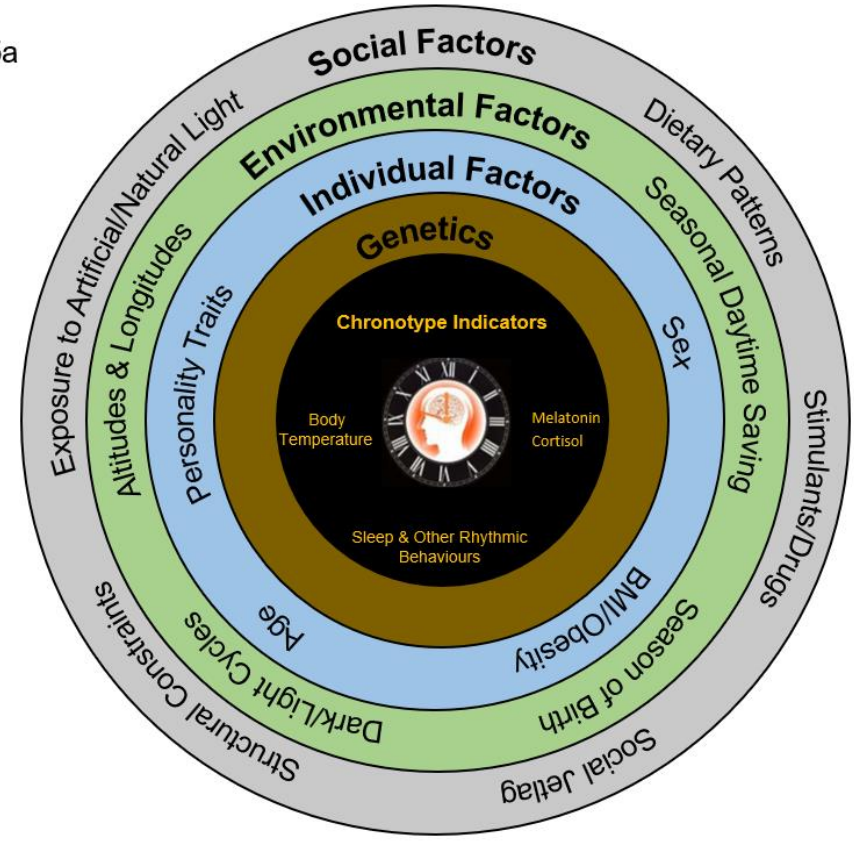
1.8 Refining the Construct of Chronotype: Need for a Multidimensional Model

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 1.5) 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 1.5a), 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 1.5b), and outline various potential feedback loops between these factors (Figure 1.5c). We acknowledge that directionality in some of the loops we have proposed (Figure 1.5c) 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 1.5c). 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 1.5 *The schematic representation of (1.5a) the proposed multidimensional model of chronotype integrating various social, environmental and individual factors (1.5a; the clock in the centre represents an individual's circadian preference or chronotype, and each circle represents a factor), (1.5b) the known or likely association of these factors with morningness or eveningness, and (1.5c) 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).*

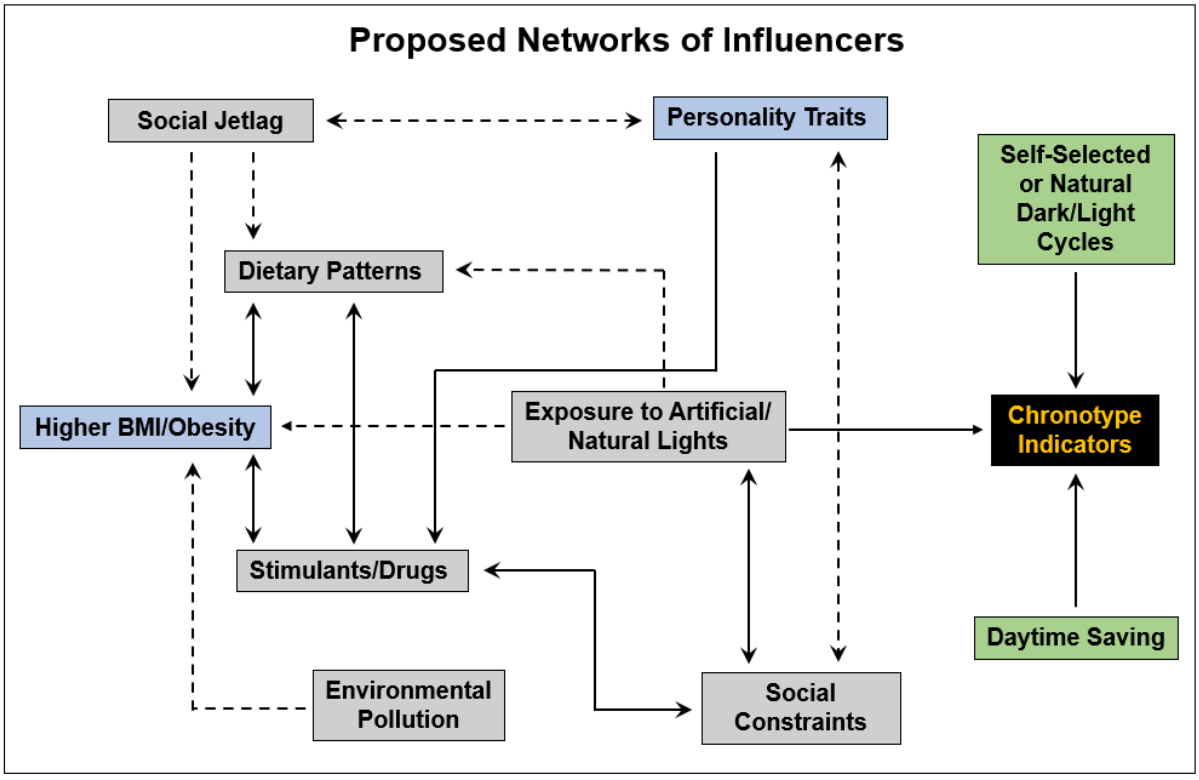
1.5a


Social Factors
Environmental Factors
Individual Factors
Genetics
Chronotype Indicators
Body Temperature
Melatonin Cortisol
Sleep & Other Rhythmic Behaviours
Exposure to Artificial/Natural Light
Altitudes & Longitudes
Personality Traits
Sex
Seasonal Daytime Saving
Dietary Patterns
Stimulants/Drugs
Social Jetlag
Season of Birth
BMI/Obesity
Age
Dark/Light Cycles
Structural Constraints

1.5b

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

1.5c



1.9 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 ECs (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 1.7.2.1), 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 ECs.

Chapter 2: Chronotype-Mental Health Relationship: Making a Case for Sleep Quality as a Mediator

Abstract

Considerable evidence suggests that EC is associated with sleep-related disturbances and shares similar comorbidities with certain mental health issues and psychopathology-related personality traits. However, the role of sleep quality in the chronotype-mental health association remains unclear. A brief literature review was conducted to provide an overview of the current evidence on chronotype-mental health relationship, with a particular focus on the role of sleep quality. The observations suggests that EC is negatively linked with various mental health conditions, with the strongest and most consistent association observed with depression. Sleep quality is associated with various mental health issues, but its mediating role in chronotype-mental health relationship remains debatable. The prevailing view in chronobiology research suggests that chronotype functions as an "independent transdiagnostic factor" for poor mental health outcomes, beyond the influence of sleep-related disturbances. Further research is needed to clarify the distinct contributions of sleep quality and chronotype to mental health. Identifying these independent effects will be crucial for developing early interventions aimed at improving mental health outcomes.

2.1 Chapter Aims and Overview

The previous chapter highlighted that chronotype is a multidimensional construct known to exist on a continuum between two extremes, MCs and ECs, with most individuals falling in the intermediate range, known as ICs. EC has been linked to poor quality of sleep and shares similar comorbidities with certain mental health issues and psychopathology-related personality traits. This chapter aims to briefly define sleep and review chronotype-mental health and sleep-mental health associations, and then consider the role of sleep quality in chronotype-mental health relationships.

2.2 Defining Sleep and Its Dimensions

Sleep is a complex phenomenon, more than an amalgamation of physiological mechanisms occurring at the intersection of circadian and homeostatic oscillators. It is a fundamental biological need, alongside other needs such as nutrition, hydration, and oxygen. However, sleep also requires an individual to engage in volitional behaviours, at least to some extent. Environmental and social factors often influence these volitional behaviours, causing considerable intra and inter-individual variability in sleeping patterns. Healthy sleep is vital for human survival, better lifestyle, well-being, and cognitive functioning (Medic et al., 2017) and typically requires appropriate sleep duration (≥6 hours), adequate sleep timings, regularity and consistency, all of which contribute towards good sleep quality (Ramar et al., 2021). Buysse (2014) established five global dimensions of sleep, namely, *sleep duration* (i.e., the number of hours an individual has slept over 24 hours), *sleep efficiency* (i.e., the ease of falling or returning to sleep), *sleep timings* (i.e., period of falling asleep over 24 hours), *alertness/sleepiness* (i.e., ability to be attentively awake), and *sleep quality* (i.e., effectiveness and restorative nature of an individual's sleep).

Sleep is regulated by two interconnected systems: *sleep homeostasis* and *circadian system* (Borbley & Achermann, 1999). Sleep homeostasis refers to a state of equilibrium between sleep and wakeful processes (Borbely, 1981, 1982), with sleep pressure building up as wakefulness increases. This increased pressure results in deeper and more restorative sleep. As previously described in Chapter 1 (Section 1.1), the circadian system regulates various endogenous biological rhythms, including sleep-wake cycles and can be influenced by exogenous factors, including natural/artificial light or lifestyle choices (Aschoff, 1967; Aschoff & Wever, 1976; Wever, 1986; Duffy & Czeisler, 2009). The interaction of the two mechanisms, *sleep*

homeostasis and *circadian system,* determine the sleep timings and structure as highlighted in the two-process model of sleep (Borbely, 1982; Borbley & Achermann, 1999). Individual differences in sleep homeostasis have also been found to influence chronotype variations. For example, research by Mongrain and colleagues (2004) showed that MCs exhibit higher slow-wave activity during non-rapid eye movement sleep and experience faster dissipation of homeostatic sleep pressure compared to ECs (Mongrain et al., 2005, 2006). These findings suggest MCs recover faster from sleep propensity, and may require less time to restore cognitive and psychological functioning upon waking up.

2.3 Sleep and Mental Health

Historically, altered sleep patterns were considered a secondary consequence of various mental health disorders (e.g., psychosis; Waite et al., 2020). However, over the past 20 years, many studies have documented a bidirectional relationship between sleep and adverse mental health outcomes, suggesting sleep disruption as a transdiagnostic factor responsible for the onset and persistence of mental health disorders (Baglioni et al., 2011; Harvey, 2001; Gregory et al., 2009; Waters et al., 2017) as well as it being a by-product of poor mental health. This shift acknowledges sleep as an essential treatment target in various disorders (e.g., depression and psychosis; Chauhan et al., 2023). Many studies have linked disrupted sleep patterns in both healthy and clinical populations with detrimental mental health outcomes, including depressive symptomatology and anxiety (Alvaro et al., 2013; Okun et al., 2018; Tsuno et al., 2005), post-traumatic stress disorder (Agoratos & Olff, 2021), psychosis (Cosgrave et al., 2018; Kumari & Ettinger, 2020; Yates, 2016), eating disorders (Allison et al., 2016; Lauer & Krieg, 2004), substance abuse (Hasler et al., 2011; Meneo et al., 2023), impulsive and aggressive behaviour (Kamphuis et al., 2012; Li et al., 2020), personality disorders (Selby, 2013; Winsper et al., 2017), childhood trauma and abuse (Shehann et al., 2020), as well as mood and emotion dysregulation (Tomaso et al., 2021). Recently, in a meta-analysis of 65 studies, Scott and colleagues (2021) reported that improved sleep quality had medium-size effects on mental health (g+=-0.53) regardless of any comorbid condition (physical or mental), suggesting that improving sleep quality may reduce levels of depression, anxiety and stress.

2.4 Chronotype and Mental Health

There is increasing recognition of chronotype as a transdiagnostic risk factor for poor mental health due to its potential association with a range of mental health outcomes including, mood

disorders (review, Au & Reece, 2017; Norbury, 2021), anxiety (Passos et al., 2017; Walsh et al., 2021), eating disorder (review, Kivela et al., 2018), psychosis-like symptoms (review, Kivela et al., 2018; Taylor & Hasler, 2018), substance use disorder (review, Adan et al., 2012; Zou et al., 2022), and attention deficit hyperactivity disorder (Coogan & McGowan, 2017). A number of comprehensive reviews (Zou et al., 2022) and meta-analyses (Au & Reece, 2017; Kivela et al., 2018; Norbury, 2021; Taylor & Hasler, 2018) have confirmed an association between EC and depressive symptoms (though with varying effect sizes) in healthy and clinical samples, with there being relatively less support for an association of chronotype with anxiety, stress-related disorders (including trauma), eating disorders, schizophrenia, and attention-deficit hyperactive disorder.

EC has also been associated, though not consistently, with certain personality traits; of note, extraversion, neuroticism, and impulsivity (review, Adan et al., 2012; Chauhan et al., 2023; Randler et al., 2017). Studies also show ECs to be more likely to consume substances (e.g., nicotine and drugs), engage in compulsive and addictive behaviours, be less conscientious, have more impulsive and risky behaviour, negative cognitive bias, poor emotion regulations, which may further contribute to their chances of developing and sustaining depression and other adverse mental health outcomes (review, Adan et al., 2012; Kivela et al., 2018; Zou et al., 2022). Chronotype continues to be a variable of interest in the context of psychiatric illnesses, although the underlining mechanisms are not yet fully elucidated.

2.5 The Role of Sleep in Chronotype-Mental Health Relationship

ECs have been found to report various sleep-related disturbances, including poor sleep quality, latency, duration, daytime dysfunction, sleep maintenance and restoration, irregular sleep-wake cycles, and accumulate higher sleep debt and build higher sleep pressures on weekends (Carciofo et al., 2014; Fernández-Mendoza et al., 2010; Muzni et al., 2021; Roenneberg et al., 2003; Sun et al., 2019; Taillard et al., 2003; Vadar et al., 2008). These findings are consistently reported for healthy adolescents and young adults (Glavin et al., 2021; Silva et al., 2020; Walsh et al., 2022), students (Jankowski, 2016; Mokros et al., 2017), athletes (Litwic-Kaminska & Kotysko, 2020), and shift workers (Khan et al., 2020; Lee et al., 2015; Yun et al., 2015). Given that ECs struggle to maintain and restore good sleep, they also develop higher SJL (i.e., misalignment between an individual's circadian and social clock; Roenneberg et al., 2003).

Some studies have also reported moderate yet significant associations between poor sleep quality and SJL (Juda et al., 2013; Harfmann et al., 2020).

A substantial body of evidence also suggests the potential role of sleep quality as a mediating factor influencing the EC and poor mental health relationship (of note, depression) in both healthy and clinical populations (Bradford et al., 2021; Lin et al., 2021; Muzni et al., 2021; van Den Berg et al., 2018). Chan and colleagues (2020) reported improved depressive symptoms after curing insomnia and improving sleep in EC adolescents. However, some studies also dismiss the role of sleep quality in mediating the chronotype-mental health relationship (Antypa et al., 2016), or emphasise hopelessness (Uzer & Yucens, 2020), sleep-related dysfunctional beliefs (Roeser et al., 2012), and resilience (Zhou et al., 2021) as relevant mediating influences.

2.6 Conclusions

The general view in the chronobiology research has been that chronotype is an 'independent transdiagnostic factor' for poor mental health outcomes (Taylor & Hasler, 2018; Norbury, 2021) beyond the apparent effect of sleep disruption. More recent literature, however, suggests an overlap between the effects of sleep quality and chronotype on mental health outcomes which needs to be clarified. Specifically, since sleep and chronotype share some physiological processes (see Chapter 1), and are also associated with some common mental health outcomes, it is essential to delineate their independent roles in mental health outcomes.

Chapter 3: Chronotype Influences in Neurocognitive Functions: A Systematic Review

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Chauhan, S., Vanova, M., Tailor, U., Asad, M., Faßbender, K., Norbury, R., Ettinger, U., & Kumari, V. (under-review). Chronotype and synchrony effects in neurocognitive functions: A systematic review.

Abstract

Chronotype is a proxy for various intra-individual rhythms (e.g., sleep-wake cycles) which fluctuate throughout the day. The extent to which chronotype modulates cognitive performance remains unclear. Here, existing evidence was systematically reviewed studies to determine the influence of chronotype on its own, and/or interactions with ToD (optimal/non-optimal), in cognitive function in healthy adults. Following PRISMA guidelines, data searches were conducted in PubMed and Web of Science databases (11 March 2024), yielding 65 studies (53 in adults aged 18-45 years; 11 comparing adults aged 18-32 and 50-95 years; one involving only MC adults aged 60-76 years). Most of the reviewed studies (>80%) indicated no main effect of chronotype on cognitive function. There was evidence from 29 (45.31%) of 64 studies involving adults aged 18-45 years of a synchrony effect (i.e., superior performance at optimal ToD) in MCs and/or ECs, mostly in attention, inhibition, and memory. In older adults, there was evidence of a synchrony effect from 10 (83.33%) of 12 studies, especially on tasks involving fluid abilities. Limited evidence suggested higher activation of inhibition-related brain regions at optimal ToD in both chronotypes, and synchrony effects being impacted by certain exogenous factors known to affect arousal and performance (e.g., task characteristics and complexity, lighting conditions). These findings highlight the need to carefully consider age along with endogenous and exogenous sources of intra-individual variations in arousal while determining synchrony effect in cognitive functions. Not acknowledging these synchrony effects may also result in exaggerated cognitive deficits especially in the elderly.

3.1 Chapter Aims and Overview

This chapter reports a systematic review conducted to synthesise and critically appraise the existing evidence for chronotype and synchrony effects in performance across and within general and specific cognitive domains.

3.2 Introduction

In humans, CRs oscillate with periodicity in length, causing considerable intra-individual variations (Czeisler & Gooley, 2007) in various neurophysiological, behavioural, and cognitive domains (Xu et al., 2021). These intra-individual variations are commonly referred to as '*chronotype*'(Adan et al., 2012). The multidimensional construct of chronotype (Chauhan et al., 2023) exists on a continuum between two extremes, MCs and ECs, with most individuals falling in the intermediate range, known as ICs. There is growing interest in how chronotype impacts human cognitive function but, despite a broadening corpus of literature, there is no consensus on the nature of this relationship. There are reports of MCs performing better academically (Cohen-Zion & Shiloh, 2018) and having better fine motor skills and short-term memory relative to ECs (Atkinson & Speirs, 1998; Drust et al., 2005; Facer-Childs et al., 2018), but there are also reports of no association between chronotype and cognitive function (Adan, 1991; Cox et al., 2019), or of better performance in ECs compared to MCs (review, Preckel et al., 2011).

Over the years, it has been assumed that *'early to bed and early to rise, makes a man healthy, wealthy, and wise'* (Franklin, 1855) but without clear empirical support for this assumption (Gale & Martyn, 1998). On the contrary, a substantial body of evidence pointing towards optimal cognitive performance when tested in synchrony with an individual's biological rhythm (Barner et al., 2019; May & Hasher, 1998; Taillard et al., 2021; Wyatt et al., 1999). This concept is known as the *'synchrony effect'* (May & Hasher, 1998). Some studies report synchrony effects in attention (Martínez-Pérez et al., 2020), vigilance (Mongrain et al., 2008), inhibition (Lara et al., 2014; May & Hasher, 1998), and memory (Schmidt et al., 2015) but its impact may not be the same across different cognitive tasks and domains (Barner et al., 2019; Bennett et al., 2008; Fabbri et al., 2013; Natale et al., 2003; Wieth & Zacks, 2011), especially in tasks demanding well-practised responses (May et al., 2023). Furthermore, synchrony effect might be age-dependent and not similarly present in different age groups (review, Adan et al.,

2012; Schmidt et al., 2007). The aim of this review, therefore, is to systematically review, synthesise and critically appraise the existing evidence for chronotype and synchrony effects in performance across and within general and specific cognitive domains.

3.3 Methodology

The protocol for this systematic review was registered with PROSPERO (CRD42024498808). The review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) structure and guidelines (Page et al., 2021).

3.3.1 Information Source and Research

A literature search in PubMed, and Web of Science databases was conducted on 11th March 2024 using the following search terms: (chronot* OR "diurnal preference" OR "circadian preference" OR "morning type" OR "evening type") AND (cognit* OR memory OR attent* OR "verbal recall" OR "problem solving" OR "executive func*" OR "verbal fluency"). Search results were restricted to English, with no specific time window for publication. Cited references in the selected studies were also examined to identify further eligible literature.

3.3.2 Eligibility Criteria

Searched studies were assessed against the following inclusion criteria and deemed eligible for inclusion if they:

- Included adult (≥ 18 years) participants with no history or current diagnosis of mental illness, neurological impairment, and major physical illnesses.
- Determined chronotype via a standardised self-report assessment, actigraphy, and/or physiological data.
- Included at least one measure (experimental or standardised assessment) of cognitive function/s (attention, executive functions, working memory, reasoning, problem solving, and/or verbal learning).
- Were peer-reviewed primary research articles.

Studies without full text and methodology, meta-analyses, dissertation/PhD theses, unpublished papers, pre-prints, books, scoping and systematic reviews, animal studies, genetic

and metabolic studies, were excluded. Studies examining only ToD effect without consideration of chronotype were also excluded.

3.3.3 Study Selection

All studies meeting our eligibility criteria were exported to Zotero (Zotero, 2016). Titles and abstracts were screened for relevance by two independent reviewers (SC, UT). If the abstract did not contain sufficient information, the full text was retrieved before deciding regarding its eligibility. The two reviewers (SC, UT) independently read the study title, abstracts, and full texts (where needed) and assigned each study a score of 0 (not suitable), 1 (probably suitable), or 2 (suitable). Subsequently, all the full-text articles rated as suitable for inclusion (i.e., received a score of 2) by both researchers were reviewed by a third reviewer (MV). The selection ratings of the two reviewers (SC, UT) were compared, and the degree of agreement was assessed. Any discrepancies, as well as any studies with at least one score of 1, were discussed with a fourth reviewer (VK) to reach a consensus. The reasons for excluding studies at all stages were documented (Figure 3.1).

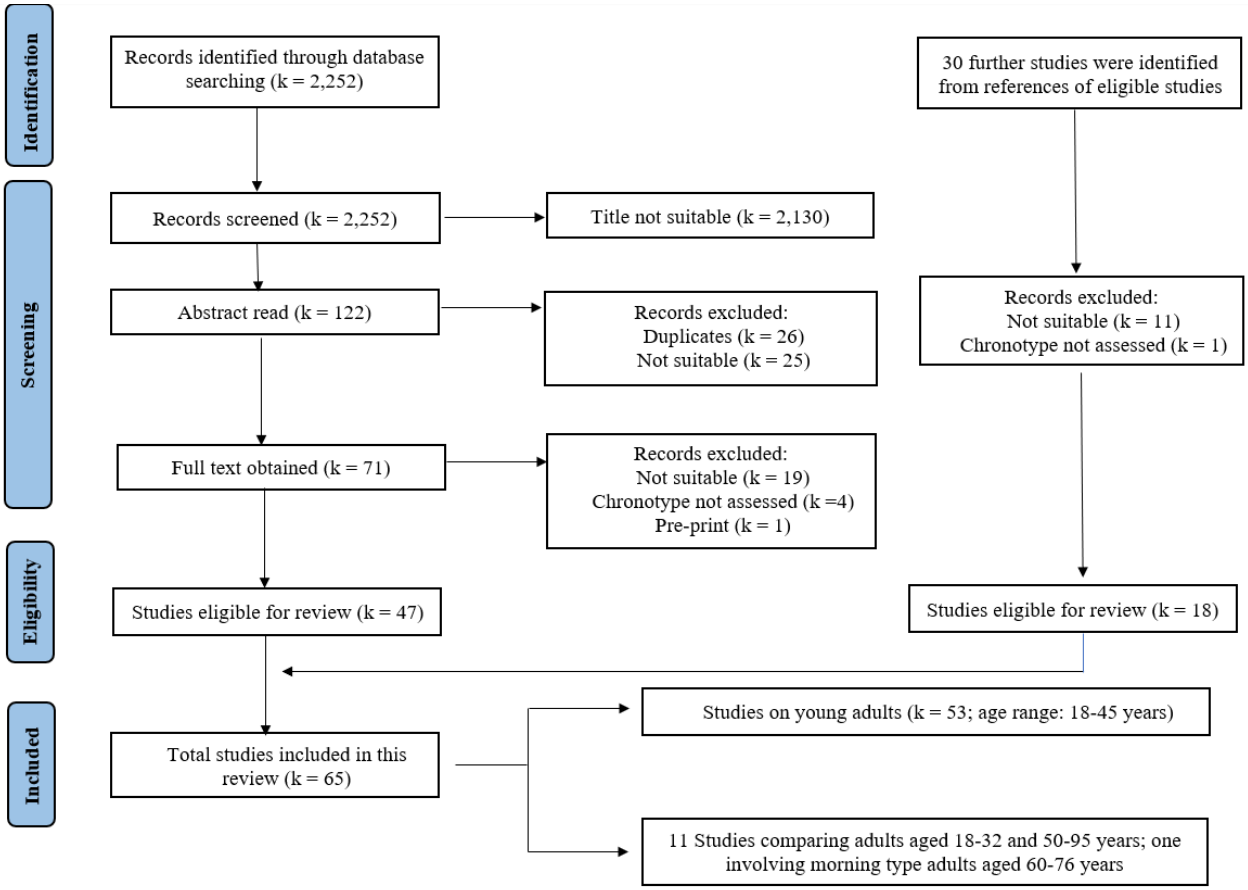
3.3.4 Data Collection, Items, and Statistical Analysis

For each of the selected studies, the following data were extracted independently by SC and MA: authors, study year, month and time of testing, sample characteristics (sample size, mean age, and sex and chronotype distribution), study population, methods for assessing chronotype, measures/tasks used to assess the cognitive functions, and key study outcomes (Tables 3.1 and 3.2). If any of these factors were not reported, we made no specific assumptions regarding whether or not they had been assessed in the study, and noted them as ‘not reported’ in our dataset. Extracted data were compiled into a Microsoft Excel spreadsheet and analysed descriptively, with regards to the significance of the findings as reported by the study authors.

3.3.5 Quality Appraisal

The quality of selected studies was assessed (SC, MA) using the Joanna Briggs Institute Quality Appraisal Rating for cross-sectional studies (Zeng et al., 2015). All eight criteria were graded as ‘yes’, ‘no’, ‘unclear’ or ‘not applicable’. One point was given for scoring ‘yes’ on each criterion and then a total sum of all points was derived (Table 3.3).

Figure 3.1 *PRISMA flowchart.*



3.4. Result

Overall, we analysed 65 studies conducted in 18 countries (Australia, Belgium, Brazil, Canada, China, Czech Republic, France, Germany, Hungary, Ireland, Israel, Italy, Netherlands, Poland, Spain, Switzerland, United Kingdom, and USA) examining one or more cognitive functions (Tables 3.1-3.2). There was considerable variability in the sample size, ranging between 15 and 1131. Most studies (57 of 65) employed a mixed factorial design with ToD as a within-subject and chronotype as a between-subject factor and received acceptable quality ratings (Table 3.3). Of 65 in total, 53 studies investigated the effect of chronotype and/or ToD as well as their interaction in various cognitive functions in young adults (age range: 18-45; Table 3.1). The remaining 12 investigated the influence of age in the chronotype and/or synchrony effects in cognitive performance or simply investigated chronotype or synchrony effects in older adults (Table 3.2).

We grouped the findings of eligible studies, based on the cognitive parameters used and functions examined, as pertaining to intelligence, sensory processing, perception, attention,

inhibition, working memory, decision-making, problem-solving, thinking, reasoning, verbal fluency, learning and memory (Table 3.4). We now report the findings for chronotype, also for ToD and synchrony effect in young (k=53) and older adults (k=12), respectively.

Table 3.1 *Summary of key data extracted from selected studies in young adults.*

Author & Year (In chronological order)	**Month and Time of Testing**	**Sample Characteristics** (n, sex, age, chronotype)	**Chronotype Method** (Questionnaire/ actigraphy, and/or physiological data)	**Other Measures Used**	**Cognitive Tasks/ Measures Used**	**Key Outcomes**		**Other Findings**
						Main Effect of CT and ToD	**Synchrony Effect**	
Petros et al. (1990)	Season of testing not reported. Participants were tested in groups of 1-4 either at 9:00, 14:00, or 20:00 h	79 university students (all F; age range not reported; 40 MCs/39 ECs)	Morningness-Eveningness Questionnaire; Body Temperature	Eysenck Personality Questionnaire	Passage Difficulty Task	ECs recalled more idea units than MCs. A significant ToD effects was observed only for difficult passages.	A significant synchrony effect in both chronotypes with a linear increase in recall throughout the day for MCs and vice-versa for ECs.	
Anderson et al. (1991)	Season of testing not reported Participants were tested randomly either at 9:00, 14:00, or 20:00 h.	99 university students (all F; mean age not reported; 45MCs/54ECs)	Morningness-Eveningness Questionnaire; Body Temperature		Word-Pair Recognition	No significant CT effect. A significant ToD on speed of word encoding, lexical access, and semantic memory.	A significant synchrony effect in both chronotypes with a linear increase in semantic memory throughout the day for MCs and vice-versa for ECs.	
Song & Stough (2000)	Season of testing not reported. Participants were tested at 9:00 and 15:00 h.	70 university students (50 F, 20 M; mean age: 24.9±8.3) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire Body Temperature MCs (9:00 h): 36.1±.9; (15:00 h): 36.2±.8 ECs (9:00 h): 35.9±.50; (15:00 h): 36.2±.5		Inspection Time; Digit Span; Picture Completion; Spatial subtest of MAB; Picture Arrangement; Object Assembly	No significant CT effect. No significant ToD effect.	A synchrony effect was observed with MCs performing better in the morning only on spatial subtest of MAB and vice-versa for ECs.	
Natale et al. (2003)	Season of testing not reported Participants were familiarised with	48 university students (24F/24M; mean age: 25.04±2.92;	Morningness-Eveningness Questionnaire; Body Temperature	Global Vigour Scale; Wechsler Adult Intelligence Scale	Two-Letter Search; Syllogistic Reasoning; Overlapping;	No significant CT effect. No significant ToD effect.	A significant synchrony effect was observed on Two-Letter Task with MCs and ECs	MCs reported higher subjective alertness at 8:00 h than 23:00 h, vice-versa for ECs.

	the tasks a week before testing and were tested repeatedly over a period of 15 hours at 8:00 h, 11:00 h, 14:00 h, 17:00 h, 20:00 h, and 23:00 h.	12MCs/24ICs/12ECs)			Crypto-Arithmetic		performing faster at their optimal ToD. A synchrony effect was found with highest speed of execution at optimal ToD for MCs and ECs on Syllogistic Reasoning, Overlapping and Crypto-Arithmetic Tasks.	
Hidalgo et al. (2004)	Data were collected between October-November (year not reported) Participants were tested at 7:30 h and 18:00 h.	47 adults (26F/21M; age range: 20-35 years; 14MCs/16ICs/17ECs)	Morningness-Eveningness Questionnaire	Self-Report Questionnaire-20	Metamemory Questionnaire; Scale-Semantic Memory; Digit Span; Word List with Emotional Content Test; Word-pair Associated; Visual Memory Scale; Verbal Fluency Test	No significant CT effect. A significant ToD was found during second recall on *'word list with positive emotional content test'*, with all participants showing better performance in the evening.	A synchrony effect was found with both chronotypes showing better performance on metamemory test at their optimal ToD.	ICs showed better performance on Word List with Positive Content and Scale-Semantic Memory Tests in the evening.
Killgore & Killgore (2007)	Season and time of testing not reported.	54 young adults (25F/29M; age range: 23.5±4) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire		Wechsler Abbreviated Intelligence Scale	No relationship between MEQ scores and full-scale IQ and performance IQ. Although, MEQ was negatively correlated with verbal IQ. ToD effect not examined.	Not examined	Higher evening- ness was associated with higher verbal cognitive ability as measured only in females.

Barbosa & Albuquerque (2008)	Season of testing not reported 32 participants were tested between 7:30-9:30 h and 36 between 16:30-18:30 h. A week later 35 participants took part in long-term memory test in morning and 33 in the evening.	68 undergraduate students (40F/28M; mean age: 21.0±2.0; 23MCs/23 ICs/25 ECs)	Morningness-Eveningness Questionnaire MCs: 66±6 ICs: 51±4 ECs: 37±4		Word-List Recognition Morning testing time: 4.25±.46 Evening testing time: 4.00±.48	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	Training*ToD effect was found with better performance on long term explicit memory in the afternoon training group.
Bennett et al. (2008)	Season of testing not reported Participants were randomly tested either between 8:00 h-10:00 h or 15:00 h-17:00 h.	77 University students (54F/23M; range: 18-29; 37MCs/40ECs)	Morningness-Eveningness Questionnaire MCs (8:00 h): 63.3±3.1; (15:00 h): 63.7±4 ECs (8:00 h): 34.3±4.6; (15:00 h): 33.5±6 Tympanic Temperature	Verbal Ability MCs (8:00 h):32.9±9.8; (15:00 h): 32.6±6.9 ECs (8:00 h):32.8±7.4; (15:00 h): 36±6.5	Continuous Performance Task; Controlled Oral Word Association Test; Digit Span Test; Wisconsin Card Sorting Task	No significant CT effect. A significant ToD only on Controlled Oral Word Association Test with more words being generated in the evening.	A significant synchrony effect was found only on Wisconsin Card Sorting Task with MCs performing better at their optimal ToD.	Overall, tympanic temperature was higher in MCs than ECs with even higher at 15:00 h.
Mongrain et al. (2008)	Season of testing not reported Participants were awakened 15 times per night and were tested every 4 h: 1.5, 5.5, 9.5 and 13.5 h after wake time, repeatedly over five days.	24 adults (12 F, 12M; age range: 19-34 years; 12MCs/12ECs)	Morningness-Eveningness Questionnaire; Actigraphy; DLMO (using saliva samples); Body Temperature	Multiple Sleep Latency test; Visual Analogue Scale	Psychomotor Vigilance Task	No significant CT effect. No significant ToD effect.	A significant synchrony effect was observed with MCs having higher subjective alertness in the morning and vice-versa for ECs.	

Matchock & Mordkoff (2009)	Season of testing not reported. Participants were tested at 8:00 h, 12 noon, 16:00 h, and 20:00 h.	80 university students (57F/23M; mean age: 21.6 ±SD not reported; 36MCs/36ICs/44ECs)	Morningness-Eveningness Questionnaire		Attention Network Task; Thayer Activation-Deactivation Check List	No significant CT effect. A ToD effect was found only on conflict scores at 12:00 noon and 4:00 pm for MCs and ECs.	A found synchrony effect was found only on alerting scores, with MCs/ICs being more alert in the morning and noon than ECs.	
Taillard et al. (2011)	Season of testing not reported. Participants were tested over 84-hour period with 48 hours observation in lab and 36 hours of wakeful period. On day 1 between 7:30-23:30 h and 00:30-6:30 h. On day 2 between 7:30-18:30 h.	18 adults (all males; mean age: 21.4±1.9; 9MCs/9 ECs)	Morningness-Eveningness Questionnaire MCs:63±3.6 ECs:32.6±6.2 Basic Nordic Sleep Questionnaire; Melatonin; Body Temperature	Maintenance Wakefulness Test; Visual Analogue Scale	Reaction Time Task	No significant CT effect. ToD effect not examined.	Not examined	During 36 hours of wakefulness, ECs maintained optimal alertness. In MCs it significantly decreased after 17 hours of wakefulness due to increased sleep pressure.
Wieth & Zacks (2011)	Season of testing not reported. Participants were either tested between 8:30-9:30 h or 16:00 h-17:30 h.	428 university students (sex not reported; mean age: 20.41±1.91; 28 MCs/205 ICs/195ECs)	Morningness-Eveningness Questionnaire		Analytic Problems; Insight Problems	No significant CT effect. No significant ToD effect.	Participants had higher significant insight problem solving rate (but not for analytic problem) at the non-optimal than optimal ToD.	
Schmidt et al. (2012a)	Participants were tested over 2 nights, 1.5 h (morning session) and 10.5 h (evening session) after waking up	31 young adults (17F/14M; age range: 22-32 years; 16MCs/ 15 ECs)	Morningness-Eveningness Questionnaire; Munich Chronotype Questionnaire; Actigraphy; Saliva	Epworth Sleepiness Scale MCs: 4.56±1.8 ECs: 5.29±3.12 Pittsburgh Sleep Quality Index MCs: 3.75±1.0 ECs: 4.05±1.03	Stroop Task	No CT effect for accuracy on Stroop task, but MCs were slower than ECs on RTs and overall Stroop task. No significant ToD effect.	No significant synchrony effect.	

Fabbri et al. (2013) (Experiment 1)	Season of testing not reported Participants were tested between 9:00-10:00 h, 13:00-14:00 h, and 17:00-18:00 h.	60 university students (39F/21M; mean age not reported; 30MCs/30 ECs)	Morningness-Eveningness Questionnaire MCs:58.4±4.35 ECs:35.95±5.12 Reduced Morningness-Eveningness Questionnaire MCs:19.9±1.37 ECs:8±2.26		Semantic Classification Task	No significant CT effect. A significant ToD effect was found with lower percentage of retrieval efficiency in the evening than in afternoon and/or morning session.	No significant synchrony effect.	Both, MCs and ECs had higher percentage of retrieval efficiency for positive than negative words.
(Experiment 2)	Season of testing not reported Participants were tested between 9:00-10:00 h, 15:00-16:00 h, and 18:00-17:00 h.	60 university students (43F/17M; Overall mean age not reported; 30MCs/30 ECs)	Morningness-Eveningness Questionnaire MCs:62.4±2.37 ECs:37.5±3.03 Reduced Morningness-Eveningness Questionnaire MCs:19.8±1.47 ECs:8.55±2.14		Number-Matching	No CT effect was found on RT and accuracy. But ECs showed a higher increase of sum interference effect than MCs. No significant ToD effect.	No significant synchrony effect.	
Baeck et al. (2014)	Season of testing not reported Participants were tested in two groups with group 1 (evening-morning-evening-morning) starting at 20:00, 21:00, or 22:00 h and group 2 (morning-evening-morning-evening) starting	32 university students (19F/13M; mean age: 21.94±1.24; 9MCs/13 ICs/10ECs)	Morningness-Eveningness Questionnaire	Raven Advanced Progressive Matrices	Visual Learning	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	Independent of CT and ToD, perceptual learning improved as a result of sleeping in-between training sessions.

	at 8:00, 9:00, or 10:00 h, followed by 3 sessions with 12 h interval.							
Correa et al. (2014)	Season of testing not reported Participants were tested on 2 consecutive days one at 8:00 and another at 20:00 h.	25 university students (all F; mean age: 21.09±2.46; 13MCs/12ECs)	Reduced Morningness-Eveningness Questionnaire MCs:18.15±1.34 ECs:9.17±.83 Body Temperature	Visual Analogue Scale; Monk's Activation Affect Scale	Psychomotor Vigilance Tast; Stimulated Driving Task	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	MCs reported higher levels of alertness at their optimal ToD.
Delpouve et al. (2014)	Season of testing not reported Participants were randomly tested at self-defined optimal (12.8±2.9 h) and non-optimal time of day (15.7±3.6 h)	36 university students (26F/10M; mean age: 25.08 (SD not reported) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire Optimal group: 49.1±6.1 Non-optimal group: 50.4±6.3	Pittsburgh Sleep Quality Index Optimal group: 4.8±1.4 Non-optimal group: 3.6±1.5 St Marry Hospital Questionnaire Optimal group: 497.9±97 Non-optimal group: 516.4±50.6 Karolinska sleepiness scale Optimal group: 2.9±1.1 Non-optimal group: 5.5±1.3	Psychomotor Vigilance Task Optimal group: 315.6±22.9 Non-optimal group: 349.6±38.5 Artificial Grammar Learning; Digit Span	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	Overall, non-optimal group reported poor sleep quality, higher subjective sleepiness, and longer RT during Psychomotor Vigilance Task than optimal group.
Lara et al. (2014)	Season of testing not reported	27 university students (25F/2M; age	Reduced Morningness-	Visual Analogue Scale; Barrett	Psychomotor Vigilance Task;	No significant CT effect.	A significant synchrony effect with MCs and ECs	

	Participants were tested at 8:00 h and 20:30 h, one week apart	range: 18-27; 13MCs/14ECs)	Eveningness Questionnaire MCs:17.85±1.14 ECs:9.64±.84 Skin Temperature	Impulsivity Scale-11 Attentional related Cognitive Error Scale: MCs: 29.18±2.13 ECs: 34.14±1.89	Sustained Attention Response Task	No significant ToD effect.	performing better at their optimal ToD in no-go accuracy and precision strategy.	
Gobin et al. (2015)	Season of testing not reported Participants were randomly assigned to either morning session at 09:00 h or an evening session at 21:00 h.	154 undergraduate students (104F/50M; mean age: 21.27±4.03) Chronotype groups (N) not reported)	Morningness-Eveningness Questionnaire	Pittsburgh Sleep Quality Index; Centre for Epidemiologic Studies Depression Scale; State–Trait Anxiety Inventory; Profile of Mood States	Negative and Neutral Image Recognition Task; Sustained Attention Response Task; Continuous Performance Task	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	ECs reported poor sleep quality, higher confusion, tension, mood disturbance, depressive symptoms and anxiety than MCs and ICs.
Reinke et al. (2015)	Data collected between April-May 2013. Participants were tested between 14:00 h-16:00 h during day-shift and 4:00h - 6:00 h at night shift.	96 Nurse (71F/25M; F/M; overall mean age not reported; 61MCs/35 ECs)	Munich Chronotype Questionnaire	Samn Perelli 7 Level Fatigue scale; Karolinska sleepiness scale	Psychomotor Vigilance Task; Two-Digit Addition Test	No significant CT effect. A significant ToD was observed with participants having higher response times, increasing RTs, and lowered numbers of correct responses during night than day shift.	No significant synchrony effect.	No significant differences in sleep quality, sleepiness, and fatigue scores of MCs and ECs. MCs were reported to take naps prior to their shiftwork.
Schmidt et al. (2015)	Season of testing not reported Participants were tested 1.5 hour and 10.5 hour of wakefulness. Testing time	32 young adults (sex not reported; mean age: MCs: 4±2.3, ECs: 24.8±4.9; 16MCs/16ECs)	Morningness-Eveningness Questionnaire; Actigraphy	Pittsburgh Sleep Quality Index; Beck Anxiety Inventory; Beck Depression Scale; Epworth Sleepiness Scale; Visual Analogue Scale	N-back	A significant CT effect with ECs having higher accuracy but longer RTs than MCs. No significant ToD effect.	No overall synchrony effect was observed. But for 3-back condition ECs performed better than MCs in the evening.	fMRI results showed the modulation of cerebral activity by working memory load in the thalamus and in the middle frontal cortex.

	for each session was adapted to participants' bedtime.							
Fimm et al. (2016)	Season of testing not reported. Participants were tested at 8:00, 11:00, 14:00, 17:00, and 20:00 h within 24 h interval.	15 university students (7F/8M; age range: 20-39 years; 1MC/9 ICs/5 ECs)	Morningness-Eveningness Questionnaire – German Version; Body Temperature	Sleepiness Rating Scale; Alertness subtest of Test of Attentional Performance	Covert and Overt Orienting of Attention Task; Neglect Task	No significant CT effect. A significant ToD effect on all cognitive tasks (bar attentional asymmetry) especially at 8:00 h than later test sessions.	No significant synchrony effect.	No significant variation in negative or positive affect during the day.
Gijselaers et al. (2016)	Data were collected between September 2012-August 2013. Secondary data (time of testing not reported).	1131 university students (697F/434M; mean age: 37.26±10.65) Chronotype groups (N) not reported	Munich Chronotype Questionnaire	Pittsburgh Sleep Quality Index; Short Questionnaire to assess Health-Enhancing Physical Activity	Trial Making Task; N-Back Substitution Test	No significant CT effect. ToD effect not examined.	Not examined	Sedimentary behaviour significantly predicted processing speed.
Maierova et al. (2016)	Season of testing not reported. Participants were tested for 3-6 days over 3 sessions (in dim light, bright light, and self-selected light) in Morning (average time: 7:16±0:34 h) and evening (average time: 11:14±1:01 h)	32 adults (18F/14M; mean age: 22.7±3.5;16MCs /16ECs)	Morningness-Eveningness Questionnaire MCs: 70.5±3.1 ECs: 30.2±5 Munich Chronotype Questionnaire MCs: 2.88±0.81 ECs: 6.53±0.82 Melatonin onset MCs: 19:33±0:56 ECs: 23:26±1:48	Pittsburgh Sleep Quality Index MCs: 2.94±1.1 ECs: 3.50±1.9 Epworth Sleepiness Scale MCs: 5.38±2.9 ECs: 5.56±2.1 Mental Effort Rating Scale	Auditory and Visual N-Back Task; Go-no-go Test; Psychomotor Vigilance Task;	Significant differences were observed in all cognitive tasks due to lighting conditions with little dependency upon chronotype. ToD effect not examined.	Not examined	Overall, ECs were significantly sleepier than MCs. Both groups were more alert in bright light condition than in dim light, with ECs showed higher alertness in self-selected light than dim light condition.
Rothen & Meier (2016)	Season of testing not reported.	160 university students	Morningness-Eveningness		184 Standardised	No significant CT effect.	A significant synchrony effect	

	31 MCs were tested at 6:00 h and 30 at 10:00 h, 49 ECs at 17:00 h and 50 at 21:00 h.	(93F/67M; mean age: 22.52±2.30; 61MCs/ 99ECs)	Questionnaire - German Version		Line Drawing (Snodgrass & Vanderwart, 1980)	No significant ToD effect.	on priming in both groups with better performance at the non-optimal than optimal ToD.
Barclay & Myachykov (2017)	Season of testing not reported Participants were tested over a period of 18 hours. Starting at 7:45 h and were required to be awake until the next session at 2:00 h.	26 young healthy adults (12F/14M; mean age: 25.58±4.26) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire	Epworth Sleepiness Scale; Pittsburgh Sleep Quality Index	Attention Network Test	No significant CT effect. A significant main effect of ToD, with longer RTs at 2:00 h than 8:00 h. But not on error rates and attentional network scores.	No significant synchrony effect.
Correa et al. (2017)	Season of testing not reported. Participants were tested within 24-h, at 9:00 h and 17:00 h.	64 university students (32F/32M; mean age: 21.6±2.3; 32 MCs/32 ECs)	Reduced Morningness-Eveningness Questionnaire; Body Temperature	Global Vigour-Affect Scale	Ultimatum game; Continuous Performance Test	No significant effects of CT on decision making pattens. Although, MCs were slower than ECs while responding to high-uncertainty offers in decision making game. No significant ToD effect.	No significant synchrony effect.
Fabbri et al. (2017)	Season of testing not reported. Participants were paired (81 pairs) and were assigned to one of three testing times: 9:00-10:00 h, 13:00-14:00 h or 17:00-18:00 h,	162 university students (81F/81M; mean age: 23.84±3.59; 30MCs/89 ICs/43Cs)	Reduced Morningness-Eveningness Questionnaire		Navon Task	No significant CT effect. A significant ToD effect with faster global and local foci of attention in the evening than morning or afternoon session.	A significant synchrony effect on joint Navon task with increased performance at optimal ToD for both MCs and ECs.

	with 27 pairs per session.					Faster RTs for global focus in the early afternoon and vice-versa for local focus.		
Ritchie et al. (2017)	Season of testing not reported Participants were tested after 8 h of sleeping at 1, 10, 20, 30, 40, 60 mins with EEG verified awakening.	18 healthy adults (5F/13M; mean age: 22.1±3.7; 7MCs/7 ECs)	Munich Chronotype Questionnaire MCs: 4.2±.1 ECs: 5.8±0.2 Melatonin onset (using saliva) MCs: 21.2±0.2 ECs: 23.2±.2		Spatial Configuration Visual Search Task	Duration of Sleep inertia for cognitive throughput and RTs was significantly longer in ECs than MCs. ToD effect not examined.	Not examined	
Simor & Polner (2017)	Season of testing not reported. 40 participants (21 ECs, 19 MCs) were tested during their off-peak times and 32 (15 ECs, 17 MCs) at their peak times between 8:00 h-18:15 h.	72 university students (27M/45F; mean range:18-30; 36MCs/36ECs)	Morningness Eveningness Scale – Hungarian version	Athens Insomnia Scale MCs: 5.47±3.71 ECs: 5.80±3.63	Compound Remote Associate Problems Tasks; Just suppose subtest of the Torrance Tests of Creative Thinking	No significant CT effect. No significant ToD effect.	Reversed synchrony was only found in convergent task scores in ECs.	Insomniac symptoms predicted lower scores in the convergent thinking task.
Facer-Childs et al. (2018)	Season of testing not reported. Participants were tested at 14:00, 20:00 and 8:00 h.	56 healthy participants (23/33F; mean age: 21.8±3.8; 25ECs/31 ECs)	Munich Chronotype Questionnaire	Karolinska Sleepiness Scale Dim light melatonin onset MCs: 20:27±00:16 ECs: 23:55±00:26 Cortisol peak time	Psychomotor vigilance task; Memory and Attention Test	No significant CT effect. No significant ToD effect.	A significant synchrony effect on PVT performance only in ECs. Also, on executive function task in MCs.	

				MCs: 7:04±00:16 ECs: 11:13±00:23				
Lewandowska et al. (2018)	Season of testing not reported. MCs were tested at 8:00 and 17:00 h and ECs at 9:00 and 18:00 h.	52 young adults (38F/14M; mean age: 23.96±3.14; 18MCs/34ECs)	Morningness Eveningness Scale	Epworth Sleepiness Scale; Sleep Quality Index	Semantic memory Task; Phonological Task; Global Processing Task; Local Processing Task	No significant CT effect. A significant ToD effect on response bias for semantic, phonological, global, and local processing tasks in evening than morning session.	No significant synchrony effect.	
Rodríguez-Morilla et al. (2018)	Study conducted between 4 April-21 June 2016 Participants were tested at 8:00 h in blue-enriched white light and dim light and before and after driving task.	17 university students (11F/6M; mean age: 20.25±1.48; 17ECs)	Reduced Morningness-Eveningness Questionnaire; Wrist Temperature	Mood State Scale; Karolinska Sleepiness Scale	Psychomotor Vigilance Task; Simulated Driving Task	No significant CT effect. ToD effect not examined.	Not examined	Faster RTs in Psychomotor Vigilance Task and driving task were attenuated under blue-enriched white light than dim light.
Song et al. (2018)	Season of testing not reported. Participants were tested between 8:00-12:00 h (morning session) and 19:00-23:00 h (evening session). The sessions were counterbalanced.	32 young adults (15F/17M; mean age: 21.7±2.1; 16MCs/16ECs)	Morningness-Eveningness Questionnaire:		Stop Signal Paradigm	No significant CT effect. A significant ToD on accuracy i.e., higher accuracy in evening than in the morning. No effect of ToD on RTs.	No significant synchrony effect.	MCs had higher brain activity than ECs in right lateral IFG, MTG, and left-lateral MCC with the BOLD responses in MFG and MCC, thalamus decreased in the evening in the MCs, while the BOLD responses remained stable in ECs.
Nowack & Van Der Meer (2018)	Season of testing not reported. 50% of both MCs and ECs were	36 university students (24F/12M; mean age: 26.4±6.4; 18MCs/18ECs)	Munich Chronotype Questionnaire MCs: 4:10±00:55 h		Semantic Analogy Task; Raven Advanced Progressive	A significant CT effect was observed only on analogical reasoning task,	MCs significantly solved the analogy detection task at their non-optimal ToD than ECs.	

	testing between 8:00-11:00 am and 50% between 2:00-4:00 pm.		ECs: 5:30±00:59h Morningness-Eveningness Questionnaire		Matrices; Mehrfachwahl Wortschatztest	with MCs showing faster processing speed and lower error rates than ECs. A significant ToD effect was observed RTs but not on error rates on analogy conditions.	
Zion & Shochat (2018)	Data were collected between August 2011 and April 2014. Participants were tested twice per night at 3:00 h and 7:00 h.	109 nurses (all F; mean age: 39.29±9.06; 73.5% participants were MCs)	Munich Chronotype Questionnaire	Pittsburgh Sleep Quality Index; Karolinska Sleepiness Scale	Digit Symbol Substitution Test; Letter Cancellation Task	No significant CT effect. Overall, performance on both tasks improved at 7:00 h, in younger nurses.	No significant synchrony effect.
Barner et al. (2019)	Season of testing not reported. Participants were either tested between 8:30 h - 11:00 h or between 19:00 h-21:30 h.	39 young healthy adults (28F/11M; overall mean age not reported; 20MCs/19ECs)	Morningness-Eveningness Questionnaire MCs tested in morning: 59.83±1.99 MCs tested in evening: 58.75±1.44 ECs tested in morning: 45.20±1.94 ECs tested in evening: 45.83±3.11	Pittsburgh Sleep Quality Index; Stanford Sleepiness Scale;	Syllable Detection Test (RT) Morning group:1042.5± 54.94ms Evening group: 971.74±60.91 ms Dresden Breakfast Task (task completion) Morning group: 70.83±3.17%	No significant CT effect. A significant ToD effect was observed with better performance in the evening than in the morning on both cognitive tasks.	No significant synchrony effect.

			Munich Chronotype Questionnaire MCs tested in morning: 3.82±.19 MCs tested in evening: 3.92±.13 ECs tested in morning: 5.44±.18 ECs tested in evening: 5.36±.24		Evening group: 971.74±60.91 ms Red Pencil Task; Colour Task (mean ± SD not reported)			
Facer-Childs et al. (2019)	Season of testing not reported. Participants were tested over 20 h at 14:00 h, 20:00 h, and 8:00 h.	38 healthy adults (24F/14M; mean age: 22.7±4.2; 16MCs/22ECs)	Munich Chronotype Questionnaire MCs: 2:24±00:10 ECs: 6:52±00:17 Melatonin onset in h) MCs: 20:27±00:16 ECs: 23:55±00:26 Cortisol peak time (in h) MCs: 7:04±00:16 ECs: 11:13±00:23	Karolinska Sleepiness Scale	Psychomotor Vigilance Task; Stroop Task	ECs performed significantly worse than MCs on Psychomotor Vigilance Task. No significant ToD effect.	A significant synchrony effect was observed only for Psychomotor Vigilance Task with both ECs and MCs showing better performance at their optimal ToD.	ECs reported higher sleepiness in morning than afternoon and evening and vice-versa for MCs.
Song et al. (2019)	Season of testing not reported. Participants were tested twice, at 8:00 h, a week apart (with a sleep deprivation session: 22:00-8:00 h).	45 university students (sex not reported; age range: 18-30years; 24MCs/21ECs)	Morningness-Eveningness Questionnaire	Pittsburgh Sleep Quality Index; Epworth Sleepiness Scale; Positive and Negative Affect Schedule; NEO Five-Factor Inventory; Barrett	Psychomotor Vigilance Task; Go/no-go task	A significant CT effect with ECs having lower stop rate than MCs. A marginally significant ToD effect on PVT with ECs performing worse at 2:00,	No significant synchrony effect.	Sleep deprivation led to decreased response inhibition-related activation of the right lateral inferior frontal gyrus in MCs and vice-versa in ECs.

				Impulsiveness Scale; Dysexecutive Questionnaire		3:00, and 6:00 h following sleep deprivation.		
Zion & Shochat (2019)	Data were collected between August 2011 and April 2014. Participants were tested on 2 nights (with and without naps) at 3:00 h and 07:00 h.	119 nurses (all females; mean age: 39.0±9.1) Chronotype groups (N) not reported	Munich Chronotype Questionnaire MCs: 71 ECs: 22 (SD not reported)	Karolinska Sleepiness Scale; Pre-Sleep Arousal Scale-Somatic Subscale; Pre-Sleep Arousal Scale-Cognitive Subscale; Pittsburgh Sleep Quality Index	Digit Symbol Substitution Test; Letter Cancellation Task	No significant CT effect. Improved cognitive at 7:00 h as compared to 3:00 h in both nap and no-nap conditions.	No significant synchrony effect.	Cognitive performance improved following a nap.
Evansová et al. (2020)	Participants were tested on two consecutive days at 8:00 h and 20:00 h.	42 young adults (25 F/17 M; mean age: 28.12±5.25; 14MCs/15ICs/13ECs)	Morningness-Eveningness Questionnaire; Actigraphy		Rey Auditory Verbal Learning Test; Trial Making Test; Digit Span; Letter-Number Sequencing; Stroop Test; Continuous Performance Test; Intelligence Quotient	MCs named more colours than ECs in naming subtest of Stroop task. A significant ToD effect on Rey Auditory Verbal Learning Test with better performance in evening than in the morning, independent of CT.	No significant synchrony effect.	
Ge et al. (2020)	Season of testing not reported. MCs were tested at 8:00 h and ECs at 16:00 h	42 young drivers (Sex not reported; mean age: 27.43±3.46; 22MCs/20ECs)	Reduced Morningness-Eveningness Questionnaire		Visual-Spatial Working Memory Task; Syllable Detection Task	MCs had higher visual-spatial working memory than ECs. ToD not applicable.	Not examined	Age significantly predicted the accuracy of visual-spatial working memory.
Martínez-Pérez et al. (2020)	Season of testing not reported.	34 university students (27F/7M	Reduced Morningness-		Optimal time	No significant CT effect.	Shorter RTs were observed in Psychomotor in	

	Participants were tested at 8:00 h and at 20:30 h, one week apart.	mean age: 21±2.3; 16MCs/18ECs)	Eveningness Questionnaire MCs: 19.4 ECs: 8.6 (SD not reported)		Psychomotor Vigilance Task (RT): 300ms Flanker Task:394ms Non-optimal time Psychomotor Vigilance Task (RT): 319ms Flanker Task:412ms (SD not reported)	No significant ToD effect.	both chronotypes at their optimal ToD in Psychomotor Vigilance Task In the flanker task, only ECs showed a significant synchrony effect.	
McGowan et al. (2020)	Data were collected between January-December (bar first weeks of December and January) (year not reported). Participants were tested between 12:00 h and 14:00 h.	188 university students (90F/98M, mean age: 22.3±3.6) Chronotype groups (N) not reported	Munich Chronotype Questionnaire	Pittsburgh Sleep Quality Index; Subjective Sleepiness Scale	Continuous Performance Test; Iowa Gambling Task	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	Poor self-reported sleep quality was correlated with poor decision making on the Iowa Gambling Task.
Ceglarek et al. (2021)	Season of testing not reported. MCs were tested between 9:25-9:55 h (morning session) and between 18:30-19:02 h (evening session). ECs between 11:00-11:30 h (morning session) and	65 young adults (40F/25M; mean age: 24.29±3.64; 33MCs/32ECs)	Chronotype Questionnaire	Epworth Sleepiness Scale	DRM paradigm (Atkins & Reuter-Lorenz, 2011)	A significant CT effect on accuracy with higher accuracy in ECs than MCs, regardless of ToD. No CT effect on RTs. Slower RTs in the morning than evening session.	No significant synchrony effect.	

	20:40-21:10 h (evening session).					No significant ToD effect for accuracy.		
Kossowski et al. (2021)	Season of testing not reported. Participants were tested over 96 hours under 4 light conditions, with MCs tested either at 8:00 or 9:00 h and ECs either at 9:00 or 10:00 h	24 young adults (all M; mean age: 22.92±1.38; 12MCs/12ECs)	Composite Scale of Morningness	Karolinska Sleepiness Scale	N-Back	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	Significantly higher brain activity in frontal areas of the precentral gyrus, middle and superior frontal gyri and in the occipital gyrus in the morning for MCs but not for ECs.
Reiter et al. (2021)	Season of testing not reported. Participants were tested for 3 consecutive days between 8:00 h - 19:00 h.	72 young adults (36F/36M; mean age: 23.1±3.6; 23MCs/24ICs/23ECs)	Melatonin Onset (via saliva over 8 hours)	Karolinska Sleepiness Scale	Psychomotor Vigilance Task	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	A significant effect of test session was found. Subjective alertness, Psychomotor Vigilance Task lapses, and RTs decreased between each consecutive test session.
Yaremenko et al. (2021)	Season of testing not reported 49 participants were tested between 7:40-9:00 h (optimal time) and 42 between 20:30-21:30 h (non-optimal time).	91 young adults (66F/25M; mean age: 21.96 (SD not reported; 39MCs/52ECs)	Morningness-Eveningness Questionnaire MCs: 63.77±4.46 ECs: 34.37±5.05		Face Recognition Task; Source Monitoring Task	No significant CT effect. No significant ToD effect.	No significant synchrony effect.	
Palmero et al. (2022)	Season of testing not reported. All participants were tested 4 times during early and mid-follicular phase at 8:00 h and 20:30 h.	32 university students (all Females; age range: 19.75±1.57; 16MCs/16ECs)	Reduced Morningness-Eveningness Questionnaire		Psychomotor Vigilance Task; Sustained Attention Response Task	MCs were slower but accurate than ECs on Sustained Attention Response Task. No significant ToD effect.	A significant synchrony effect on Psychomotor Vigilance Task, with faster RTs at optimal ToD in MCs during mid-luteal phase than follicular phase	

							and vice-versa for ECs. In Sustained Attention Response Task, higher accuracy at optimal ToD in MCs during mid-luteal phase than follicular. No synchrony effects for ECs.	
Van Opstal et al. (2022)	Season of testing not reported Participants were tested twice, first at 8:00 h and then at 20:30 h.	130 university students (96F/33M; mean age: 20.65 (SD not reported; 22MCs/56ICs/52ECs)	Morningness-Eveningness Questionnaire MCs: 64±3.95 ICs: 64±3.95 ECs: 35.6±4.25	Sleep duration (single item) MCs: 7.59±1.03 ICs: 7.3±1.13 ECs: 6.68±1.35	Sustained Attention Response Task	A significant CT effect with ECs having higher RTs and reduced accuracy on Sustained Attention Response Task than MCs and ICs. No significant ToD effect.	A significant synchrony effect with MCs and ECs performing better at their optimal ToD.	Disrupted and reduced sleep resulted in increased mind wandering in participants.
Carlson et al. (2023)	Season of testing not reported Participants completed an online battery twice: after 1h of waking up and 30 mins before going to bed.	273 university students (216F/54M; mean age: 24.3±6.69) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire; Consensus Sleep Diary	Bedtime Procrastination Scale; Self-reported cognitive difficulties; Behavioural regulation difficulties; Emotion regulation difficulties	Stroop Task; Self-Reported Executive Functioning Difficulties	No significant CT effect. ToD effects not examined.	Not examined	ECs had higher bedtime procrastination, emotional, behavioural regulation difficulties, and poorer subjective executive functioning.
(Palmero et al. (2024a) Experiment 1	Season of testing not reported. ICs were tested between 10:00 h-	24 university students (Sex not reported; mean age not reported; 24ICs)	Reduced Morningness-Eveningness Questionnaire		Psychomotor Vigilance Task; Category Semantic Priming Task			A total of 64 participants with a mean age of 21.14±5.45

	16:00 h in one single session.						Results on ICs served as a reference to assess the extreme MCs and ECs.
Experiment 2	MCs and ECs were tested in the morning at 8:00 h and 20:30 h twice, a week apart	40 university students (Sex not reported; mean age not reported; 20MCs/20ECs)			Significant controlled priming effects only in ECs. No significant ToD effect.	A significant synchrony effect on Psychomotor Vigilance Task, with shorter RTs in both chronotypes at their optimal ToD time. No synchrony effect of priming in MCs but it was present in ECs	
Palmero et al. (2024b)	Season of testing not reported. Participants were tested at 8:00 h and 20:30 h, one week apart.	40 university students (32 F/8M; mean age: 21.14±5.45; 20MCs/20ECs)	Reduced Morningness-Eveningness Questionnaire	Psychomotor Vigilance Task; Shape-Label Matching Task	No significant CT effect. No significant ToD effect.	A significant synchrony effect on Psychomotor Vigilance Task, with shorter RTs in both chronotypes at their optimal ToD time. A significant synchrony effect was found on automatic processing only in ECs.	

Abbreviations: CT, Chronotype; ECs, Evening Chronotypes; F, Females; fMRI, Functional Magnetic Resonance Imaging; H, Hour; ICs, Intermediate Chronotypes; IFG, Inferior Frontal Gyrus; IQ, Intelligence Quotient; M, Males; MCC, Middle Cingulate Cortex; MCs, Morning Chronotypes; MEQ, Morningness-Eveningness Questionnaire; MTG, Middle Temporal Gyrus; RTs, Reaction Time; ToD, Time of Day.

Table 3.2 *Summary of key data extracted from selected studies comparing young and old adults*.

Author & Year (In chronological order)	**Month and Time of Testing**	**Sample Characteristics** (n, sex age, and chronotype)	**Chronotype Method** (Questionnaire/ actigraphy, and/or physiological data)	**Other Measures Used**	**Cognitive Measures Used**	**Key Outcomes**		**Other Findings**
						CT and ToD Effect	**Synchrony Effect**	
May et al. (1993)	Season of testing not reported. 50% of the participants in both groups were tested between 8:00 h -9:00 h and remaining between 16:00 - 17:00 h.	20 young adults (Sex not reported; mean age: 18.8, all ECs) 22 old adults (Sex not reported; mean age: 70.5, all MCs) (SD not reported)	Morningness-Eveningness Questionnaire Old MCs: 70.2±3.7 Young ECs: 29.3±3.5	Vocabulary Test Old MCs: 39.7 Young ECs: 25.7 (SD not reported)	Verbatim Recognition of Sentences from a Series of Paragraphs.	Young ECs had higher recognition accuracy than the older MCs. No significant ToD effect was observed.	A significant synchrony effect was found on recognition accuracy with both groups performing better at their optimal ToD.	
May & Hasher (1998) Experiment 1	Season and time of testing not reported. 50% of the participants were tested at 8:00 h and remaining either at 16:00 or 17:00 h.	48 young adults (sex not reported; age range: 18-22 years; 5% MCs, 58% ICs, 37% ECs) 48 older adults (sex not reported; age range: 62-75 years; 73%MCs/ 25% ICs/ 2% ECs)	Morningness-Eveningness Questionnaire		Sentence Competition Task; Extended Range Vocabulary Test	No significant CT effect. No significant ToD effect.	A significant synchrony effect on priming of disconfirmed items with both younger ECs and older adults performing better at their optimal ToD.	No age-related differences in completion rates.
Experiment 2		36 young adults (sex not reported; age range: 18-21 years, all ECs) 36 older adults (sex not reported; age range: 62-76 years, all MCs)			Stop-Signal Task; Stroop Task; Trial Making Task	No significant CT effect. No significant ToD effect.	No synchrony effect on accuracy and RTs in go-trials. Younger adults were faster than older adults in Stop-Signal Task. Older adults performed better in the morning on Stroop Task and Trial Making Task. No difference in younger adults.	

May (1999)	Season of testing not reported. 50% of the participants were tested at 8:00 h and remaining either at 17:00 h.	40 younger adults (sex not reported; age range: 18-25 years, all ECs) 48 older adults (sex not reported; age range: 60-75 years, all MCs).	Morningness-Eveningness Questionnaire		Word Problem; Extended Range Vocabulary Test	No significant CT effects. Cost and benefit scores were more reliable in the evening than morning session.	A significant synchrony effect in both younger and older adults with increased distraction when tested at their non-optimal ToD.	
Hasher et al. (2002)	Season of testing not reported. 50% of the participants were tested at 8:00 h and remaining either at 16:30 h.	48 younger adults (sex not reported; mean age: 20.29±3.01, all ECs) 48 older adults (sex not reported; mean age: 67.96±1.97, all MCs)	Morningness-Eveningness Questionnaire Young adults: 19.7±6.84 Older adults: 67.3±5.71		Memory Task; Mill Hill Vocabulary Scale; Extended Range Vocabulary Test	No significant CT effect. No significant ToD effect.	A significant synchrony effect on recall with both MC older adults and EC younger adults performing better at their optimal ToD.	older adults were more vulnerable to proactive interference than younger adults with heightened interference effects at non-optimal ToD.
West et al. (2002)	Season of testing not reported Participants were tested over 4-days with 50% tested at 9:00 h and 50% at 17:00 h. These were alternated between morning and evening sessions (i.e., morning-evening-morning-evening or evening-morning-evening-morning).	20 young adults (Sex and mean age not reported; 10MCs/10ECs) 20 old adults (Sex and mean age not reported; 10MCs/10ECs)	Morningness-Eveningness Questionnaire in morning Young adults: 46.8±9.11 Old adults: 59.2±7.44 Morningness-Eveningness Questionnaire in evening Young adults: 41.7±11.72 Old adults: 58.5±7.88	Alertness Rating Scale scores in morning Young adults: 62.94±18.46 Old adults: 70.54±11.69 Alertness Rating Scale scores in evening Young adults: 72.38±16.74 Old adults: 67.73±13.95 Wechsler Adult Intelligence Scale-Revised	Four-Box Task	No significant CT effect. No significant ToD effect.	A significant synchrony effect on error rate with both older MCs and younger ECs had significantly lower error rates at their optimal ToD.	Younger adults reported higher levels of alertness in the evening than morning and vice-versa for old adults. Due to practice effect, error rates increased from morning to evening on day 1 but not on day 3 for older MCs but not for younger ECs.
Bonnefond et al. (2003)	Season of testing not reported.	12 young nurses (sex not reported; mean age:	Morningness-Eveningness Questionnaire	Visual Analogue Scale (alertness, performance, and	Visual Discrimination	No significant CT effect.	No significant synchrony effect.	No age effect was observed on RTs and error rates for the

	Participants were tested between 10:00-12:00 h, 18:00 h - 20:00 h, and 2:00-4:00 h, one week apart. Prior to the testing participants underwent 2 weeks of training.	27.5±2.1; 1MC/10ICs/1EC) 12 old nurses (sex not reported; mean age: 52.1±2.2; 2MCs/8ICs/1EC)		task duration rating)	Task; Descending Subtraction Test	A significant ToD effect was observed with both ECs and MCs having significantly longer RTs only in Visual Discrimination task at 2:00 h.		Visual Discrimination Task. Age effect was only present on tasks requiring higher cognitive load.
Yang et al. (2007) Experiment 1	Season of testing not reported. 27 participants were tested at 9:00 h and 26 at 16:00 h.	53 older adults (Sex not reported; mean age: 67.89±4.19; all MCs)	Morningness-Eveningness Questionnaire	Short Blessed Test	Four List of Critical Words, One List of Fillers, and Eight Buffers by Wilson & Horton (2002)	CT effects not applicable. A significant ToD effect was found only on control retrieval with greater priming in the morning than afternoon session.	Participants using controlled retrieval strategy showed more priming at optimal than at non-optimal ToD.	
Experiment 2	22 participants were tested at 9:00 h and 24 at 16:00 h.	46 older adults (Sex not reported; mean age: 66.24±4.51; all MCs)				CT effects not applicable. Greater priming was seen in the morning than afternoon.	A significant synchrony effect only on controlled retrieval.	
Hogan et al. (2009)	Season of testing not reported Participants were tested between 9:00-10:00 h and between 18:00-19:00 h.	48 young adults (37F/11M; mean age: 20.17±3.53; 48ECs) 48 old adults (28F/21M; mean age: 69.70±4.86; 48 MCs)	Morningness-Eveningness Questionnaire Old MCs: 63.6±3.68 Young ECs: 35.55±3.62	Hospital Depression Anxiety Scale Old MCs: 6±3.3 Young ECs: 8.70±3.98 National Adult Reading Test	Digit Symbol Paired Associate Learning Task; Wechsler Paired Associates Memory Test	A significant CT effect was found on Digit Symbol Paired Associate Learning Task with old MCs having poorer memory and slower RTs than young ECs. No significant ToD effect.	A significant synchrony effect was observed with older MCs having poorer memory at their non-optimal ToD.	
Schmidt et al. (2012b)	Season of testing not reported. Participants were tested	11 Young adults (6F/5M; mean age: 25.6±3.49)	Morningness-Eveningness Questionnaire	Pittsburgh Sleep Quality Index Young adults: 25.6±3.49	Psychomotor Vigilance Task; Stroop Task	No significant CT effect. No significant ToD effect.	A significant synchrony effects was observed with young and older adults	Young ECs woke up later and were significantly sleepy than older MCs.

	consecutively for 2 days at 9:00 h and 18:00 h.	14 Old adults (8F/6M; mean age: 67.2±3.98) Chronotype groups (N) not reported	Old adults: 72.43 ± 1.74 Young adults: 27.23 ± 1.63	Old adults: 3.86±1.96 Beck's Anxiety Inventory Young adults: 3.78±1.56 Old adults: 5.07±1.35 Beck's Depression Inventory Young adults: 4.12±1.26 Old adults: 5.18±1.58 Mattis Dementia Scale Old adults: 139.42±3.76			ECs having significantly improved RTs at their optimal time.	No age effect was found on Psychomotor Vigilance Task and Stroop task.
Anderson et al. (2014)	Season of testing not reported 16 young and older adults were tested between 13:00-17:00 h (average time: 14:42 h). Further 18 older adults tested between 8:30-10:30 h (average time: 8:47 h).	16 young adults (8 F/8 M; mean age: 23.94± 4.17) 16 old adults (10 F/4 M; mean age: 71.27±7.68; 16 MCs) 18 old adults (12 F/6 M; mean age: 68.83±7.2; 18 MCs)	Morningness-Eveningness Questionnaire Older adults tested in morning: 60.53±8.17 Older adults tested in morning: 63.67±10.81	Mini Mental State Exam	N-back; Flanker Task; Implicit Word-Fragment Completion Task	A significant CT effect was found on Flanker Task with smallest flanker effect in young adults, followed by older MCs tested in the morning and afternoon. Older adults tested in the morning ignore the unattended stimulus than older adults in the afternoon, and activate cognitive control regions (rostral prefrontal and superior parietal cortex) similar to young adults.	A significant synchrony effect on behavioural and fMRI tasks with older adults performing better at their optimal time.	

Iskandar et al. (2016)	Season of testing not reported Participants were tested for 4 consecutive days with 2 morning sessions at 9:00 h and evening sessions at 17:00 h.	20 university students (10F/10M; mean age: 24.20±3.49, all ECs) 20 old adults (10F/10M; mean age: 72.75±4.63, all MCs)	Morningness-Eveningness Questionnaire Older adults: 58.85±8.46 Younger adults: 45±10.23	Younger adults Wechsler Adult Intelligence Scale-Revised: 13.6±3.66 National Adult Reading Test Revised: 106.82±9.05 Beck Depression Scale: 5.50±4.8 Older adults Wechsler Adult Intelligence Scale-Revised:16±3.43 National Adult Reading Test Revised: 115.44±7.02 Beck Depression Scale: 4.58±2.84	Category Fluency Test; Letter Fluency Test	No significant CT effect. No significant ToD effect.	A significant synchrony effect was found for word generation, switching more between subcategory exemplars during word generation with both groups performing better at their optimal ToD.	
Rothen & Meier (2017)	Season of testing not reported. Participants were randomly tested between 8:00-12:00 h and between 16:00-20:00 h.	115 young adults (66F/49M; mean age: 23.05±3.53) 113 old adults (68F/45M; mean age: 67.58±5.97) Chronotype groups (N) not reported	Morningness-Eveningness Questionnaire Old adults: 60.37±8.95 Young adults: 49.51±9.58		Prospective Memory Task	No significant CT effect. No significant ToD effect.	A significant synchrony effect was observed for younger adults (better performance on-peak than off-peak time), but not for older adults on prospective memory task.	Younger adults performed better than older adults in all conditions.

Abbreviations: CT, Chronotype; ECs, Evening Chronotypes; F, Females; ICs, Intermediate Chronotypes; M, Males; MCs, Morning Chronotypes; RT, Reaction Time; SD, Standard Deviation; ToD, Time of Day.

Table 3.3 *The Joanna Briggs Institute quality appraisal ratings of the selected studies.*

Study Details		**JBI Criteria**								
Study	**Study Design**	Inclusion criteria clearly defined Were the criteria for inclusion in the sample clearly defined? Yes/ No / Unclear/ NA	Study subjects and setting described in detail Were the study subjects and the setting described in detail? Yes/ No/ Unclear/NA	Exposure measured in a valid and reliable way Was the exposure measured in a valid and reliable way? Yes/ No/ Unclear/NA	Objective, standard criteria used for measurement of condition Were objective, standard criteria used for measurement of the condition? Yes/No/Unclear /NA	Confounders identified Were confounding factors identified? Yes/No/Unclear/NA	Strategies to deal with confounders Were the criteria for inclusion in the sample clearly defined? Yes/No/ Unclear/NA	Outcomes measured in a valid way Were the outcomes measured in a valid and reliable way? Yes/No/ Unclear/NA	Appropriate statistical analysis Was appropriate statistical analysis used? Yes/No/ Unclear/NA	**Score**
Petros et al. (1990)	Mixed: Between and within subject factors	0	1	1	1	1	0	1	1	**6**
Anderson et al. (1991)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**
May et al. (1993)	Mixed: Between and within subject factors	0	Unclear	1	1	1	Unclear	1	1	**5**
May & Hasher (1998)	Mixed: Between and within subject factors	0	1	1	1	0	0	1	1	**5**
May (1999)	Mixed: Between and within subject factors	0	1	1	1	0	0	1	1	**5**
Song & Stough (2000)	Mixed: Between and within subject factors	0	1	1	1	1	0	1	1	**6**
Hasher et al. (2002)	Mixed: Between and within subject factors	0	1	1	1	0	0	1	1	**5**
West et al. (2002)	Mixed: Between and within subject factors	Unclear	Unclear	1	1	0	0	1	1	**4**
Bonnefond et al. (2003)	Mixed: Between and within subject factors	1	Unclear	1	1	1	0	1	1	**6**
Natale et al. (2003)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Hidalgo et al. (2004)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Killgore & Killgore (2007)	Correlational	1	1	1	1	0	0	1	1	**6**

Yang et al. (2007)	Mixed: Between and within subject factors	0	1	1	1	1	1	1	1	**7**
Barbosa & Albuquerque (2008)	Mixed: Between and within subject factors	0	1	1	1	1	1	1	1	**7**
Bennett et al. (2008)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Mongrain et al. (2008)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Hogan et al. (2009)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Matchock & Mordkoff (2009)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Taillard et al. (2011)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Wieth & Zacks (2011)	Mixed: Between and within subject factors	0	0	1	1	1	1	1	1	**6**
Schmidt et al. (2012a)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Schmidt et al. (2012b)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Fabbri et al. (2013)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Anderson et al. (2014)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Baeck et al. (2014)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Correa et al. (2014)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Delpouve et al. (2014)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Lara et al. (2014)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Gobin et al. (2015)	Mixed: Between and within subject factors	0	1	1	1	1	1	1	1	**7**
Reinke et al. (2015)	Prospective observational cohort design	Unclear	Unclear	1	1	1	1	1	1	**6**
Schmidt et al. (2015)	Mixed: Between and within subject factors	1	Unclear	1	1	1	Unclear	1	1	**6**
Fimm et al. (2016)	Mixed: Between and within subject factors	Unclear	1	1	1	1	1	1	1	**7**
Gijselaers et al. (2016)	Mixed: Between and within subject factors	Unclear	1	1	1	1	1	1	1	**7**

Iskandar et al. (2016)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Maierova et al. (2016)	Within-subjects and Cross-over	1	1	1	1	1	1	1	1	**8**
Rothen & Meier (2016)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Barclay & Myachykov (2017)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Correa et al. (2017)	Mixed: Between and within subject factors	0	1	1	1	0	0	1	1	**5**
Fabbri et al. (2017)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**
Ritchie et al. (2017)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Rothen & Meier (2017)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Simor & Polner (2017)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Facer-Childs et al. (2018)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Lewandowska et al. (2018)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Nowack & Van Der Meer (2018)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Rodríguez-Morilla et al. (2018)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Song et al. (2018)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**
Zion & Shochat (2018)	Mixed: Between and within subject factors	1	1	1	1	1	1	0	1	**7**
Barner et al. (2019)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Facer-Childs et al. (2019)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**
Song et al. (2019)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Zion & Shochat (2019)	Prospective within-subjects	1	1	1	1	1	1	1	1	**8**
Evansová et al. (2020)	Mixed: Between and within subject factors	1	1	1	1	1	Unclear	1	1	**7**
Ge et al. (2020)	Between-subjects	1	1	1	1	1	1	1	1	**8**

McGowan et al. (2020)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Martínez-Pérez et al. (2020)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Ceglarek et al. (2021)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**
Kossowski et al. (2021)	Mixed: Between and within subject factors	1	1	1	1	0	0	1	1	**6**
Reiter et al. (2021)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Yaremenko et al. (2021)	Mixed: Between and within subject factors	1	1	1	1	1	1	1	1	**8**
Palmero et al. (2022)	Mixed: Between and within subject factors	1	1	1	1	1	Unclear	1	1	**7**
Van Opstal et al. (2022)	Mixed: Between and within subject factors	0	1	1	1	1	Unclear	1	1	**7**
Carlson et al. (2023)	Correlational	1	1	1	1	1	1	1	1	**8**
Palmero et al. (2024a)	Mixed: Between and within subject factors	0	1	1	1	1	0	1	1	**6**
Palmero et al. (2024b)	Mixed: Between and within subject factors	1	1	1	1	1	0	1	1	**7**

Note: One point was given for scoring “yes” on each of the criteria, and then all applicable points added to derive the total score for each study.

Table 3.4 *List of cognitive functions examined and neuropsychological tests/subtests used.*

Cognitive function assessed		Overall Direction		Cognitive test/subtest	Studies
		Chronotype	Synchrony/ asynchrony Effect		
Intelligence	**Arithmetic, comprehension, information, spatial, vocabulary**	No evidence	No evidence	Multidimensional Aptitude Battery (Digit Symbol, Picture Completion, Spatial, Picture Arrangement, and Object Assembly Task.	Song & Stough, 2000
	Mathematical			Digit Span Task	Delpouve et al., 2014; Evansová et al., 2020
	Fluid and verbal Mathematical			Raven Advanced Progressive Matrices	Nowack & Van Der Meer, 2018
				Wechsler Adult Intelligence Scale (Digit Symbol Substitution Task)	Gijselaers et al., 2016; Zion & Shochat, 2018, 2019
				Wechsler Adult Intelligence Scale (Semantic Memory, Digit Span, Word-Pair Associates, and Verbal Fluency Test)	Hidalgo et al., 2004
	Verbal and performance			Wechsler Adult Intelligence Scale-III (Digit Span Subtest, Controlled Oral Word Association Test)	Bennett et al., 2008
				Wechsler Abbreviated Scale of Intelligence	Killgore & Killgore, 2007
Sensory Processing	**Speed**	Mixed evidence	Mixed evidence	Inspection Time	Song & Stough, 2000
				Trial Making Task	Evansová et al., 2020; Gijselaers et al., 2016; May & Hasher, 1998
				Two Digit Adding Test	Reinke et al., 2015
Perception		No evidence	No evidence	Visual Discrimination Task	Bonnefond et al., 2003
				Shape-Label Matching Task	Palmero et al., 2024b
Attention	**Control**	No evidence	Strong evidence	Two Letter Search Task	Natale et al., 2003
	Joint		Strong evidence	Navon Task	Fabbri et al., 2017
	Sustained		Mixed evidence	Letter Cancellation Task	Zion & Shochat, 2018, 2019
				Continuous Performance Task	Bennett et al., 2008; Correa et al., 2017; Evansová et al., 2020; McGowan et al., 2020
				Psychomotor Vigilance Task	Correa et al., 2014; Delpouve et al., 2014; Facer-Childs et al., 2018, 2019; Lara et al., 2014; Martínez-Pérez et al., 2020; Mongrain et al., 2008; Palmero et al., 2022, 2024a, 2024b; Reinke et al., 2015; Reiter et al., 2021; Rodríguez-Morilla et al., 2018; Schmidt et al., 2012a; Song et al., 2019
				Reaction Time Task	Taillard et al., 2011

				Sustained Attention Response Task	Correa et al., 2014; Gobin et al., 2015; Lara et al., 2014; Palmero et al., 2022; Van Opstal et al., 2022)
	Visual selective			Spatial Configuration Visual Search Task	Ritchie et al., 2017
	Visual (altering orienting, conflict)			Attentional Network Test	Barclay & Myachykov, 2017; Matchock & Toby Mordkoff, 2009
	Visuo-spatial	Mixed evidence	No evidence	Covert Orientation Task of attention Overt Orienting Task of attention Neglect Task	Fimm et al., 2016
Inhibition		No evidence (Mixed for Stroop task)	Mixed evidence	Flanker Task	Anderson et al., 2014; Martínez-Pérez et al., 2020
				Go-No-Go Task	Maierova et al., 2016; Song et al., 2019
				Memory Task	Hasher et al., 2002
				Sentence Competition Task	May et al., 1993
				Stop-Signal Task	May & Hasher, 1998; Song et al., 2018
				Stroop Task	Carlson et al., 2023; Evansová et al., 2020; Facer-Childs et al., 2019; May & Hasher, 1998; Schmidt et al., 2012a, 2012b
				Word Problem Task	May, 1999
Working memory		No evidence	No evidence	Descending subtraction test	Bonnefond et al., 2003
				Global Processing Task	Lewandowska et al., 2018
				Local Processing Task	Lewandowska et al., 2018
				Phonological Task	Lewandowska et al., 2018
				Four box tasks	West et al., 2002
				N-back	Anderson et al., 2014; Gijselaers et al., 2016; Kossowski et al., 2021; Maierova et al., 2016; Schmidt et al., 2015
				Number-Letter Sequencing Task	Evansová et al., 2020
				Semantic Processing Task	Lewandowska et al., 2018
				Visual-Spatial Working Memory Task	Ge et al., 2020
				Wisconsin Card Sorting Test	Bennett et al., 2008
Multi-tasking		No evidence		Stimulated Driving Task	Ge et al., 2020; Rodríguez-Morilla et al., 2018
Decision making		No evidence	No evidence	Iowa Gambling Task	McGowan et al., 2020
				Ultimatum Game	Correa et al., 2017
Problem solving		No evidence	Strong evidence	Analytic and Insight problems	Wieth & Zacks, 2011)
				Crypto-arithmetic tasks	Natale et al., 2003
Thinking	**Convergent-Divergent**	No evidence	Strong evidence	Compound Remote Associate Problems Tasks	Simor & Polner, 2017
Reasoning	**Analogical**	No evidence	Strong evidence	Semantic Analogy Task	Nowack & Van Der Meer, 2018
	Syllogistic			Syllogistic Reasoning Task	Natale et al., 2003
				Language Dependent Task	Iskandar et al., 2016

Verbal fluency		No evidence	Strong evidence	Letter Fluency Task	Iskandar et al., 2016
				Verbal fluency task	Hidalgo et al., 2004
Learning	**Associate**	No evidence	Mixed evidence	Digit Symbol Paired Associate Learning Task	Hogan et al., 2009
	Implicit			Artificial Grammar Learning Task	Delpouve et al., 2014
	Perceptual			Visual Learning Task	Baeck et al., 2014
Memory	**Emotional**	No evidence	No evidence	Negative and Neutral Image Recognition Task	Gobin et al., 2015
	Implicit		Mixed evidence	Number-Matching Task	Fabbri et al., 2013
				184 standardised line drawing (Snodgrass & Vanderwart, 1980)	Rothen & Meier, 2016
				Four list of critical words, one list of fillers, and eight buffers by Wilson & Horton (2002)	Yang et al., 2007
	Explicit			Word-List Recognition Test	Barbosa & Albuquerque, 2008
				Facial Recognition Task	Yaremenko et al., 2021
	Prospective			Colour Task	Barner et al., 2019
				Dresden Breakfast Task	Barner et al., 2019
				Prospective Memory Task	Rothen & Meier, 2017
				Red Pencil Task	Barner et al., 2019
				Syllable Detection Task	Barner et al., 2019
	Prose	Strong evidence	Strong evidence	Passage Difficulty Task	Petros et al., 1990
	Semantic	Mixed	No evidence	Category Semantic Priming Task	Palmero et al., 2024a
				Word-pair Recognition Test	Anderson et al., 1991
				Semantic Classification Task	Fabbri et al., 2013
	Short-Term	No evidence	No evidence	DRM Paradigm (Atkins & Reuter-Lorenz, 2011)	Ceglarek et al., 2021
				Rey Auditory Verbal Learning Test	Evansová et al., 2020
	Source			Source Monitoring Task	Yaremenko et al., 2021
	Verbal		Strong evidence	Verbatim Recognition of Sentences from a Series of Paragraphs.	May et al., 1993
				Wechsler Paired Associates Memory Test	Hogan et al., 2009
				Word List with Emotional Content test	Hidalgo et al., 2004)
	Visual		No evidence	Visual memory scale	Hidalgo et al., 2004

3.4.1 Effects of Chronotype on Cognitive Performance in Young Adults

Five of the 53 studies (Ceglarek et al., 2021; Ge et al., 2020; Palmero et al., 2022; Petros et al., 1990; Schmidt et al., 2015) reported significant main effects of chronotype. Ge and colleagues (2020) reported better visuo-spatial working memory in MCs vs ECs. Petros and colleagues (1990) reported greater recall in ECs vs MCs in prose memory tasks. Some studies reported higher accuracy (Schmidt et al., 2015, N-Back; Ceglarek et al., 2021), although not consistently (see Palmero et al., 2022, Sustained Attention Response Task), and longer reaction time (RT; Palmero et al., 2022; Schmidt et al., 2015) in ECs than MCs.

In addition, four other studies (Evansová et al., 2020; Killgore & Killgore, 2007; Nowack & Van Der Meer, 2018; Palmero et al., 2024a) reported a main effect of chronotype on some but not all cognitive domains that were tested. Killgore and Killgore (2007), although not finding any chronotype effect on overall verbal IQ and performance, reported an association between a higher preference for eveningness (i.e., lower scores on the Morningness-Eveningness Questionnaire) and higher verbal cognitive ability in females (not in males). In other three studies, MCs were found to have faster processing speed and lower error rates (Nowack & Van Der Meer, 2018), generate more colour names in the naming subtest of the Stroop task (Evansová et al., 2020), or easily shift from automatic to controlled processing-based responses, regardless of ToD during Category Sematic Priming Task (Palmero et al., 2024a).

As evident in Table 3.1, the remaining studies found no significant effect of chronotype on *intelligence* (Bennett et al., 2008; Evansová et al., 2020; Gijselaers et al., 2016; Hidalgo et al., 2004; Killgore & Killgore, 2007; McGowan et al., 2020; Nowack & Van Der Meer, 2018; Song & Stough, 2000; Zion & Shochat, 2018, 2019), *processing speed* (Evansová et al., 2020; Gijselaers et al., 2016; Reinke et al., 2015; Song & Stough, 2000), *perceptual learning* (Baeck et al., 2014), *visual attention* (Matchock & Mordkoff, 2009), *visuo-spatial attention* (Fimm et al., 2016), *sustained attention* (Correa et al., 2014; Delpouve et al., 2014; Evansová et al., 2020; Facer-Childs et al., 2018; Gobin et al., 2015; Lara et al., 2014; Martínez-Pérez et al., 2020; Mongrain et al., 2008; Palmero et al., 2024a, 2024b; Reinke et al., 2015; Reiter et al., 2021; Rodriguez-Morilla et al., 2018; Taillard et al., 2011; Zion & Shochat, 2018, 2019), *joint attention* (Fabbri et al., 2017), *attentional control* (Natale et al., 2003), *inhibition* (Carlson et al., 2023; Facer-Childs et al., 2019; Martínez-Pérez et al., 2020; Schmidt et al., 2012a; Song et al., 2018), *executive functions* (Facer-Childs et al., 2018; Rodriguez-Morilla et al., 2018),

working memory (Bennett et al., 2008; Evansová et al., 2020; Gijselaers et al., 2016; Kossowski et al., 2021; Lewandowska et al., 2018), *reasoning* (Natale et al., 2003), *verbal fluency* (Hidalgo et al., 2004), *problem-solving* (Natale et al., 2003; Wieth & Zacks, 2011), *decision making* (Correa et al., 2014; McGowan et al., 2020), *convergent and divergent thinking* (Simor & Polner, 2017), *implicit memory* (Fabbri et al., 2013; Rothen & Meier, 2016), *explicit memory* (Barbosa & Albuquerque, 2008; Yaremenko et al., 2021), *semantic memory* (Anderson et al., 1991; Fabbri et al., 2013), *prospective memory* (Barner et al., 2019), *visual memory* (Hidalgo et al., 2004), *verbal memory* (Hidalgo et al., 2004), *short-term memory* (Evansová et al., 2020), *source memory* (Yaremenko et al., 2021), and *emotional memory* (Gobin et al., 2015). Lastly, in two studies, regardless of chronotype, better cognitive performance was attributed to lower sleep inertia (Ritchie et al., 2017) or appropriate lighting during testing (Maierova et al., 2016).

In addition to chronotype, 45 of 53 studies in young adults (Table 3.1) also examined ToD effect. In 37 of these 45 studies (82.22%), there was no significant main effect of ToD on *intelligence* (Bennett et al., 2008; Evansová et al., 2020; Hidalgo et al., 2004; McGowan et al., 2020; Song & Stough, 2000), *processing speed* (Evansová et al., 2020; Song & Stough, 2000), *perceptual learning* (Baeck et al., 2014), *sustained attention* (Correa et al., 2014; Delpouve et al., 2014; Evansová et al., 2020; Facer-Childs et al., 2018, 2019; Gobin et al., 2015; Lara et al., 2014; Martínez-Pérez et al., 2020; Mongrain et al., 2008; Palmero et al., 2022, 2024b; Reiter et al., 2021; Van Opstal et al., 2022), *attentional control* (Natale et al., 2003), *attentional asymmetry* (Fimm et al., 2016), *verbal fluency* (Hidalgo et al., 2004), *inhibition* (Facer-Childs et al., 2019; Martínez-Pérez et al., 2020; Schmidt et al., 2012a), *executive functions* (Facer-Childs et al., 2018), *working memory* (Evansová et al., 2020; Kossowski et al., 2021; Schmidt et al., 2015), *reasoning* (Natale et al., 2003; Nowack & Van Der Meer, 2018), *thinking* (Simor & Polner, 2017), *problem solving* (Natale et al., 2003; Wieth & Zacks, 2011), *decision-making* (Correa et al., 2017; McGowan et al., 2020), *verbal fluency* (Iskandar et al., 2016), *implicit memory* (Fabbri et al., 2013; Rothen & Meier, 2016), *explicit memory* (Barbosa & Albuquerque, 2008; Yaremenko et al., 2021), *visual memory* (Hidalgo et al., 2004), *emotional memory* (Gobin et al., 2015), *short-term memory* (Evansová et al., 2020), *sematic memory and associated processing* (Palmero et al., 2024a) or *source memory* (Yaremenko et al., 2021). Five of these 37 studies, however, did find a ToD effect in some but not all cognitive measures that were tested (Bennett et al., 2008; Evansová et al., 2020; Fabbri et al., 2013, Fimm et al., 2016; Hidalgo et al., 2004). For instance, some studies reported greater word recall and generation, and better short-term memory in the evening (i.e., between 17:00-

20:00 hour) than morning session (Bennett et al., 2008; Evansova et al., 2020; Hidalgo et al., 2004). Two studies (Fabbri et al., 2013; Fimm et al., 2016) reported a poorer retrieval efficiency on semantic classification and higher visual-spatial attention in the evening session.

The remaining eight of 45 studies (Anderson et al., 1991; Barner et al., 2019; Ceglarek et al., 2021; Fabbri et al., 2017; Lewandowska et al., 2018; Matchock & Mordkoff, 2009; Petros et al., 1990; Song et al., 2018) reported a main effect of ToD. Five of these studies reported a ToD effect, regardless of chronotype, with majority suggesting better performance in late afternoon or evening in measures of prospective memory (Barner et al., 2019), response bias in working memory (Lewandowska et al., 2018), executive control (indicated via higher conflict scores; Matchock & Mordkoff, 2009), and faster global and local attentional foci (Fabbri et al., 2017). Song and colleagues (2018) reported higher accuracy (on go trials of Stop-Signal Task) but no effects on RT in the evening than in the morning. ToD was reported to influence comprehension and reading processing (Petros et al., 1990), and speed of access to long-term memory (Anderson et al., 1991), with better performance either in the morning or evening depending upon the type of person tested (i.e., the ToD effect attributable to chronotype characteristics of the sample). Ceglarek and colleagues (2021) reported faster RTs (but only in ECs and with greater efforts) on a test of short-term memory in the evening than morning session.

3.4.2 Synchrony Effect: Chronotype × ToD Interaction in Young Adults

In total, 45 of 53 studies examined the synchrony effect in cognitive function (Table 3.1). Twenty-two (48.88%) of these 45 studies reported a synchrony effect in MCs and/or ECs. Of these 22 studies, nine (40.90%) reported better performance in both chronotypes or selectively in MCs/ECs at their optimal ToD. Petros and colleagues (1990) reported a significant synchrony effect on probe memory with a linear decrease in performance across the day for MCs and vice-versa for ECs. Similar findings were reported by Anderson and colleagues (1991) on long-term memory access using the Word-Pair Recognition Test. Synchrony effect in both chronotypes was also found in *sustained attention* (Mongrain et al., 2008; Van Opstal et al., 2022), *response inhibition* (Lara et al., 2014), *metamemory* (Hidalgo et al., 2004), *joint attention* (Fabbri et al., 2017), *attentional control*, *reasoning* and *problem-solving* (Natale et al., 2003). Lastly, Palmero and colleagues (2022) found a synchrony effect using sustained

attention response task only in MCs females when they were tested during the luteal phase, relative to the follicular phase.

Nine (40.90%) of 22 studies found synchrony in some cognitive functions but not in others. For example, majority of the studies examining *sustained attention* especially using the Psychomotor Vigilance Task (PVT) reported a synchrony effect in both chronotypes (Facer-Childs et al., 2019; Lara et al., 2014; Martínez-Pérez et al., 2020; Palmero et al., 2024a, 2024b). However, Facer-Childs and colleagues (2018) found this effect only in ECs. These studies (Facer-Childs et al., 2018, 2019; Martínez-Pérez et al., 2020; Palmero et al., 2024a, 2024b) also reported selective or no synchrony in other cognitive functions. For instance, better *inhibition* (Martínez-Pérez et al., 2020), priming and automatic processing (Palmero et al., 2024a, 2024b) was found only in ECs at their optimal ToD. Conversely, Facer-Childs and colleagues (2018) reported better executive functioning only in MCs at their optimal ToD. Lastly, Facer-Childs and colleagues (2019) reported no synchrony effect on inhibition using Stroop Task. Four further studies found expected synchrony in some tasks and no synchrony in other tasks. Song and Stough (2000) reported a synchrony effect only in MCs on the Spatial Subtest of Multidimensional Amplitude Battery and showed no synchrony on the Inspection Time, Digit Span, Picture Completion, Picture Arrangement, and Object Assembly Tests. Similarly, Bennett and colleagues (2008) reported selective synchrony (in MCs) in executive functioning (Wisconsin Card Sort Task) but not in working memory, fluency or memory measures (Digit Span, Controlled Oral Word Association, and Continuous Performance Test). Matchock and Mordkoff (2009) reported increased alertness scores, but not on orienting and conflict scores, on the attentional network task in MCs. Schmidt and colleagues (2015) observed no synchrony effect in overall working memory (N-Back) performance but found the ECs to perform better during 3-Back condition at their optimal ToD.

Four (of 22; 18.88%) studies found reversed synchrony with better performance at non-optimal ToD. Rothen and Meier (2016) reported increased effect on priming at non-optimal ToD in both chronotypes. Similarly, Wieth and Zacks, (2011) also reported reversed synchrony in both chronotypes on an insight problem task, but showed no effect analytical problems. Nowack and Van Der Meer (2018) found MCs to be better at analogical reasoning and to show fewer difficulties than ECs in reverse analogy conditions at their non-optimal ToD. Conversely, Simor and Polner (2017) observed better convergent thinking (but not divergent thinking) performance in ECs than MCs when tested at their non-optimal ToD.

The remaining 23 (of 45; 51.11%) studies found no synchrony effect in *Intelligence* (Delpouve et al., 2014; McGowan et al., 2020; Zion & Shochat, 2018, 2019), *processing speed* (Evansova et al., 2020; Reinke et al., 2015;), *perceptual learning* (Baeck et al., 2014), *implicit learning* (Delpouve et al., 2014), *visual attention* (Barclay & Myachykov, 2017), *visuo-spatial attention* (*Fimm et al., 2016*), *sustained attention* (Correa et al., 2014; Gobin et al., 2015; *Reinke et al., 2015;* Reiter et al., 2021; Song et al., 2019; Zion & Shochat, 2018, 2019*), inhibition (*Evansova et al., 2020; *Koss*owski et al., 2021; Schmidt et al., 2012a, Song et al., 2018, 2019), *working me*mory (Evansova et al., 2020; Lewandowska et al., 2018), *decision making* (Correa et al., 2017; McGowan et al., 2020), *short-term memory* (Ceglarek et al., 2021; Evansova et al., 2020*), explicit memory* (Barbosa & Albuquerque, 2008; Yaremenko et al., 2021), *prospective memory* (Barner et al., 2019), *source memory* (Yaremenko et al., 2021), *and emotional memory* (Gobin et al., 2015).

Notably, four of 23 studies that we described earlier as showing no significant synchrony effect in cognitive data also obtained neuroimaging data, and their findings hinted towards a synchrony effect in brain activity. Specifically, while Schmidt and colleagues (2012a) reported no synchrony effect on the overall Stroop Task, they did find a stable or increased interference-related hemodynamic responses from morning to evening in the ECs, while it decreased in the MCs under similar conditions. Schmidt and colleagues (2015) did not find a synchrony effect in the overall N-Back task performance, but observed better performance and increased thalamic activity during the 3-Back condition in ECs, and higher middle frontal gyrus activation in MCs, at their optimal times. Similarly, Kossowski and colleagues (2021) did not find a synchrony effect in the overall N-Back task but reported higher brain activity in frontal areas of the precentral gyrus, middle and superior frontal gyri and in the occipital gyrus in the MCs at their optimal ToD. Song and colleagues (2018) also did not find an overall synchrony effect in the Stroop Task but did report a significant decrease in the medial frontal gyrus, middle cingulate cortex, and thalamus in the MCs at their non-optimal time, while the activity in right inferior frontal gyrus, medial frontal gyrus, and middle cingulate cortex either remained stable in ECs.

3.4.3 Modulation of Chronotype, ToD, and Synchrony Effect by Age

Of 12 (of 65) studies that examined age-related influences, 11 studies examined synchrony effect comparing young and older adults (Anderson et al., 2014; Bonnefond et al., 2003; Hasher et al., 2002; Hogan et al., 2009; Iskandar et al., 2016; May, 1999; May et al., 1993; May & Hasher, 1998; Rothen & Meier, 2017; Schmidt et al., 2012b; West et al., 2002), and one study used a within-subject design assessing older MCs (but not ECs) in the morning and late afternoon (Yang et al., 2007).

Of 11 studies comparing younger (18-32 years) and older adults (50-95 years), seven studies reported a significant synchrony effect with both younger ECs and older MCs performing better at their optimal ToD on *verbal fluency* (Iskandar et al., 2016), *recognition* (May et al., 1993), *memory* (Hasher et al., 2002; May, 1999; May & Hasher, 1998), had lower error rates (West et al., 2002) and faster RTs (Schmidt et al., 2012b). However, Hogan and colleagues (2009) reported a synchrony effect on *associate learning* only in older MCs adults.

Anderson and colleagues (2014) reported a synchrony effect in priming only in old adults. They also conducted fMRI analysis in the same sample and reported that older adults tested in the morning were able to ignore more unattended stimuli than older adults tested in the afternoon and also showed higher activation in the rostral prefrontal and superior parietal cortex (similar to young adults). Rothen and Meier (2017) reported a significant synchrony effect in prospective memory in younger ECs adults but not in older MCs adults. Bonnefond and colleagues (2003) did not report any synchrony effect on visual discrimination and descending subtraction tasks. Lastly, Yang and colleagues (2007) reported that older MCs using a controlled retrieval strategy showed higher priming at optimal ToD; however, this relationship was not found for automatic retrieval.

3.5 Discussion

In this systematic review, we evaluated existing evidence to identify possible chronotype, ToD and synchrony effects in cognitive function in healthy adults. Our findings are discussed below.

3.5.1 Chronotype, ToD and Synchrony Effects

Our review showed no main effect of chronotype in the majority of reviewed studies (>80%; Section 3.1). The findings concerning the main effect of ToD also indicated no significant ToD effect in more than 2/3 of the studies (>70%; Section 3.1).

Our review concerning the synchrony effect revealed a mixed picture with about 45.31% of the examined studies in young adults (k=64, including 11 studies that examined both young and older age groups) reporting synchrony in both chronotypes or selectively in MCs or ECs. Synchrony effects were majorly but not entirely seen in three interrelated cognitive functions of *memory* (Anderson et al., 1991; Bennetts et al., 2008; Hasher et al., 2002; Hidalgo et al., 2004; Iskandar et al., 2016; May et al., 1993; May, 1999; Petros et al., 1990), *attention* (Facer-Childs et al., 2018, 2019; Fabbri et al., 2017; Lara et al., 2014; Martínez-Pérez et al., 2020; Matchock & Mordkoff, 2009; Mongrain et al., 2008; Natale et al., 2003; Palmero et al., 2022, 2024a, 2024b; Van Opstal et al., 2022), and *inhibition* (Lara et al., 2014; Martínez-Pérez et al., 2020) using different neuropsychological tests (e.g., PVT, Spatial Subtest of Multidimensional Aptitude Battery, Wisconsin Card Sorting Test, Attentional Network Task, Analogy Detection Task). It can be argued that cognitive parameters used in these studies required participants to suppress irrelevant thoughts, demanded higher attention, and critical information processing, suggesting cognitive operations involving executive control are more sensitive to synchrony effect. Furthermore, fMRI results also hinted towards an increased activation of inhibition-related brain regions [prefrontal cortex areas including percental, occipital gyrus and middle and superior frontal gyri (Kossowski et al., 2021), lateral inferior frontal gyrus (Song et al., 2018), and thalamus (Schmidt et al., 2012a, 2015)], in both chronotypes during the inhibition tasks.

Interestingly, an asynchrony effect or better performance at a non-optimal time on the Insight Problems, 184 Standardised Line Task, Convergent Task, and Semantic Analogy Task can also be observed (Nowack & Van Der Meer, 2018; Rothen & Meier, 2016; Simor & Polner, 2017; Wieth & Zacks, 2011) especially when attentional and inhibitory controls are weakened, which allows infiltration of stimuli less relevant to working memory, leading to novel, divergent, and creative ideas (Radel et al., 2015).

3.5.2 Chronotype, ToD, and Synchrony Effect Modulation by Age

About 63.63% (7 of 11) of the studies reported a significant synchrony effect with both young ECs and old MCs performing better at their optimal ToD on tasks involving memory and recognition (Hasher et al., 2002; Iskandar et al., 2016; May et al., 1993; May, 1999; May & Hasher, 1998), higher accuracy (West et al., 2002) and RTs (Schmidt et al., 2012b). Furthermore, there was evidence of a synchrony effect in older adults from the three of 12 studies that involved individuals aged 50-95 years on priming (Anderson et al., 2014; Yang et al., 2007) and associate learning (Hogan et al., 2009). The diurnal preference shifts from eveningness to morningness in adults aged over 55 (review, Adan et al., 2012; Chauhan et al., 2023), and this may make older adults more vulnerable towards cognitive deficits when tested in the evening. Therefore, the time when testing occurs is crucial in determining age-related differences in cognitive performance both in healthy and clinical samples, of note, neurocognitive disorders (e.g., dementia). These findings are clinically relevant, especially when conducting assessments for diagnosis of potential dementia or other cognitive disorders in older adults and determining treatments based on the assessment outcomes. Therefore, not acknowledging these synchrony related influences may result in exaggerated deficits and biased test outcomes in cognitive performance.

3.5.3 Limitation of the Reviewed Studies

In this section, we discuss some of the key methodological issues that are likely to have impacted the findings of the reviewed studies.

a) Inconsistency in Testing Time and Sub-Optimal Study Designs

There's no consensus in chronobiology literature regarding time of testing to best capture chronotype and/or synchrony effects. The examined studies employed a range of methods to investigate chronotype and/or ToD effects, as well as their interactions at various time points ranging from a 24-hours (Natale et al., 2003) to an extended period of two to five days (e.g., Baeck et al., 2014; Barclay & Myachykov, 2017; Correa et al., 2014; Facer-Childs et al., 2019; Iskandar et al., 2016; Mongrain et al., 2008; Reiter et al., 2021; Schmidt et al., 2012a, 2012b; Song et al., 2019; West et al., 2002), under different conditions including 36-hour wakefulness (Taillard et al., 2011), nap vs no nap (Zion & Shochat, 2019), and using bright vs dim light (Kossowski et al., 2021; Maierova et al., 2016; Rodríguez-Morilla et al., 2018). The testing period shows significant variability with morning sessions starting at 7:30 and/or 8:00 hour in

some studies (e.g., Barbosa & Albuquerque, 2008; Hidalgo et al., 2004; Lara et al., 2014; Rothen & Meier, 2016; Song & Stough, 2000), afternoon sessions at 12 noon, 14:00, 15:00, 16:00 hour and/or 18:00 hour (Anderson et al., 2014; Barbosa & Albuquerque, 2008; Hidalgo et al., 2004), and night session at 8:00 pm, 10:00 pm, midnight, and/or 2 am (e.g., Gobin et al., 2015; Lara et al., 2014; Martínez-Pérez et al., 2020; Reinke et al., 2015; Rothen & Meier, 2016; Van Opstal et al., 2022; Yaremenko et al., 2021). Furthermore, some studies did not report the exact time of testing (Carlson et al., 2023; Gijselaers et al., 2016; Killgore & Killgore, 2007; Ritchie et al., 2017; Schmidt et al., 2012a, 2012b). The reviewed studies varied considerably in procedures and cognitive parameters, and some studies had very limited range of chronotype scores which may have led to attenuated synchrony effects.

b) Individual Differences

Chronotype is a heavily studied construct, from Asia to Europe and the Americas to Oceania, with consistent findings reporting that chronotype may be sex- and age-dependent (Adan et al., 2012). The findings of this review, as discussed earlier, suggest a more consistent synchrony effect in older adults. Of the 65 studies we reviewed, 12 studies considered a potential influence of sex. Of these 12 studies, six controlled for seven (Gijselaers et al., 2016; Kossowski et al., 2021; McGowan et al., 2020; Song et al., 2018, 2019; Zion & Shochat, 2018, 2019), two reported not finding any sex-related differences in decision-making (Correa et al., 2017) and memory (Fabbri et al., 2013), and the remaining three reported sex-related differences in cognitive performance (Ceglarek et al., 2021; Killgore & Killgore, 2007; Palmero et al., 2022). Ceglarek and colleagues (2021) found males exert more effort on short-term memory in the evening while females remain unaffected. Killgore and Killgore (2007) found a positive association between higher eveningness and higher verbal cognitive ability in females. Recently, Palmero and colleagues (2022) reported an increased performance in MCs females and a decreased performance in the ECs, especially in the mid-luteal phase, compared to the follicular phase in sustained attention assessed using SART and PVT. Chronotype has also been linked to certain personality traits (Adan et al., 2012; Chauhan et al., 2024; Randler et al., 2017; Tsaousis, 2010), for example, extraversion and neuroticism (Chauhan et al., 2023). Most of the literature examining chronotype effects on cognitive functions, however, does not take into account or control for sex differences and/or personality traits.

c) Overseeing Seasonal Variations

Only six of the examined studies provided information on the season/s of testing (Gijselaers et al., 2016; Hidalgo et al., 2004; McGowan et al., 2020; Reinke et al., 2015; Zion & Shochat, 2018, 2019), with the majority (k=59) not reporting variations in day length over the year, especially in countries which use daytime saving methods (e.g., UK, USA, Germany, Poland). Seasonal changes and daytime saving temporarily disrupt the human circadian system, further influencing sleep-wake patterns and chronotypes (review, Adan et al., 2012; Chauhan et al., 2023).

d) Neglecting Reporting of Physiological Markers of Chronotype

Melatonin and cortisol secretion, as well as body temperature, are considered the gold-standard physiological biomarkers of chronotype, with studies reporting that peak secretion level and offset occur 3 hours earlier in MCs than ECs, at least in healthy samples (review, Adan et al., 2012; Chauhan et al., 2023). Forty-eight of the 65 examined studies did not examine any physiological data. Only 17 used a physiological marker (melatonin and/or body temperature), alongside a subjective measure of chronotype (Bennett et al., 2008; Bonnefond et al., 2003; Correa et al., 2014, 2017; Facer-Childs et al., 2019; Fimm et al., 2016; Lara et al., 2014; Maierova et al., 2016; Mongrain et al., 2008; Natale et al., 2003; Petros et al., 1990; Reiter et al., 2021; Ritchie et al., 2017; Rodríguez-Morilla et al., 2018; Schmidt et al., 2012a; Song & Stough, 2000; Taillard et al., 2011), which provides more comprehensiveness and robustness to the reported chronotype and/or ToD findings.

e) Environmental and Other Potential Confounding Factors

As expected, all examined studies were based on the chronotype approach, with some also measuring sleep quality, latency, inertia, alertness/arousal levels, daytime sleepiness, light conditions, napping, and wakefulness, task familiarisation in either laboratory settings or online. However, most of the reviewed studies did not report controlling for confounding variables. Not surprisingly, some studies reported that independent of chronotype, improved sleep quality was linked to better memory, sustained attention (Gobin et al., 2015), and decision-making (McGowan et al., 2020). Other studies reported the role of sedimentary behaviour in predicting processing speed (Gijselaers et al., 2016), poor cognitive performance attributed to sleep inertia (Ritchie et al., 2017), severe social jetlag (McGowan et al., 2020), dim light condition (Maierova et al., 2016; 1000lx), and sleep deprivation (Song et al., 2019), and good performance after napping (Zion & Shochat, 2019). It is worth mentioning the role

of environmental temperature (e.g., testing laboratory) in influencing an individual's arousal level and cognitive performance (Zhang et al., 2019).

3.5.4 Conclusion and Future Directions

Based on the findings of this review, we conclude that chronotype (on its own) does not strongly or consistently impact cognitive function in healthy adults. We highlight the importance of synchrony (chronotype x ToD) effects in inter-individual differences in cognitive performance, especially in older adults. These effects have far-reaching implications ranging from education, well-being to clinical diagnosis and treatment. To capture them more fully and accurately, we make a number of recommendations for future research.

First, we suggest that future studies should aim to employ a consistent testing time within a study and transparency in reporting the season of testing to allow robust replication studies and reduce between-study variations. This is particularly relevant given that post-COVID-19 work lifestyle and work-schedule are largely influenced by individuals' abilities and preferences for setting their schedules, making it harder to replicate any previously reported chronotype and synchrony related effects.

Second, we recommend future studies to control for season of testing, seasonal daytime changes, light conditions in the laboratory, room temperature, and other relevant exogenous factors that might influence chronotype and certain cognitive indices (e.g., alertness and vigilance) in all age groups.

Third, we recommend future studies to use comprehensive cognitive batteries to delineate chronotype, ToD and synchrony effects. Cognitive domains are not unitary in nature and involve a cohesive set of functions which could be measured via various parameters, both simple and complex, requiring crystallised and fluid sources of information, respectively (e.g., Hopkins Verbal Learning Test vs N-Back). With respect to task sensitivity, they may not behave similarly to circadian fluctuations and produce non-existent, attenuated or strong synchrony effects.

Fourth, we recommend future studies to also control for sleep-wake patterns, sleep disruption and quality, personality and to have large enough samples to accurately detect the relationship. We further call for transparency in reporting chronotype classification (e.g., the exact criteria

for defining MCs, ECs, and ICs rather than groups based on arbitrary median splits). Studies should also aim to have a sufficient number of males and females to allow meaningful investigation of sex differences and control for or report hormonal variations and contraception use, given their influence on cognitive performance (Munro et al., 2012; Palmero et al., 2022; Warren et al., 2014).

Lastly, we encourage future studies to examine physiological data (e.g., body temperature, melatonin and cortisol levels, heart rate, actigraphy, and skin conductance) while studying chronotype and ToD effects on cognition, considering that chronotype has a specific physiological manifestation which fluctuates throughout the day and is linked to arousal, alertness, and attentional levels.

Chapter 4: Thesis Aims and Objectives

For centuries, the phrase '*early to bed and early to rise, makes a person healthy, wealthy, and wise*' has highlighted the role of morningness in good mental, physical, and cognitive health. This phrase, deeply embedded in many cultures, may drive our modern-day society and human consciousness. It is based on one of the most studied biological rhythms in humans, called CRs, a masterstroke of natural selection which oscillates periodically over a 24-hour cycle to facilitate our adaptability to the Earth's rotation (Foster & Kreitzman, 2004). CRs oscillates periodically causing considerable inter-individual variations, known as chronotype (Adan et al., 2012). Chronotype is a multidimensional construct (Chauhan et al., 2023) that reflects an individual's circadian preference for sleep cycle and optimal task performance (Adan et al., 2012). In relation to chronotype and human cognitive performance, individuals are typically categorised as MCs (i.e., morning preference for task performance), ECs (i.e., evening preference for task performance), and ICs (i.e., no preference for task performance).

As discussed in Chapter 2, a vast amount of literature has repeatedly argued that sleep timings (early or late) influence mental and cognitive health (Chapter 3). A growing number of studies have also indicated an overlap between the effects of sleep quality, certain personality traits, and chronotype on mental health outcomes (Chapter 2, Section 2.5). Despite this, the general view in the chronobiology research has been that chronotype is an 'independent transdiagnostic risk factor' for poor mental health beyond the apparent effect of sleep quality. Similarly, the literature generally suggests that chronobiological variables (i.e., chronotype, ToD, synchrony effect) influence cognitive functions, especially in older adults. However, as highlighted in Chapter 3 (Section 3.5.3), various methodological limitations (of note, limiting the testing sample to either MCs or ECs, comparison of young ECs vs old MCs, failure to report or control for personality, sleep-related disturbance and variable testing times) make it difficult to draw a clear picture about the unique influence of chronotype on mental health and cognition.

This PhD thesis, therefore, aimed to investigate the influence of chronotype and sleep quality on mental health and cognitive functions, while also considering psychopathology-related personality traits, in young non-clinical adults in related empirical studies.

4.1 Aims and Objectives

The empirical chapters reported in this thesis present data collected from young non-clinical adults residing in the UK (Chapters 6-8), India (Chapter 5), and Germany (Chapter 6) and address the following overarching aims:

i. To examine the inter-relationships of chronotype, mental health, sleep quality, psychopathology-related personality traits and childhood trauma.

ii. To examine the role of sleep quality in the chronotype-mental health relationship.

iii. To examine chronotype, ToD, synchrony effects on verbal learning and memory and sensorimotor processing.

For these empirical investigations (Chapters 5-8), all participants provided demographic information (age, sex, ethnicity, BMI, shiftwork and employment/education status, medication use, drug/stimulant consumption) and were assessed on psychometric measures of chronotype, sleep quality, personality, schizotypy, impulsivity, and childhood trauma. For the experimental work conducted to address the third aim (Chapters 7 and 8), MC, IC and EC participants from the UK-based sample were invited to partake in two identical sessions, once in the morning (8:00-10:00 hour) and once in the late afternoon (16:00-18:00 hour), one week apart. They were assessed on verbal learning and memory and PPI of the acoustic startle response (a measure of sensorimotor gating), and completed a sleep questionnaire on both occasions.

4.2 Plan of Investigation

This thesis contains results from four empirical investigations:

i. Two psychometric studies investigating the relationship between chronotype, mental health, sleep quality, psychopathology-related personality traits, and childhood trauma, as well as the role of sleep quality in the chronotype-mental health relationship (Chapters 5 and 6).

ii. A behavioural study investigating the effects of chronobiological variables on verbal learning and memory (Chapter 7); and

iii. A psychophysiology study investigating the effects of chronobiological variables on PPI of the acoustic startle response (Chapter 8).

PART II

Chapter 5: Examining the role of Sleep Quality in Chronotype-Mental Health Relationship: A Psychometric Study in Young Indian Adults
Chapter 6: Chronotype and Mental Health Relationship: Evidence from the UK and Germany
Chapter 7: Influence of Chronotype and Sleep Quality in Verbal Learning and Memory: An Experimental Study
Chapter 8: Circadian Rhythmicity in Prepulse Inhibition of the Acoustic Startle Response: A Study of Chronotype and Time-of-Day Effects in Young Healthy Adults

Chapter 5: Examining the role of Sleep Quality in Chronotype-Mental Health Relationship: A Psychometric Study in Young Indian Adults

The work reported in this chapter has been published in *NPJ Mental Health* as:

Chauhan, S., Pandey, R., Vakani, K., Norbury, R., Ettinger, U., & Kumari, V. (2024). Sleep quality mediates the association between chronotype and mental health in young Indian adults. *NPJ Mental Health Research*, *3*(1), 31. https://doi.org/10.1038/s44184-024-00076-9 (Appendix 9.2).

Abstract

There is increasing recognition of EC as a potential independent risk factor for poor mental health. To examine the chronotype-mental health relationship while also quantifying the potential roles of poor sleep quality, relevant personality traits, and childhood trauma, 282 young adults (18–40 years; 195 females) residing in North India, were assessed between January and March 2023 (to control for seasonal variation), using self-report measures of chronotype, sleep patterns, mental health (depression, anxiety, and stress), personality traits (extraversion, neuroticism, schizotypy, and impulsivity), and childhood trauma. The results showed a significant association between EC and poor mental health but this association was fully mediated by poor sleep quality. Neuroticism, emotional abuse and cognitive disorganisation were correlated with EC as well as with poor mental health and sleep quality. Neuroticism and emotional abuse, but not cognitive disorganisation, also had indirect effects on mental health via sleep quality. These findings highlight the crucial role played by sleep quality in the chronotype-mental health relationship.

5.1 Chapter Aims and Overview

This chapter reports an empirical study conducted to examine the inter-relationship between chronotype, sleep quality, mental health, psychopathology-related personality traits, and childhood trauma as well as the role of sleep quality in chronotype-mental health relationship within the homogenous sample of non-clinical Indian adults.

5.2 Introduction

Chronotype is a multidimensional construct which reflects behavioural consequences and manifestations of various circadian mechanisms (Chauhan et al., 2023). It is known to exist on a continuum between two extremes, i.e., MCs and ECs. Most individuals, however, fall in the middle of this continuum and are called ICs. There is considerable evidence that EC is associated with adverse mental health outcomes, such as depression (Norbury, 2021; Taillard et al., 2021; Taylor et al., 2020; Walsh et al., 2022), anxiety (Ashi et al., 2022; Evans & Norbury, 2021), psychosis (Lemoine et al., 2013; Linke et al., 2021), impulsive and maladaptive behaviour (Deibel et al., 2020; Yilbas & Günel Karadeniz, 2022), and substance abuse (Taylor & Hasler, 2018). Furthermore, personality traits that are known to be associated with a higher risk of developing these mental disorders or problematic behaviours, namely, neuroticism (linked to depression and anxiety disorders; Kang et al., 2023), schizotypy (psychosis; Ettinger et al., 2014) and impulsivity (substance abuse; Kozak et al., 2019) also show a positive association with EC in non-clinical samples in some studies (Adan et al., 2012; Chauhan et al., 2023; Metts et al., 2021). On the other hand, extraversion which is associated with a lower risk for mental disorders (Adan et al., 2012; Chauhan et al., 2023) may have a small association with the MC (Muzni et al., 2021).

There are reports of ECs having poor quality or altered sleep patterns (Nielsen, 2010; Vardar et al., 2008), including spending less time in bed during weekdays, shorter sleep duration, daytime sleepiness and dysfunction, irregular sleep-wake cycles, and a need for more sleep on weekends (Carciofo et al., 2014; Fernandez-Mendoza et al., 2010; Sun et al., 2019; Vardar et al., 2008). Such self-reported sleep alterations are also common in various mental illnesses, for example major depression or anxiety disorders (Alvaro et al., 2014; Okun et al., 2018; Scott et al., 2021; Tsuno et al., 2005). Furthermore, poor sleep quality has been consistently found in people with a history of childhood abuse/trauma (Brindle et al., 2018; McKay et al., 2021;

Sheffler et al., 2023), and childhood maltreatment is an established risk factor for many disorders, including depression, anxiety, psychosis, personality disorder, post-traumatic stress disorder, and substance abuse (Beards et al., 2020; Pandey et al., 2020; van Nierop et al., 2012). Whether and to what extent a history of childhood trauma might influence any relationship between chronotype and mental health, however, remains unclear.

Against the backdrop of previous findings supporting a direct association between EC and poor mental health (Ashi et al., 2022; Evans & Norbury, 2021: Taillard et al., 2021), a study conducted in the UK by Horne and colleagues (2018) reported a positive association between EC and depressive symptomatology and this association was partly mediated by subjective sleep quality. A more recent UK study by Muzni and colleagues (2021) involving a large non-clinical adult sample suggested a much stronger relationship between poor sleep quality and adverse mental health (with medium-to-large effect sizes), relative to that observed between EC and poor mental health (negligible-to-small effect sizes), especially in females. These findings raise doubts about the widely publicised association of EC with poor health outcomes, at least in the general population. There are, however, no data examining the chronotype-mental health relationship while also quantifying the influence of sleep quality, chronotype-relevant personality traits, and childhood trauma within the same homogenous sample of non-clinical adults.

The main aim of the present study, therefore, was to determine the association between chronotype and mental health (depression, anxiety, and stress) in young (18-40 years) males and females, with a particular focus on the roles of sleep quality, relevant personality traits (neuroticism, schizotypy, impulsiveness, and extraversion), and childhood trauma. We tentatively hypothesised, based on the findings of Muzni and colleagues (2021), that both EC and poor sleep quality would be associated with higher levels of depression, anxiety, and stress, with these associations being stronger for sleep quality than for EC. Lastly, we explored possible associations between chronotype, sleep quality, personality traits, childhood trauma and mental health, and examined the influence of personality traits and childhood trauma, while also considering sleep quality, in the chronotype-mental health relationship.

5.3 Methods

5.3.1 Participants

The data were collected from young adults (N=313, age range 18-40 years) residing in different parts of Northern India between January and March 2023 with average daytime temperatures ranging between 14 and 23 degrees Celsius. The age range was restricted to 18-40 years given previous evidence of age-related changes in chronotype (Ronneberg et al., 2003).

Of 313, 31 participants had to be excluded for failing our attention check criteria (i.e., failed to enter a given response to one or more of the four catch items; N=20) or due to non-completion of some measures (N=11), leaving a final sample of 282 participants (195 females, 87 males) who completed all self-report measures online in a single session. The inclusion criteria required all participants to be aged between 18-40 years and living in India, be fluent in English, not be on any regular medication, not have a history of any diagnosed mental disorders or drug abuse (any past or current use of non-prescribed drugs), and be able to provide written informed consent. Their participation was voluntary, and no compensation was provided. This study was approved by the Research Ethics Committee, College of Health, Medicine, and Life Sciences, Brunel University of London (ref no. 41125-MHR-Mar/2023- 44225-4).

5.3.2 Self-Report Measures

5.3.2.1 Chronotype

The MEQ (Horne & Ostberg, 1976), which is a self-report questionnaire comprising of 19 items, was used to assess chronotype. The questionnaire has both a Likert scale (e.g., *item 19: are you a morning or evening type?*) and time scale (e.g., *item 18: at approximately what time of the day do you usually feel your best?).* Twelve items on the Likert scale present four options, with the lowest values indicating definite eveningness. The remaining seven items on the time scale are divided into periods of 15 minutes, spanning a time frame of seven hours. Higher scores indicate a preference for morningness and lower scores indicate a preference for eveningness. The scale has high internal consistency (*a*=0.83; Horne & Ostberg, 1976, *a*=0.76 in the current sample).

5.3.2.2 Mental Health

Depression, anxiety, and stress levels were assessed using the 21-item *Depression, Anxiety and Stress Scale* (DASS-21; Lovibond & Lovibond, 1995). It has three sub-scales: Depression, Anxiety, and Stress. Each sub-scale consists of seven items. The participants respond to each

item based on their feelings on most days over the past week. The Depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest, anhedonia, and inertia. The Anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The Stress scale assesses difficulty relaxing, nervous arousal, getting easily upset, agitated, irritable, over-reactive, and impatient. The sub-scales are reported to have high reliability coefficients (Depression, a=0.83-0.94; Anxiety, a=0.66-0.87; Stress, a=0.79-0.91; Lee et al., 2019). The Cronbach's alphas for Depression (a=0.88), Anxiety (a=0.84), and Stress (a=0.81) sub-scales also indicated good internal consistency in the current sample.

5.3.2.3 Sleep Quality

Sleep quality was assessed using the *Pittsburgh Sleep Quality Index* (PSQI; Buysse et al., 1989). The PSQI is a 19-item scale assessing daytime dysfunction, use of sleeping medication, sleep disturbances, habitual sleep efficiency, sleep duration, sleep latency, and subjective sleep score. Participants answer the PSQI questions for each of these components by relating them to their past month. Each component is scored from "No difficulty" (0) to "Severe difficulty" (3) and tallied up to yield a total score (range 0-21). Higher scores indicate poor sleep quality. The PSQI (global score) is reported to have a high internal consistency (a=0.83) and test-retest reliability (r=0.85), with a sensitivity of 89.6% and a specificity of 86.5% (Buysse et al., 1989). Cronbach's alpha for the PSQI (global score) in the current sample was 0.67.

5.3.2.4 Personality Traits

Extraversion, Neuroticism, and Psychoticism were measured using the short 48-item *Eysenck Personality Questionnaire-Revised* (EPQR-S; Eysenck & Eysenck, 1992). It has three sub-scales, corresponding to the three personality dimensions in the Eysenck's model of personality, plus a lie scale (Eysenck & Eysenck, 1992). Each scale contains 12 items with a binary response, 'Yes' or 'No' (scored as 1 or 0). Extraversion (a=0.74-0.84) and Neuroticism scales (a=0.70-0.77) are known to have good reliability but the Psychoticism scale is reported to have less-than-satisfactory reliability (a=0.33-0.52, Forrest et al., 2000; as was also the case in the current sample (Extraversion, α=0.82; Neuroticism, α=0.82; Psychoticism, α=0.27).

Schizotypal personality traits were assessed using the short version of the *Oxford-Liverpool Inventory of Feelings and Emotions* (s-OLIFE; Mason et al., 1995, 2005). It is a 43-item

questionnaire with high reliability (*a*=0.78-0.87) as well as good convergent and discriminant validity (Fonseca-Pedrero et al., 2015). Each item belongs to one of the four sub-scales: (i) Unusual Experiences (12 items; describing perceptual aberrations, magical thinking, and hallucinations), (ii) Cognitive Disorganization (11 items; covering aspects of poor attention, concentration, decision-making, and social anxiety), (iii) Introvertive Anhedonia (10 items; describing a lack of enjoyment from social and physical sources of pleasure as well as avoidance of intimacy), and (iv) Impulsive Non-conformity (10 items; describing impulsive, anti-social, and eccentric forms of behaviour, often suggesting a lack of self-control). All items require a Yes/No response (scored 1 or 0). Higher scores indicate higher levels of schizotypy. Cronbach's alphas in the current sample for Unusual Experiences, Cognitive Disorganisation, Introvertive Anhedonia, and Impulsive Nonconformity were 0.75, 0.81, 0.44, and 0.54, respectively.

Impulsivity was assessed using the *Impulsive Behaviour Scale-Short Version* (S-UPPS-P; Cyders et al., 2014). It is a 20-item self-report measure with adequate reliability (*a*=0.74-0.88; Cyders et al., 2014). Each item is rated on a four-point Likert scale (1: disagree strongly, 2: disagree some, 3: agree some, and 4: agree strongly). There are five (5-item) sub-scales: Lack of Perseverance (inability to stay focused on a task), Lack of Premeditation (inability to account to the repercussions of actions), Sensation Seeking (tendency to seek unique and exciting experiences), Negative Urgency (tendency to react rashly in an intense negative mood), and Positive Urgency (tendency to react rashly in an intense positive mood). Higher scores indicate higher levels of impulsivity. Cronbach's alphas in the current sample for Negative Urgency, Lack of Perseverance, Lack of Premeditation, Sensation Seeking, Positive Urgency were 0.73, 0.55, 0.73, 0.66, and 0.78, respectively.

5.3.2.5 Childhood Trauma

Childhood trauma was assessed using the short form of the *Childhood Trauma Questionnaire* (CTQ-SF; Bernstein et al., 2003). It consists of 28 items on histories of abuse and neglect. It has five 5-item sub-scales, measuring emotional, physical, and sexual abuse, and emotional and physical neglect. All items are rated from ‘never true’ (score 1) to ‘very often true’ (score 5), and after reversing seven items, the scores on all sub-scales can range between 5 and 25. The final scores are classified as ‘none to minimal’, ‘low to moderate’, ‘moderate to severe’, and ‘severe to extreme’. Three additional items compose the minimisation/denial sub-scale for

detecting socially desirable responses or false-negative trauma reports. The total CTQ score reflects the severity of multiple forms of abuse and neglect. These sub-scales are reported to have high test-retest reliability (α=0.79-0.86) and internal consistency (α=0.66-0.92; Bernstein et al., 2003), though in the current sample, Cronbach's alphas for Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, and Physical Neglect were 0.81, 0.87, 0.89, 0.82, and 0.58, respectively.

5.4 Statistical Analysis

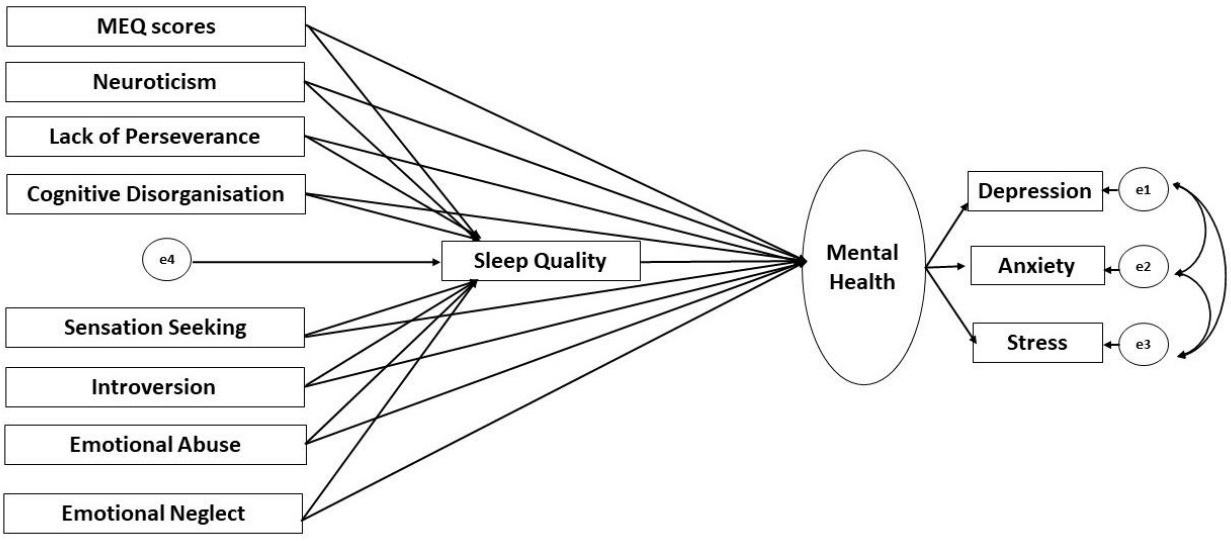
Data were analysed using Statistical Package for Social Sciences (SPSS, for macOS, version 28; IBM, New York, United States), unless specified otherwise. Alpha level for testing the significance of effects was maintained at $p \leq 0.05$, unless stated.

The data on all self-report measures were examined and found to be suitable (skewness and kurtosis <±2) for parametric statistical approaches. The Psychoticism sub-scale of the EPQR-S was excluded from all analysis due to its low reliability in the current sample (α=0.27) (a common problem with this sub-scale, as mentioned earlier). We explored possible sex differences in various self-report measures using independent sample *t*-tests. Since we considered chronotype as a continuous variable, Pearson's *r* was used to examine the associations of chronotype with mental health (Depression, Anxiety, Stress), personality traits (Extraversion, Neuroticism, Schizotypy, and Impulsivity), and childhood trauma scores, followed by Fisher's Exact *z*-test to test for significant differences in chronotype-mental health and sleep-mental health correlations as well as any sex differences in these correlations. Effect sizes for correlation coefficients were interpreted based on Cohen (1988) (*r* value +/-0.1 to +/-0.29 as small, +/-0.3 to +/-0.49 as medium, and +/- 0.5 to +/- 1 as large).

Given significant associations of EC with mental health, sleep quality, certain personality traits (Extraversion, Neuroticism, Cognitive Disorganisation, Lack of Perseverance, Lack of Premeditation, Sensation Seeking), and childhood emotional abuse and neglect (see Results), we conducted structural equation modelling (SEM) in SPSS AMOS with scores on the MEQ, personality traits, childhood emotional abuse and neglect as predictors, PSQI scores (sleep quality) as a mediator, and mental health (a latent construct, incorporating depression, anxiety, and stress) as the outcome variable (Figure 5.1). All predictor, mediator, and outcome variables were checked for multicollinearity, with no significant violation (variance inflation factor <5, tolerance >0.2) found in the measured cases. The predictors were allowed to covary in the

proposed model (see Figure 5.1) and the maximum likelihood method was used to test the model fit and calculate the parameter estimates of path coefficients. We used the comparative fit index (CFI; >0.95 represents good model fit), root mean square of approximation (RMSEA; value <0.80 represents good fit), the ratio of maximum-likelihood chi-square to the degree of freedom (χ^2/df; acceptable value <5), the goodness of fit index (GFI; acceptable value >0.95), Tucker Lewis Index (TLI;>0.95), and adjusted goodness of fit index (AGFI, acceptable value >0.90) to evaluate the global fit of the model (Hooper et al., 2008). A global fitting model may have local misfit (i.e., presence of nonsignificant direct/indirect effects), therefore, the statistical significance of the indirect and direct effects was tested based on bias-corrected 95% bootstrap confidence intervals and associated *p* values. The model was then revised to exclude non-significant paths (Figure 5.2; see Results) one-by-one leaving us with the significant direct or indirect paths in the final model (Figure 5.3). The invariance of the model was inferred if the fully constrained model (measurement weights of measurement model of mental health as well as the structural weights, covariances and residuals were constrained to be equal in males and females) did not differ significantly from the unconstrained model. A non-significant chi-square difference ($\Delta\chi 2$ with p>0.05), ΔCFI $\leq$0.005, and ΔRMSEA $\leq$0.01 is considered as evidence for invariance of a given model (Chen, 2007; Yuan & Chan, 2016).

Figure 5.1 *Schematic representation of proposed structural model showing the direct and indirect effects (via sleep quality) of chronotype (higher MEQ scores represent a greater preference for morningness and lower scores a greater preference for eveningness), personality traits, and childhood trauma (predictors) and mental health (outcome) relationship using SEM framework. All predictors were allowed to covary. The latent variable is indicated*



in an oval shape, observable variables in a rectangle shape, and e1, e2, e3, and e4 are residuals.

5.5 Results

5.5.1 Sample Characterisation

The majority of the sample comprised of Asian Indians (92.2%), pursuing a bachelor's degree or above (95.7%). Just over half (54.3%) of the sample self-reported consuming caffeine, and only 0.7% self-reported consuming alcohol (Table 5.1). About half of the sample (47.51) reported normal BMI, and a significant proportion (46.45%) reported being underweight (as also seen in other young North Indian cohorts; Dutta et al., 2019). Just over half of sample (55.3%) met the PSQI criteria for good sleep (score ≤5).

Table 5.1 *Demographic characteristics of the study sample.*

Demographic Characteristics	N=282	Frequency (%) of N=282
Ethnicity	Asian Indian	92.2%
	European White	0.8%
	Other Ethnic Groups	4.1%
	Prefer not to say	2.8%
Stimulant/Sedative Consumption	Caffeine	54.3%
	Nicotine	4.3%
	Alcohol	0.7%
	None	40.8%
Body Mass Index (BMI)[a]	Underweight (<18.5)	46.45%
	Normal (18.5-24.9)	47.51%
	Overweight (25-30)	4.25%
	Obese (30 and above)	0%
Education/Employment	Student	95.7%
	Full-time Work	4.3%
	Part-time Work	0%
Medication	Yes	0%
	No	92.6%
	Prefer not to say	7.4%
Sleep Quality[b]	Good (≤5)	55.3%
	Poor (6-15)	44.7%

[a]BMI data missing for 5 participants
[b]Individuals scoring 5 or below on the PSQI were categorised as good sleepers and those scoring above 5 and below 15 (highest score in our sample) as poor sleepers.

Females were younger than males (t_{280}=4.04, p<0.001), had significantly lower BMI (t_{275}=4.24, p<0.001), had a higher morning preference (t_{280}=4.53, p<0.001), and rated themselves as having poorer sleep quality (t_{280}=4.09, p<0.001). They also scored higher than males on Neuroticism (t_{280}=5.62, p<0.001), Depression (t_{280}=2.14, p=0.033), Anxiety (t_{280}=2.07, p=0.039), Stress (t_{280}=3.48, p<0.001), Cognitive Disorganisation (t_{280}=3.11, p=0.002), Lack of Perseverance (t_{280}=3.06, p=0.002), Lack of Premeditation (t_{280}=2.85, p=0.005), and Emotional Abuse (t_{280}=2.56, p=0.011) (Table 4.2). Males had higher scores than females for Sensation Seeking (t_{280}=7.30, p=0.001), Positive Urgency (t_{280}=3.84, p=0.001), and Physical Neglect (t_{280}=3.49, p=0.001) (Table 5.2).

Table 5.2 *Descriptive statistics for self-report measures (chronotype, mental health, sleep quality, personality traits and childhood trauma).*

Study Variables			Males (*n*=87)		Females (*n*=195)		Entire Sample (N=282)	
			Mean ± SD	**Sample Range**	**Mean ± SD**	**Sample Range**	**Mean ± SD**	**Sample Range**
Age			26.26±4.80	18-40	23.98±4.17	18-40	24.68±4.49	18-40
Chronotype	MEQ		53.31±9.05	31-77	47.98±9.11	27-70	49.63±9.40	27-77
Mental Health	DASS-21	Depression	11.90±10.24	0-42	14.98±11.50	0-42	14.03±11.20	0-42
		Anxiety	11.60+9.33	0-42	14.28±10.32	0-42	13.46±10.08	0-42
		Stress	12.20±8.59	0-42	16.25±9.18	0-42	15.00±9.18	0-42
Sleep Quality	PSQI	Sleep Quality	0.91±0.66	0-3	1.22±0.78	0-3	1.13±0.76	0-3
		Sleep Latency	0.80±0.69	0-2	1.02±0.71	0-2	0.95±0.71	0-2
		Sleep Duration	1.03±0.78	0-3	1.03±0.83	0-3	1.03±0.81	0-3
		Sleep Efficiency	0.66±1.01	0-3	0.80±1.02	0-3	0.76±1.02	0-3
		Sleep Disturbance	1.09±0.49	0-3	1.29±0.53	0-3	1.23±0.53	0-3
		Sleep Medication	0.05±0.23	0-1	0.22±0.67	0-3	0.17±0.58	0-3
		Daytime Dysfunction	0.75±0.80	0-3	1.2±0.85	0-3	1.06±0.86	0-3
		Global Score	4.67±2.31	0-13	6.02±2.63	1-15	5.60±2.61	0-15
Personality Traits	EPQ-S	Extraversion	7.28±3.02	0-12	6.56±3.52	0-12	6.79±3.39	0-12
		Neuroticism	5.47±3.23	0-12	7.80±3.20	0-12	7.08±3.38	0-12
	s-OLIFE	Unusual Experience	5.34±3.172	0-12	5.43±2.89	0-12	5.40±2.97	0-12
		Cognitive Disorganisation	4.95±3.16	0-11	6.23±3.20	0-11	5.84±3.24	0-11
		Introvertive Anhedonia	3.48±1.80	0-8	3.66±1.93	0-9	3.60±1.89	0-9
		Impulsive Nonconformity	3.56±2.03	0-9	3.54±2.12	0-9	3.54±2.09	0-9
		s-OLIFE Total	17.34±8.05	1-36	18.87±7.71	3-36	18.40±7.84	1-36
	S-UPPS-P	Negative Urgency	10.49±2.98	4-16	9.98±2.97	4-16	10.14±2.98	4-16
		Lack of Perseverance	6.72±1.87	4-11	7.52±2.10	4-14	7.28±2.06	4-14
		Lack of Premeditation	6.27±1.95	4-11	7.08±2.28	4-14	6.83±2.21	4-14
		Sensation Seeking	12.74±2.16	7-16	10.43±2.70	4-16	11.14±2.76	4-16
		Positive Urgency	10.26±3.21	4-16	8.75±2.95	4-16	9.22±3.10	4-16
		Emotional Abuse	9.56±4.26	5-25	11.15±5.031	5-25	10.66±4.85	5-25

Childhood Trauma	CTQ-SF	Physical Abuse	8.49±4.24	5-25	8.14±4.58	5-25	8.25±4.47	5-25
		Sexual Abuse	8.13±4.31	5-21	9.04±5.20	5-25	8.76±4.95	5-25
		Emotional Neglect	11.55±4.26	5-21	11.98±4.97	5-25	11.85±4.76	5-25
		Physical Neglect	9.85±3.27	5-17	8.35±3.22	5-19	8.81±3.30	5-19
		CTQ Total	47.59±16.37	25-100	48.68±17.49	25-110	48.35±17.13	25-110

Abbreviations: MEQ, Morningness-Eveningness Questionnaire; PSQI**,** Pittsburgh Sleep Quality Index; EPQ-SF, Eysenck Personality Questionnaire-Revised; DASS-21, Depression Anxiety and Stress Scale-21 Items; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; S-UPPS-P, Impulsive Behaviour Scale-Short Version; CTQ-SF, Short Form of Childhood Trauma Questionnaire.

5.5.2 Chronotype, Sleep Quality, Mental Health, Personality Traits and Childhood Trauma

EC (i.e., lower MEQ scores) correlated with higher scores on Depression (r=-0.308, p=0.001), Anxiety (r=-0.213, p=0.001), Stress (r=-0.267, p=0.001) scales; higher scores on personality measures of Neuroticism (r=-.299, p=0.001), Cognitive Disorganisation (r=-0.287, p=0.001), Lack of Perseverance (r=-0.181, p=0.002), Lack of Premeditation (r=-.180, p=0.002), and Sensation Seeking (r=-.215, p=0.001); as well as Emotional Abuse (r=-0.196, p=*0*.001) and Emotional Neglect (r=-0.153, p=0.001) (Table 5.3). MC was associated with higher Extraversion scores (r=0.222, p=0.001) (Table 5.3). Of these correlations, the correlation between eveningness and Lack of Premeditation appeared stronger in males than females (Fisher's Exact z=2.01, p=0.044) though this sex difference failed to maintain statistical significance after Bonferroni correction for multiple comparisons (p>0.0025). BMI did not correlate significantly with chronotype, any personality traits, sleep quality, and mental health.

Poor sleep quality (i.e., higher PSQI scores) correlated with higher levels of Depression (r=0.489, p<0.001), Anxiety (r=0.474, p<0.001), Stress (r=0.518, p<0.001); higher scores on personality measures of Neuroticism (r=0.433, p<0.001), Unusual Experiences (r=0.168, p=0.001), Cognitive Disorganisation (r=0.294, p=0.001), Introvertive Anhedonia (r=0.150, p=0.012), Impulsive Nonconformity (r=0.198, p=0.001), and Negative Urgency (r=0.141, p=0.017); and severity of self-reported Emotional Abuse (r=0.377, p=0.001), Emotional Neglect (r=0.275, p=0.001), and Physical Abuse (r=0.164, p=0.006). Poor sleep also correlated with lower scores on Extraversion (r=-0.125, p<0.001) (Table 5.4). Poor sleep quality correlated with EC (r=-0.389, p<0.001); although this correlation appeared stronger in females than males (Fisher's Exact z=2.17, p=0.029), this sex difference did not survive correction for multiple comparisons (p>0.0025). Lastly, compared to EC, poor sleep quality showed significantly stronger correlations, as expected, with Depression (Fisher's Exact

z=2.55, p=0.01), Anxiety (Fisher's Exact z=3.53, p<0.001), and Stress (Fisher's Exact z=3.54, p<0.001).

Table 5.3 *Correlations (Pearson's r) between chronotype and measures of mental health, sleep quality, personality traits and childhood trauma.*

	Mental Health			Sleep Quality	Personality Traits										Childhood Trauma					
	DASS-21				EPQ-SF		s-OLIFE				S-UPPS-P				CTQ-SF					
	D	A	S	PSQI	E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN
MEQ (Overall)	-0.308 (0.001)	-0.213 (0.001)	-0.267 (0.001)	-0.389 (0.001)	0.299 (0.001)	-0.222 (0.001)	-0.078 (0.194)	-0.287 (0.001)	-0.086 (0.152)	-0.084 (0.157)	-0.067 (0.265)	-0.181 (0.002)	-0.180 (0.002)	0.215 (0.001)	0.079 (0.186)	-0.196 (0.001)	0.034 (0.567)	0.073 (0.219)	-0.153 (0.001)	0.006 (0.923)
Males	-0.204 (0.057)	-0.057 (0.597)	-0.111 (0.307)	-0.163 (0.132)	0.274 (0.010)	-0.199 (0.065)	-0.103 (0.341)	-0.267 (0.012)	-0.103 (0.343)	-0.017 (0.879)	-0.028 (0.796)	-0.288 (0.007)	-0.326 (0.002)	0.198 (0.066)	0.025 (0.817)	-0.193 (0.073)	0.012 (0.912)	0.062 (0.566)	-0.093 (0.393)	-0.106 (0.328)
Females	-0.320 (0.001)	-0.241 (0.001)	-0.274 (0.001)	-0.421 (0.001)	0.179 (0.012)	-0.252 (0.001)	-0.064 (0.376)	-0.245 (0.001)	-0.066 (0.357)	-0.119 (0.097)	-0.118 (0.099)	-0.084 (0.245)	-0.075 (0.299)	0.103 (0.151)	0.020 (0.781)	-0.153 (0.033)	0.032 (0.662)	0.113 (0.114)	-0.168 (0.019)	-0.028 (0.702)

Abbreviations: MEQ, Morningness-Eveningness Questionnaire; D, Depression; A, Anxiety; S, Stress; DASS-21, Depression Anxiety and Stress Scale-21 Items; PSQI**,** Pittsburgh Sleep Quality Index; E, Extraversion; N, Neuroticism; EPQ-SF, Eysenck Personality Questionnaire-Revised; UE, Unusual Experience; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; NU, Negative Urgency; LP, Lack of Perseverance; LPr, Lack of Premeditation; SS, Sensation Seeking; PU, Positive Urgency; S-UPPS-P, Impulsive Behaviour Scale-Short Version; EA, Emotional Abuse; PA, Physical Abuse; SA, Sexual Abuse; EN, Emotional Neglect; PN, Physical Neglect; CTQ-SF, short form of Childhood Trauma Questionnaire.

Table 5.4 *Correlations (Pearson's r) between measures of mental health, sleep quality, personality traits and childhood trauma.*

	Mental Health			Sleep Quality	Personality Traits															Childhood Trauma	
	DASS-21				EPQ-SF		s-OLIFE					S-UPPS-P								CTQ-SF	
	D	A	S	PSQI	E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN	
D		0.704	0.758	0.489	-0.261	0.526	0.288	0.496	0.305	0.376	0.324	0.236	0.325	-0.204	0.169	0.457	0.230	0.141	0.374	0.262	
	1	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.004)	(0.001)	(0.001)	(0.018)	(0.001)	(0.001)	
A			0.743	0.474	-0.133	0.461	0.380	0.369	0.291	0.368	0.268	0.065	0.193	-0.152	0.208	0.371	0.238	0.179	0.250	0.214	
		1	(0.001)	(0.001)	(0.026)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.277)	(0.001)	(0.011)	(0.001)	(0.001)	(0.001)	(0.003)	(0.001)	(0.001)	
S				0.518	-0.169	0.562	0.277	0.464	0.252	0.342	0.301	0.112	0.234	-0.234	0.135	0.418	0.207	0.197	0.280	0.118	
			1	(0.001)	(0.004)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.061)	(0.001)	(0.001)	(0.023)	(0.001)	(0.001)	(0.001)	(0.001)	(0.048)	
PSQI					-0.125	0.433	0.168	0.294	0.150	0.198	0.141	0.080	0.160	-0.145	0.069	0.377	0.164	0.092	0.275	0.049	
				1	(0.036)	(0.001)	0.005	(0.001)	(0.012)	(0.001)	(0.017)	(0.181)	(0.007)	0.015	(0.250)	(0.001)	(0.006)	(0.125)	(0.001)	(0.414)	
E						-0.248	-0.025	-0.283	-0.486	0.009	-0.058	-0.235	-.0124	0.334	0.100	-0.111	0.010	0.069	-0.217	0.076	
					1	(0.001)	(0.671)	(0.001)	(0.001)	(0.877)	(0.330)	(0.001)	(0.038)	(0.001)	(0.094)	(0.063)	(0.869)	(0.245)	(0.001)	(0.206)	
N							0.355	0.609	0.311	0.358	0.428	0.053	0.238	-0.237	0.247	0.342	0.123	0.121	0.345	0.142	
						1	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.375)	(0.001)	(0.001)	(0.001)	(0.001)	(0.039)	(0.043)	(0.001)	(0.017)	
UE								0.530	0.298	0.523	0.340	0.072	0.159	0.061	0.451	0.324	0.282	0.201	0.314	0.358	
							1	(0.001)	(0.001)	(0.001)	(0.001)	(0.231)	(0.008)	(0.310)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	
CD									0.370	0.518	0.442	0.250	0.349	-0.117	0.362	0.353	0.199	0.136	0.408	0.254	
								1	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.050)	(0.001)	(0.001)	(0.001)	(0.022)	(0.001)	(0.001)	
IA										0.306	0.286	0.212	0.214	-0.193	0.182	0.288	0.225	0.126	0.381	0.213	
									1	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.002)	(0.001)	(0.001)	(0.034)	(0.001)	(0.001)	
IN											0.425	(0.075)	0.235	(0.085)	0.463	0.363	0.295	0.206	0.414	0.363	
										1	(0.001)	(0.212)	(0.001)	(0.154)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	
NU												-0.141	0.075	0.134	0.649	0.182	0.249	0.151	0.345	0.294	
											1	(0.018)	(0.209)	(0.024)	(0.001)	(0.002)	(0.001)	(0.011)	(0.001)	(0.001)	
LP													0.535	-0.191	-0.135	0.190	0.100	0.087	0.087	0.119	
												1	(0.001)	(0.001)	(0.023)	(0.001)	(0.094)	(0.147)	(0.143)	(0.046)	
LPr														-0.188	0.123	0.229	0.205	0.136	0.141	0.180	
													1	(0.002)	(0.039)	(0.001)	(0.001)	(0.023)	(0.018)	(0.002)	
SS															0.318	-0.234	-0.050	-0.077	-0.075	0.098	
														1	(0.001)	(0.001)	(0.401)	(0.196)	(0.207)	(0.101)	
PU																0.108	0.251	0.143	0.297	0.394	
															1	(0.071)	(0.001)	(0.016)	(0.001)	(0.001)	
EA																	0.656	0.520	0.570	0.416	
																1	(0.001)	(0.001)	(0.001)	(0.001)	
PA																		0.562	0.391	0.499	
																	1	(0.001)	(0.001)	(0.001)	

SA	1	0.278 (0.001)	0.378 (0.001)
EN		1	0.529 (0.001)
PN			1

Abbreviations: D, Depression; A, Anxiety; S, Stress; DASS-21, Depression Anxiety and Stress Scale-21 Items; PSQI, Pittsburgh Sleep Quality Index; E, Extraversion; N, Neuroticism; EPQ-SF, Eysenck Personality Questionnaire-Revised; UE, Unusual Experience; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; NU, Negative Urgency; LP, Lack of Perseverance; LPr, Lack of Premeditation; SS, Sensation Seeking; PU, Positive Urgency; S-UPPS-P, Impulsive Behaviour Scale-Short Version; EA, Emotional Abuse; PA, Physical Abuse; SA, Sexual Abuse; EN, Emotional Neglect; PN, Physical Neglect; CTQ-SF, short form of Childhood Trauma Questionnaire.

5.5.3 The Mediating Role of Sleep Quality in Chronotype Mental Health Relationship

Our initial model (see statistical analysis) was found to be a very good fit [($\chi 2/df$=2.11, p<0.001), RMSEA (0.06), GFI (0.97), AGFI (0.90), and CFI (0.98)] to the data, though some direct effects (paths) were non-significant (see Figure 5.2). The model was, therefore, revised because of poor local fit (i.e., presence of nonsignificant path coefficients) by removing the non-significant paths leaving us with the final model [model fit indices: $\chi 2/df$=1.18; GFI=0.98; TLI=0.99; CFI=0.99; RMSEA=0.02)] (Figure 5.3). As shown in Figure 5.3, we did not find any direct effect of EC on mental health (β=-0.001, p=0.961), and found its relationship with (poor) mental health to be fully mediated by poor sleep quality (β=-0.10, p<0.001). Poor sleep quality also partially mediated the relationship between childhood emotional abuse and poor mental health (β=0.96, p<0.001), and between higher neuroticism and poor mental health (β=0.11, p<0.001), but not between Cognitive Disorganisation and poor mental health (β=-0.040, p=0.427).

While exploring sex differences, we observed that the comparison of model fit of unconstrained and fully constrained model revealed a non-significant chi-square difference $\Delta\chi 2$(20 =25.87, p=0.156 and a non-significant difference in CFI (ΔCFI=0.005), suggesting the model to be invariant in males and females. However, the difference in RMSEA was found to be higher than the prescribed cut-off of 0.01 (ΔRSMEA=0.02) suggesting non-invariance. Therefore, we tested pairwise difference in the path coefficients of unconstrained model in males and females and found a significant difference (stronger in females) in the direct path linking Cognitive Disorganization to mental health (Critical ratio=2.138, p<0.05).

Figure 5.2 *Results of the SEM analyses, with solid lines representing significant paths (**p<0.001, *p<0.005) and dotted lines representing non-significant paths.*

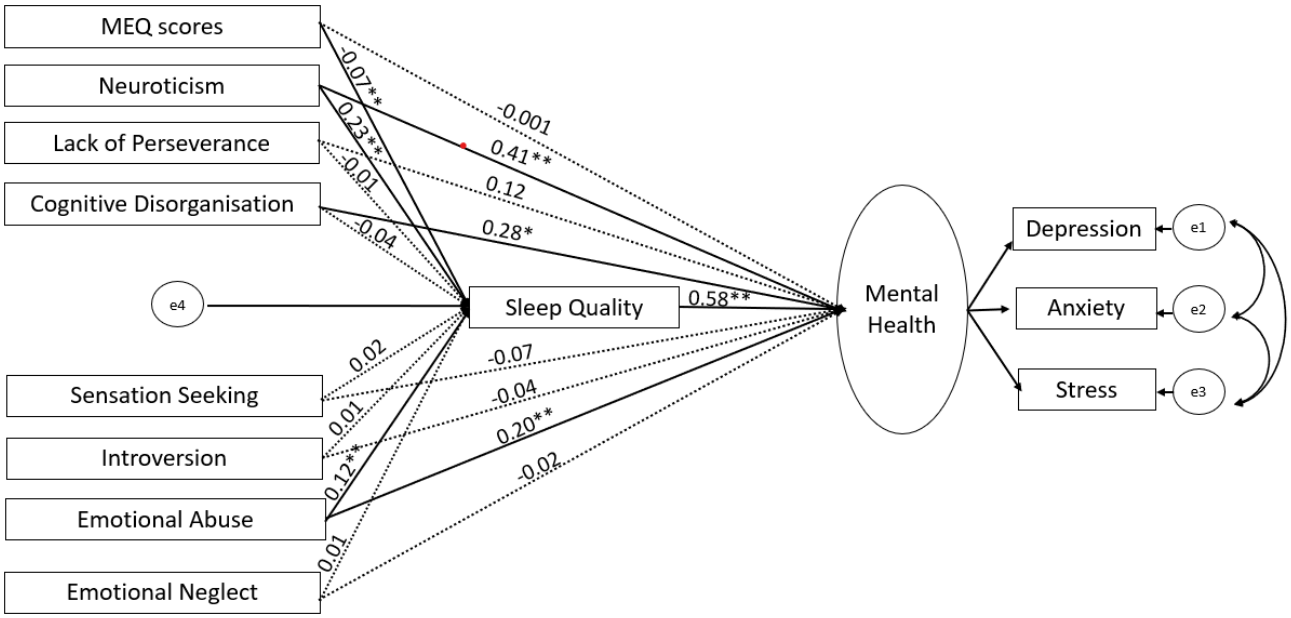
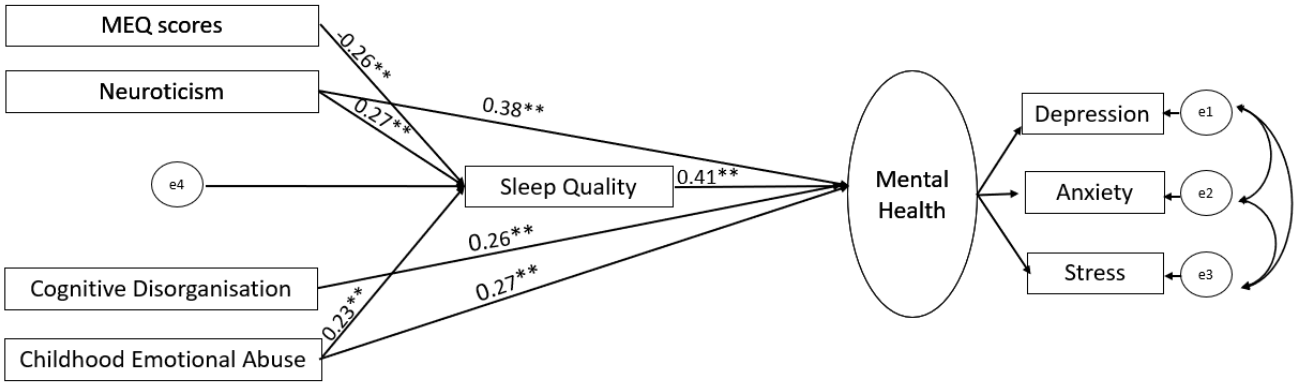


Figure 5.3 *Results of the SEM analyses for the revised model showing all significant paths (**p<0.001).*



5.6 Discussion

This is the first study, to our knowledge, to investigate chronotype-mental health associations while also examining the roles of sleep quality, clinically relevant personality traits and childhood trauma in this association. The main findings were: (i) EC had small-to-medium correlations (*r* values: 0.20-0.30) while poor sleep quality had medium-to-large correlations (*r* values: 0.47-0.52) with mental health outcomes (depression, anxiety, and stress), (ii) EC had significant but mostly small-sized (*r* values >0.30) associations with various personality traits and self-reported history of childhood emotional abuse and neglect, and (iii) there was no significant direct effect of EC on mental health outcomes, with sleep quality fully mediating

the chronotype-mental health relationship. Although, on average, females displayed more morningness than males, sex did not significantly influence any chronotype-mental health associations.

The findings in relation to our first hypothesis demonstrated only small-to-medium (at best) positive associations between EC and poor mental health outcomes (depression, anxiety, stress) in a North Indian, young and healthy volunteer sample, as also found in previous studies of general population samples in Western countries (UK; Muzni et al., 2021, f^2=0.024; Canada; Walsh et al., 2022, ηp^2=0.02-0.04). Our finding of relatively stronger (medium-to-large) positive associations between poor sleep quality and poor mental health outcomes, compared to those seen between EC and mental health outcomes, confirm our hypothesis, and offers further support to earlier findings in a non-clinical sample in the UK (Muzni et al., 2021). Furthermore, this study supports previous findings (Chauhan et al., 2023) in showing significant but mostly small associations between EC and higher scores on measures of neuroticism (Muzni et al., 2021; Randler et al., 2017) and impulsivity (Caci et al., 2005; Selvi et al., 2011; Yilbaş & Günel Karadeniz, 2022). Extraversion has also been found to have a small positive association with EC (Randler et al., 2017), though not consistently (Adan et al., 2012; Chauhan et al., 2023). Interestingly, our findings also revealed a significant positive association (r=0.299) between EC and the cognitive disorganisation aspect of schizotypy with non-significant associations in the same direction for other aspects of schizotypy. In a previous study by Dopierala and colleagues (2016) that did not find any relationship between EC and schizotypy, a positive association between all schizotypy (s-OLIFE) dimensions and altered biological rhythms in patients with bipolar disorder and healthy controls was observed, and it was present most strongly for Cognitive Disorganisation, although the mechanisms underlying such an association, remain unclear at present.

The findings in relation to our second hypothesis demonstrated no direct effect of EC on mental health outcomes, and instead showed that EC-poor mental health relationship was fully mediated by poor sleep quality. It is well known that numerous environmental and social factors associated with modern-day lifestyles hinder regular sleep patterns (Preisegolaviciute et al., 2010; Roenneberg et al., 2003), and contribute to irregular secretion of melatonin which in turn has been linked to mental disorders, such as psychosis and major depression (Chauhan et al., 2023; Moon et al., 2022). Not surprisingly, most EC individuals accumulate higher social jetlag, sleep pressure, and sleep deprivation (Carciofo et al., 2014; Fernández-Mendoza et al.,

2010; Roenneberg et al., 2003). Sleep disturbances affect the reactivity of neuroendocrine stress systems and responsivity, reducing the ability to cope with emotional dysfunction (Meerlo et al., 2008). Chronic and acute sleep-related issues may fundamentally change the brain chemistry and neuroendocrine systems (e.g., altered hypothalamic pituitary adrenal axis; Meerlo et al., 2008). Poor sleep may further sensitise people with high levels of neuroticism to experience negative affect and emotional (limbic) arousal (Calkins et al., 2013). Individuals with a history of emotional abuse are also reported to experience emotional dysfunction and distress, which in turn may contribute to poor sleep quality and altered CRs (Boyko et al., 2017; Francis & Porcu, 2023) and elevate risk for affective and stress-related disorders (Beards et al., 2013; Park, 2019; Sheffler et al., 2023). In this context, it is noteworthy that emotional abuse appeared relatively more important than other types of abuse for mental health, as also argued in the context of prevalence of mental disorders in children with a history of physical abuse (Kumari, 2020; Pandey et al., 2020). Individuals with high levels of schizotypy also often experience low mood (Kemp et al., 2018) and report social anxiety, distress as well as higher sensitivity to social rejections (Premkumar et al., 2020), all of which contribute to poor mental health. Therefore, prolonged and/or acute poor sleep quality, neuroticism, history of emotional abuse, and schizotypy may explain why EC has been associated with poor mental health, though with a marked variation in effect sizes (Norbury et al., 2021; Papaconstantinou et al., 2019) possibly due to its dependency on the quality of sleep.

5.6.1 Limitations and Future Directions

The present study had a number of strengths. First, it used a homogenous sample of young English-speaking, healthy adults residing in North India, with <5% consuming nicotine and alcohol as self-reported. Second, all data were collected over a brief period to minimise any season-related influences. Third, chronotype was used as a continuous variable to preserve power. Our study also had a number of limitations. First, although we used validated self-report questionnaires with sensitivity ranging between 73 and 97.7% (Ibáñez et al., 2018), there were no objective markers of chronotype. This, however, may not be a serious concern given significant correlations and overlaps between subjective and objective chronotype measures even in a clinical sample (Gershon et al., 2018). Second, we did not collect information on natural and/or artificial light exposure that causes phase delay in CRs (Czeisler et al., 1989; Duffy & Czeisler, 2009; Roenneberg et al., 2007). Third, our sample was predominantly female, limiting our ability to investigate sex differences adequately. Additionally, we did not

collect information on cyclic fluctuation of reproductive hormones which may act as a potential confounding variable. Fourth, we did not examine the influence of socioeconomic status, family dynamics or cultural beliefs, which may also directly or indirectly influence an individuals' mental health. Fifth, our findings from a young North Indian sample may or may not generalise to non-Indian or older age-groups. Sixth, the study did not collect data on participants' nationality, focusing solely on ethnicity. This could be a limitation, as nationality may provide additional insights, such as differences in cultural norms or geographic influences, which ethnicity alone might not fully capture. Lastly, as this was a correlational study, the findings cannot conclusively speak to causation. Despite these limitations, our findings might still have important implications. Specifically, we speculate that personal and societal interventions aiming to promote good sleep, especially in high-risk groups (e.g., with high neuroticism or emotional abuse), may help to promote good mental health in the general population.

5.6.2 Conclusions

In conclusion, this study found no direct relationship between EC and poor mental health outcomes (depression, anxiety, and stress) in young adults. Instead, this relationship was mediated by poor sleep quality. Our findings argue against EC as an independent risk factor for poor mental health, and indirectly suggest that promotion of good quality sleep may provide a more helpful strategy than those aiming to shift diurnal preferences towards morningness for improving mental health, especially in high-risk groups. Further studies in other cultures, settings, age groups, and using direct measures of circadian (mis)alignments and sleep quality along with self-report measures to collect data on more than one occasion within the same individuals, are needed to examine the stability and generalisability of these findings and realise their full potential for promoting mental health in the general population.

Chapter 6: Chronotype and Mental Health Relationship: Evidence from the UK and Germany

The work reported in this chapter has been published in *Brain Sciences* as:

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Abstract

There is considerable evidence supporting the elevated risk of mental health problems in individuals with EC relative to those with MC or IC. Recent data, however, suggest that this risk may be explained, at least partially, by poor sleep quality. This study aimed to further clarify the roles of chronotype and sleep quality in mental health outcomes (depression, anxiety, stress) in young individuals (18–40 years) living in the UK (N=213) or Germany (N=247). Consistent with our recent observations in a comparable North Indian sample, poor sleep quality was found to have significantly positive associations with adverse mental health outcomes both in the UK and Germany-based samples. Significant associations between EC and poor mental health were also evident, but these associations were fully mediated by poor quality of sleep in both samples. These observations suggest that efforts to identify sleep disruption in a timely manner and promotion of good sleep may prevent mental health problems, especially in individuals with EC and other known risks for mental disorders.

6.1 Chapter Aims and Overview

This chapter reports an empirical study conducted to further examine the mediating role of sleep quality in chronotype-mental health association in two European (UK and Germany) non-clinical samples while also quantifying for psychopathology-related personality traits and childhood trauma.

6.2 Introduction

In humans, the intra-individual variation in CRs is commonly known as '*chronotype*' (Adan et al., 2012). It is a multidimensional construct (Chauhan et al., 2023), ranging from MCs to ECs, with most individuals falling in the intermediate range, known as ICs. MCs and ECs strongly prefer different sleep–wake timings, and the phenomenon may also impact their sleep behaviour (Randler et al., 2017). A considerable body of evidence has shown an association between EC and various mental disorders, including depression (Au & Reece, 2017; Norbury, 2021), anxiety (Passos et al., 2017), substance-use disorder (Adan et al., 2012; Zou et al., 2022), and schizophrenia (Kivela et al., 2018; Taylor & Hasler, 2018). Of these, the most consistent association of EC has been reported to be with depression (Au & Reece, 2017; Norbury, 2021; Zou et al., 2022). Additionally, ECs are also known to display compulsive, aggressive, and addictive behaviours, be less conscientious, have more impulsive and risky behaviour, and display negative cognitive bias, further contributing to a higher likelihood of developing mental illnesses (Adan et al., 2012; Zou et al., 2022; Kivela et al., 2018).

Given that sleep timings and duration are regulated via sleep homeostatic processes (Deboer, 2018), it is obvious to expect some form of relationship between chronotype and sleep-related disruptions. For instance, studies have shown that ECs report poor sleep quality, latency, duration, daytime dysfunction, irregular sleep–wake cycles, accumulate higher sleep debt or social jetlag, have difficulties falling and/or maintaining sleep, build higher sleep pressures, and sleep inertia (Carciofo et al., 2014; Fernández-Mendoza et al., 2010; Ma et al., 2022; Muzni et al., 2021; Roenneberg et al., 2007; Vardar et al., 2008). These disturbed sleep–wake patterns have been considered to be transdiagnostic determinants for the onset and persistence of various mental health and behavioural problems, including depression and anxiety (Scott et al., 2021), psychosis (Cosgrave et al., 2018; Kumari & Ettinger, 2020), eating disorders (Allison et al., 2016), substance abuse (Meneo et al., 2023), impulsive and aggressive behaviour (Kamphuis et al., 2012), personality disorders (Winsper et al., 2017), as well as mood and

emotion dysregulation (Tomaso et al., 2021). Both EC and poor sleep quality are found to be linked with elevated scores on psychometric measures of certain psychopathology-related personality traits, for example, neuroticism and impulsivity (Adan et al., 2012; Chauhan et al., 2023; Randler et al., 2017), as well as with self-reported childhood maltreatment (Chauhan et al., 2024a). Given these findings, there is clearly a need to better understand the influence of chronotype and sleep quality in mental health outcomes.

Against the backdrop of some studies dismissing any influence of poor sleep in chronotype-mental health association (Antypa et al., 2016; Uzer & Yucens, 2020), a recent study by Muzni and colleagues (2021) observed mental health problems to be more strongly (medium-to-large effect sizes) associated with poor sleep quality than with EC (small effect sizes) in young adults recruited from the general population in the UK (n=675). Two very recent studies, both conducted in southeast Asian non-clinical young adult populations [North India, N=282 (Chauhan et al., 2024a); HongKong, N=200 (Poon et al., 2024)], have also shown a strong mediating influence of sleep quality in the chronotype–mental health link. Although climate may impact chronotype (Adan et al., 2012; Chauhan et al., 2023; Randler et al., 2015), recent findings emerging from different parts of the world (Chauhan et al., 2024a; Muzni et al., 2021; Poon et al., 2024) question the widely reported role of chronotype as an 'independent' transdiagnostic risk factor for mental disorders, at least in non-clinical young adult populations.

The present study aimed to further clarify the influence of chronotype and the extent to which it might be mediated by poor sleep quality [a modifiable risk factor (Scott et al., 2021)] in mental health outcomes in a European sample (from the UK and Germany). The methods and procedures used in this study matched closely with those employed in our recent study (Chauhan et al., 2024a). We hypothesised, based on our recent observations in a comparable North Indian sample (Chauhan et al., 2024a), that there will be a stronger relationship between sleep quality and mental health than between chronotype and mental health, and that any relationship between chronotype and mental health will be mediated via sleep quality. The possible influence of neuroticism, impulsivity, schizotypal personality traits, and adverse childhood experiences (McKay et al., 2021) in the chronotype–mental health association were also explored.

6.3 Methods

6.3.1 Participants

The study involved 460 young healthy adults (aged 18-40 years) who resided in the UK (N=213) or Germany (N=247) at the time of their participation. Of 460, 394 participants provided usable data (UK: 185; Germany: 209). Power analysis for multiple linear regression with eight predictors, including chronotype, quality of sleep, and relevant personality traits [as in (Chauhan et al., 2024a), in G*Power (Faul et al., 2007), using an alpha of 0.01, a power of 0.90, and a medium effect size (0.15), based on our recent observations (Chauhan et al., 2024a), indicated that we required 179 participants to test our hypothesis. We aimed to recruit a minimum of 200 participants in the UK and 200 in Germany to allow sufficient power to probe our hypothesis across and within these countries.

All included participants met the study inclusion criteria of (i) being aged between 18 and 40 years (ii) being a UK/Germany resident and a native or proficient English/German speaker, (iii) not taking any regular medication (bar contraceptives and multivitamins), and (iv) having no current or previous diagnosis of a mental disorder and/or drug abuse. Of the 213 non-clinical adults assessed in the UK, 28 were excluded because they either failed our (online) attention checks [i.e., provided an answer that differed by two or more rating points for the same (duplicated) questions; N=26)] or did not fully complete all study measures (N=2). Of the 247 non-clinical adults assessed in Germany, 38 were excluded for failing our attention checks. The final study sample consisted of 185 UK residents (86 males, 99 females) and 209 Germany residents (67 males, 142 females).

The study was approved by the College of Health, Medicine, and Life Science Research Ethics Committee, Brunel University of London (ref no. 36745-MHR-May/2022- 39617-2), and the Research Ethics Committee of the Department of Psychology at the University of Bonn (ref no. 23-03-14). All participants signed an online consent form prior to their participation. All UK-based participants were compensated with a GBP 5 Amazon gift voucher for their time to complete the survey, while those recruited in Germany were enrolled in a lottery system for winning EUR 50.

6.3.2 Assessment of Chronotype, Mental Health, Sleep Quality, Personality Traits and Childhood Trauma

6.3.2.1 Chronotype

The 19-item self-report MEQ (Horne & Ostberg, 1976) was used to assess chronotype in the UK-based sample, and its German version (Griefahn et al., 2001) in Germany-based sample. The questionnaire has 12 items which are rated on a Likert scale (e.g., *item 6: how hungry would you be during the first hour of waking-up?*), and the remaining seven items are rated on a time scale (e.g., *item 1: approximately at which hour would you wake up if you were free to plan your day?*). Higher MEQ scores indicate higher preference for morningness. The MEQ has been reported to have high internal consistency [*a*=0.83 (Horne & Ostberg, 1976)], as was also the case in our study (*a*=0.82 and 0.87 in the UK and German-based samples, respectively).

6.3.2.2 Mental Health

The DASS-21 (Lovibond & Lovibond, 1995) was used to assess mental health in the UK-based sample and its German version (Nilges & Essau, 2015) in Germany-based sample. The DASS-21 has three subscales: *Depression, Anxiety, Stress.* Each subscale consists of 7 items which are rated by the participants according to their feelings over the past one week (possible score range on each scale: 0-42). Higher scores indicate higher levels of *Depression, Anxiety or Stress*. Previous studies have indicated high internal consistency for all three DASS-21 subscales [Depression, *a*=0.83-0.94; Anxiety, *a*=0.66-0.87; Stress, *a*=0.79-0.91 (Lee et al., 2019)]. Cronbach's alphas in the current samples for Depression (UK, *a*=0.89; Germany, *a*=0.85), Anxiety (UK, *a*=0.83; Germany, *a*=0.78), and Stress (UK, *a*=0.83; Germany, *a*=0.82) also indicated high reliability coefficients.

6.3.2.3 Sleep Quality

The PSQI (Buysse et al., 1989) was used to assess sleep quality in the UK-based sample, and its German version (Backhaus & Riemann, 1996) in Germany-based sample. The PSQI is a 19-item self-report measure assessing seven sleep facets (i.e., sleep quality, sleep efficiency, sleep disturbance, sleep dysfunction, sleep duration, daytime dysfunction, and use of sleep medication). Participants answer each item based on their sleep habits in the past month, with higher scores indicating poor sleep quality. The scale is reported to have a high internal consistency [*a*=0.83 (Buysse et al., 1989)]. The Cronbach's alpha coefficients in the current study were *a*=0.73 (UK) and *a*=0.70 (Germany).

6.3.2.4 Personality Traits

The EPQ-RS (Eysenck & Eysenck, 1992) was used to assess levels of Extraversion, Neuroticism, and Psychoticism in the UK-based sample, and its German version (Francis et al., 2006) in Germany-based sample. The EPQ-RS has four 12-item subscales: *Extraversion, Neuroticism, Psychoticism,* and *Lie* (48 items in total). Higher scores indicate higher levels of Extraversion, Neuroticism, and Psychoticism. The EPQ-RS is reported to have good internal consistency [Extraversion: *a*=0.74-0.84, Neuroticism: *a*=0.70-0.77; bar Psychoticism: *a*=0.33-0.52 (Forrest et al., 2000)]. The Cronbach's alphas in the current sample were similar to what has been reported in the literature for Extraversion (UK, *a*=0.83; Germany, *a*=0.86), Neuroticism (UK, *a*=0.82; Germany, *a*=0.79), and Psychoticism (UK, *a*=0.39; Germany, *a*=0.35).

The s-OLIFE (Mason et al., 2005) was used to assess schizotypy in the UK-based sample, and its German version (Grant et al., 2013) in Germany-based sample. The s-OLIFE is a 43-item self-report measure comprising four subscales assessing levels of *Unusual Experiences* (12 items), *Cognitive Disorganisation* (11 items), *Introvertive Anhedonia*, and *Impulsive Nonconformity* (10 items each), with each item rated as 'Yes' or 'No'. Higher scores indicate higher levels of schizotypy. This scale is found to have high internal consistency [*a*=0.78-0.87 (Fonseca-Pedrero et al., 2015)]. The Cronbach's alpha coefficients in the current sample were acceptable-to-high for Unusual Experiences (UK, *a*=0.80; Germany, *a*=0.69) and Cognitive Disorganisation (UK, *a*=0.82; Germany, *a*=0.78) and lower for Introvertive Anhedonia (UK, *a*=0.49; Germany, *a*=0.53) and Impulsive Nonconformity (UK, *a*=0.55; Germany, *a*=0.42).

The S-UPPS-P (Cyders et al., 2014) was used to assess impulsivity in the UK-based sample, and its German version (Schmidt et al., 2008), with four additional Positive Urgency items as in Keidel and colleagues (2022), in Germany-based sample. It is a 20-item self-report measure assessing levels of *Lack of Perseverance, Lack of Premeditation, Positive Urgency, Negative Urgency, and Sensation Seeking*, with each item rated on a four-point Likert scale in English and a five-point Likert scale in German as in Keidel and colleagues (2022). Higher scores indicate higher levels of impulsivity. This scale is reported to have a high internal consistency [*a*=0.74-0.88 (Cyders et al., 2014)]. The Cronbach's alpha coefficients in the current sample were in the acceptable range for Lack of Perseverance (UK, *a*=0.63; Germany, *a*=0.58), Lack of Premeditation (UK, *a*=0.76; Germany, *a*=0.65), Sensation Seeking (UK, *a*=0.69; Germany,

a=0.66), Negative Urgency (UK, *a*=0.80; Germany, *a*=0.67), and Positive Urgency (UK, *a*=0.82; Germany, *a*=0.79).

6.3.2.5 Childhood Trauma

The CTQ-SF (Bernstein et al., 2003) was used to assess childhood trauma in the UK-based sample, and its German version (Klinitzke et al., 2012) in Germany-based sample. The CTQ is a 28-item self-report measure for assessing the history and severity of *Abuse* (*Physical, Emotional, Sexual), Neglect* (i.e., *Emotional, Physical),* and *Denial*, with each item being rated on a five-point Likert scale. Higher scores indicate severity of abuse and neglect. This scale is reported to have a high internal consistency [α=0.66-0.92 (Bernstein et al., 2003)]. In the current sample, the Cronbach's alpha coefficients were high for Physical Abuse (UK, *a*=0.83; Germany, *a*=0.83), Sexual Abuse (UK, *a*=0.94; Germany, *a*=0.88), Emotional Abuse (UK, *a*=0.81; Germany, *a*=0.83), and Emotional Neglect (UK, *a*=0.83; Germany, *a*=0.88), but was considerably lower for Physical Neglect (UK, *a*=0.62; Germany, *a*=0.42).

6.4 Statistical Analysis

All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) or SPSS Amos (Windows version 28; IBM, New York, NY, USA), with alpha value maintained at $p<0.05$ unless specified otherwise.

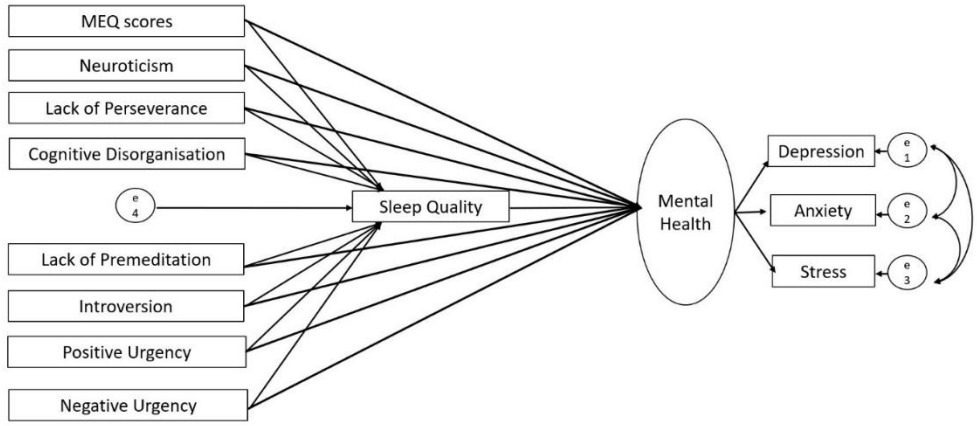
To begin with, all data properties (skewness and kurtosis <±2) were examined, followed by a reliability assessment of the various self-report scales. Since the Psychoticism subscale of the EPQ-RS showed poor reliability (UK, α=0.39; Germany, *a*=0.35), it was not included in any further analyses. Prior to running any statistical analyses to probe our hypothesis, we conducted a series of independent sample *t*-tests to compare the UK- and Germany-based participants on mental health, sleep, chronotype, personality traits, and childhood trauma parameters to rule out any major differences between them. Given that the UK-based sample, on average, had significantly poor mental health and sleep quality scores (as well as larger range of scores on these variables) compared to the Germany-based sample (see Section 6.5.1), all further analyses were conducted separately for the UK- and Germany-based samples, and then significant effects were statistically evaluated for any UK versus Germany differences. Given that chronotype may be sex-dependent (Adan et al., 2012), we also explored sex-related

differences (separately in the UK- and Germany-based samples) in mental health, sleep quality, personality traits, and childhood trauma measures using a series of independent sample *t*-tests.

Pearson correlations were employed to investigate the potential relationships of chronotype with mental health, sleep quality, personality traits, and childhood trauma, as well as the relationship of sleep quality with mental health variables. We interpreted effect sizes for observed correlation coefficients (*r* values) based on the recommendations of Cohen (1988) (absolute *r* value 0.1 to 0.29: small; 0.3 to 0.49: medium; 0.5 to 1: large), as in our previous study (Chauhan et al., 2024a). A Fisher's Exact *z*-test was used to test for statistically significant sex-related differences in these relationships.

Based on the correlations of EC with mental health, quality of sleep, and relevant personality measures (see Section 6.5.2), we ran SEM using SPSS Amos (version 28; IBM, New York, NY, USA), first in the UK and then in Germany-based sample, with chronotype and personality traits as predictors (allowed to covary), sleep quality as a mediator, and mental health (a latent construct integrating depression, anxiety and stress subscales) as an outcome (Figure 6.1). Following our earlier study (Chauhan et al., 2024a), we used the maximum likelihood method to assess model parameters. A good model fit was based on the following criteria: (a) CFI>0.95, (b) RMSEA<0.08, (c) ratio of maximum-likelihood chi-square to the degree of freedom (χ^2/df)<5, (d) GFI>0.95, (e) AGFI>0.90, (f) and TLI>0.95 (Hooper et al., 2008). We tested the statistical significance of direct and indirect paths using a bias-corrected 95% bootstrap confidence interval and corresponding *p* values. After testing our initially proposed model (Figure 6.1), first in the UK and then in Germany, we revised it by removing all non-significant paths (UK, Figures 6.2 and 6.3; Germany, Figures 6.4 and 6.5; reproduced in Microsoft Power Point, Windows version 2019 based on SPSS Amos generated outputs). Lastly, to explore any sex-related differences, we compared the fully constrained model (measurement weights of the measurement model of mental health, structural weights, covariances and residuals constrained to be equal in males and females) with the unconstrained model. A non-significant chi-square difference ($p>0.05$), $\Delta CFI \leq 0.005$, and $\Delta RMSEA \leq 0.01$ indicated invariance (Chen, 2007; Yuan & Chan, 2016). A similar approach was taken to examine country (UK versus Germany)-related differences.

Figure 6.1 *Schematic representation of proposed structural model showing the direct and indirect effects (via sleep quality) of chronotype, and personality traits (predictors) on mental health (outcome) within the SEM framework. All predictors were allowed to covary.*



6.5 Results

6.5.1 Sample Characterisation

The demographic information is presented in Table 6.1. Overall, the UK sample scored higher than German sample on Depression (t_{391}=4.00, p<0.001), Anxiety (t_{391}=5.18, p<0.001), Stress (t_{391}=2.69, p=0.004), Neuroticism (t_{391}=5.23, p<0.001), Unusual Experiences (t_{391}=8.32, p<0.001), Cognitive Disorganisation (t_{391}=4.05, p<0.001), Introvertive Anhedonia (t_{391}=7.19, p<0.001), Emotional Abuse (t_{391}=4.15, p<0.001), Physical Abuse (t_{386}=6.43, p<0.001), Sexual Abuse (t_{390}=5.85, p<0.001), Emotional Neglect (t_{389}=4.12, p<0.001), Physical Neglect (t_{391}=5.22, p<0.001), Negative Urgency (t_{391}=2.99, p<0.001), Sensation Seeking (t_{391}=5.57, p<0.001), and Positive Urgency (t_{391}=6.04 , p<0.001), as well as rated themselves having poor sleep quality (t_{391}=3.30, p<0.001). German sample scored higher on Lack of Perseverance (t_{391}=30.02, p<0.001) and Lack of Premeditation (t_{391}=25.77, p<0.001).

In the UK sample, on average, females were younger than males (t_{183}=2.03, p=0.022) and scored higher on Anxiety (t_{183}=2.45, p=0.007), Stress (t_{183}=3.28, p<.001), Neuroticism (t_{183}=5.13, p<0.001), Sleep Quality (t_{183}=2.56, p=0.006), Unusual Experiences (t_{183}=2.26, p=0.012), Cognitive Disorganisation (t_{183}=3.80, p<0.001), Negative Urgency (t_{183}=2.12, p=0.017), and Emotional Abuse (t_{183}=2.28, p=0.012), while males scores higher on Sensation Seeking (t_{183}=2.38, p=0.009) (Table 6.2). In the German sample, females, on average, scored higher than males on Stress (t_{207}=2.36, p=0.009), Neuroticism (t_{207}=3.66, p<0.001), Sleep Quality (t_{207}=2.78, p=0.003), Unusual Experiences (t_{207}=1.74, p=0.041), Cognitive

Disorganisation (t_{207}=2.77, p=0.003), and Emotional Abuse (t_{207}=2.09, p=0.019), while males scored higher on Sensation Seeking (t_{207}=3.06, p<0.001) and Negative Urgency (t_{207}=1.98, p=0.024) (Table 6.2).

Table 6.1 *Demographic characteristics of the study sample.*

		UK	Germany
Demographic Characteristics		Frequency (**%**) of N=185	Frequency (**%**) of N=209
Ethnicity	White European	30.3%	79.4%
	Any Other White	0%	1%
	South Asian	46.5%	6.7%
	East Asian	3.8%	1.9%
	West Asian	0.5%	1.4%
	Mixed	7.6%	4.3%
	Black	7%	0.5%
	Other Ethnicities	4.3%	3.8%
	Prefer Not to Say	0%	1%
Stimulant/Sedative Consumption[a]	Caffeine	39.5%	-
	Nicotine	49.2%	-
	Alcohol	7%	-
	Others	2.7%	-
	Prefer Not to Say	1.6%	-
Body Mass Index (BMI)[b]	Underweight (<18.5)	39.5%	42.1%
	Normal (18.5-24.9)	45.4%	52.6%
	Overweight (25-30)	8.6%	4.8%
	Obese (30 and above)	3.2%	0.5%
Education/Employment	Student	73.5%	95.2%
	Full-time Work	26.5	4.8%
	Part-time Work	0%	0%
Sleep Quality[c]	Good (≤5)	57.8%	65.6%
	Poor (6-14)	42.2%	34%

[a] Data not collected in the German sample.
[b] BMI data missing for 6 participants in the UK.
[c] Score 0-5: good sleepers; score 6 and above: poor sleepers.

Table 6.2 *Descriptive statistics for self-report measures.*

Study Variables			UK						Germany					
			Males (*n*=86)		Females (*n*=99)		Entire Sample (N=185)		Males (*n*=67)		Females (*n*=142)		Entire Sample (N=209)	
			Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range
Age			25.13±5.27	18-39	23.77±3.77	18-38	24.41±4.57	18-39	23.81±4.12	18-36	23.05±3.39	18-38	23.29±3.65	18-38
Chronotype	MEQ		47.59±8.89	21-68	49.68±11.05	27-78	48.71±10.13	21-78	49.19±10.71	22-74	50.04±9.73	22-71	49.77±10.04	22-74
Mental Health	DASS-21	Depression	10.23±9.62	0-42	12.57±10.77	0-42	11.48±10.29	0-42	8.03±8.66	0-38	7.76±7.07	0-36	7.85±7.60	0-38
		Anxiety	8.74±8.26	0-40	12.02±9.67	0-40	10.50±9.16	0-40	5.46±6.21	0-34	6.59±7.33	0-34	6.23±7.00	0-34
		Stress	10.72±8.14	0-32	15.05±9.58	0-38	13.04±9.18	0-38	8.78±8.31	0-38	11.58±7.83	0-34	10.68±8.08	0-38
Sleep Quality	PSQI	Sleep Quality	1.02±0.61	0-2	1.17±0.59	0-3	1.10±0.60	0-3	0.96±0.58	0-2	1.02±0.53	0-3	1±0.55	0-3
		Sleep Latency	1.30±0.97	0-3	1.41±0.93	0-3	1.36±0.95	0-3	1.01±0.80	0-3	1.15±0.88	0-3	1.11±0.86	0-3
		Sleep Duration	0.73±0.78	0-3	0.78±0.73	0-3	0.75±0.75	0-3	0.08±0.26	0-1	0.2±0.48	0-2	0.16±0.43	0-2
		Sleep Efficiency	0.56±0.91	0-3	0.77±1.05	0-3	0.67±0.99	0-3	0.32±0.53	0-2	0.47±0.74	0-3	0.42±0.68	0-3
		Sleep Disturbance	1.05±0.44	0-3	1.30±0.50	0-2	1.18±0.49	0-3	0.92±0.40	0-2	1.04±.38	0-3	1.00±0.39	0-3
		Sleep Medication	0.03±0.18	0-1	0.16±0.48	0-3	0.10±0.38	0-3	0.01±0.12	0-1	0.06±0.34	0-3	0.05±0.29	0-3
		Daytime Dysfunction	1.05±0.83	0-3	1.26±0.82	0-3	1.16±0.83	0-3	1.07±0.70	0-2	1.25±0.67	0-3	1.2±0.69	0-3
		Global Score	5.21±2.31	0-11	6.12±2.5	1-14	5.70±2.45	0-14	4.35±1.76	0-8	5.21±2.20	0-13	4.94±2.11	0-13
Personality Traits	EPQ	Extraversion	6.71±3.40	0-12	7.40±3.41	0-12	7.08±3.41	0-12	7.93±3.70	0-12	7.31±3.49	0-12	7.51±3.56	0-12
		Neuroticism	5.57±3.44	0-12	7.99±2.96	2-12	6.86±3.40	0-12	4.01±3.21	0-12	5.66±2.93	0-12	5.13±3.11	0-12
	sO-LIFE	Unusual Experience	4.62±3.10	0-12	5.68±3.22	0-11	5.19±3.20	0-12	2.44±2.31	0-10	3.04±2.28	0-9	2.83±2.31	0-10
		Cognitive Disorganisation	5.20±3.25	0-11	6.96±3.03	0-11	6.15±3.25	0-11	4.01±2.91	0-11	5.24±3.03	0-11	4.82±3.05	0-11
		Introvertive Anhedonia	3.19±1.95	0-8	3.35±1.94	0-8	3.28±1.94	0-8	1.97±1.76	0-8	1.96±1.70	0-9	1.95±1.72	0-9
		Impulsive Nonconformity	2.75±1.92	0-8	3.07±2.057	0-8	2.92±1.98	0-8	2.79±1.73	0-7	2.64±1.73	0-7	2.67±1.74	0-7
	S-UPPS-P	Negative Urgency	8.94±3.04	4-16	9.90±3.11	4-16	9.45±3.11	4-16	8.19±2.50	4-16	8.85±2.10	4-13	8.64±2.25	4-16
		Lack of Perseverance	6.55±1.77	4-11	6.89±2.01	4-14	6.74±1.91	4-14	12.05±1.64	9-16	12.29±1.72	7-16	12.22±1.69	7-16
		Lack of Premeditation	6.67±2.27	4-15	7.14±2.06	4-13	6.92±2.17	4-15	12.09±1.63	8-16	11.82±1.66	8-16	11.91±1.65	8-16
		Sensation Seeking	11.89±2.79	5-16	10.90±2.82	5-16	11.36±2.84	5-16	10.61±2.71	5-16	9.45±2.47	4-16	9.82±2.60	4-16
		Positive Urgency	8.30±3.19	4-16	8.66±3.04	5-16	8.49±3.11	4-16	7.18±2.52	4-15	6.67±2.19	4-12	6.83±2.31	4-15
		Emotional Abuse	9.14±3.91	5-22	10.67±5.02	5-25	9.96±4.59	5-25	7.38±3.49	5-23	8.55±3.88	5-25	8.18±3.79	5-25
		Physical Abuse	7.73±3.62	5-19	7.62±4.17	5-24	7.67±3.91	5-24	5.42±1.15	5-11	5.74±2.39	5-24	5.64±2.08	5-24

Childhood Trauma	CTQ-SF	Sexual Abuse	7.02±4.32	5-21	8.02±5.51	5-25	7.56±5.00	5-25	5.14±1.00	5-13	5.50±1.93	5-22	5.38±1.69	5-22
		Emotional Neglect	10.87±4.46	5-25	11.41±4.6	5-23	11.16±4.53	5-25	8.90±4.02	5-19	9.49±4.34	5-25	9.30±4.24	5-25
		Physical Neglect	8.35±3.20	5-17	8±3.19	5-18	8.16±3.19	5-18	6.67±2.21	5-16	6.69±2.42	5-17	6.68±2.35	5-17

Abbreviations: MEQ, Morningness-Eveningness Questionnaire; PSQI, Pittsburgh Sleep Quality Index; EPQ-SF, Eysenck Personality Questionnaire-Revised; DASS-21, Depression Anxiety and Stress Scale-21 Items; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; S-UPPS-P, Impulsive Behaviour Scale-Short Version; CTQ-SF, Short Form of Childhood Trauma Questionnaire.
Note: Physical abuse data missing for 4 participants and sexual and emotional abuse data missing for 1 participant (all German females).

6.5.2 Association Between Chronotype, Sleep Quality, Mental Health, Personality Traits and Childhood Trauma

6.5.2.1 UK

EC was correlated with higher levels of Depression (r=-0.242, p<0.001) and higher Extraversion scores (r=0.226, p=0.002). EC was also correlated significantly with higher BMI (r=-0.227, p=0.002). While some correlations appeared numerically stronger in females than males, these differences did not reach statistical significance (p>0.05) (see Table 6.3).

As expected, poor sleep quality, indicated by higher PSQI scores, correlated with higher levels of Depression (r=0.565, p<0.001), Anxiety (r=0.535, p<0.001), Stress (r=0.510, p<0.001); higher scores on psychopathology-related personality traits, including Neuroticism (r=0.379, p<0.001), Unusual Experiences (r=0.236, p<0.001), Cognitive Disorganisation (r=0.363, p<0.001), Introvertive Anhedonia (r=0.175, p=0.017), Impulsive Nonconformity (r=0.203, p=0.006), Negative Urgency (r=0.315, p<0.001), and Positive Urgency (r=0.175, p=0.017); and severity of self-reported Emotional Abuse (r=0.422, p<0.001) and Sexual Abuse (r=0.230, p=0.002) (Table 6.4). Poor sleep quality also correlated with EC (r=-0.296, p<0.001); although this correlation appeared numerically stronger in males than females, this sex difference was not statistically significant (p>0.05). Overall, chronotype had small-sized correlations with mental health outcomes, whereas sleep quality had large sized correlations with mental health outcomes.

6.5.2.2 Germany

In line with the UK findings, EC significantly correlated with higher levels of Depression (r=-0.299, p<0.001) and Stress (r=-0.234, p<0.001) as well as with higher scores on personality measures of Neuroticism (r=-0.206, p=0.003), Cognitive Disorganisation (r=-0.302, p<0.001), Negative Urgency (r=-0.147, p=0.033), and Lack of Premeditation (r=0.159, p=0.022). Again, some correlations appeared numerically stronger in females than males but these differences did not reach statistical significance (p>0.05) (see Table 6.3).

As expected, poor sleep quality correlated with higher levels of Depression (r=0.275, p<0.001), Anxiety (r=0.305, p<0.001), Stress (r=0.271, p<0.001); higher scores on personality measures of Neuroticism (r=0.244, p<0.001), Unusual Experiences (r=0.308, p<0.001), Cognitive

Disorganisation (r=0.289, p<0.001), Introvertive Anhedonia (r=0.196, p=0.005), Impulsive Nonconformity (r=0.186, p=0.007), Negative Urgency (r=0.157, p=0.024); and severity of self-reported Emotional Abuse (r=0.261, p<0.001), Physical Abuse (r=0.181, p=0.010), and Sexual Abuse (r=0.188, p=0.007) (Table 6.5). Poor sleep quality also correlated with EC (r=-0.276, p<0.001); although this correlation appeared numerically stronger in females than males, this sex difference did not reach any statistical significance (p>0.05). Lastly, compared to EC, poor sleep quality showed significantly stronger correlations, as expected, with Anxiety (Fisher's Exact z=4.51, p<0.001) and Stress (Fisher's Exact z=5.24, p<0.001). Overall, both chronotype and sleep quality had small-to-medium-sized correlations with mental health outcomes.

Table 6.3 *Correlations (Pearson's r) between chronotype and measures of mental health, sleep quality, personality traits and childhood trauma.*

	Mental Health			Sleep Quality	Personality Traits															Childhood Trauma
	DASS-21				EPQ-SF		s-OLIFE				S-UPPS-P					CTQ-SF				
	D	A	S	PSQI	E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN
										UK										
MEQ (Overall)	-0.242 (<0.001)	-0.130 (0.077)	-0.101 (0.172)	-0.296 <0.001	0.226 (0.002)	-0.079 (0.287)	0.059 (0.426)	-0.112 (0.128)	0.055 (0.461)	-0.043 (0.562)	-0.027 (0.713)	-0.135 (0.067)	-0.093 (0.210)	-0.005 (0.941)	-0.084 (0.255)	-0.113 (0.125)	-0.035 (0.637)	0.046 (0.535)	-0.071 (0.336)	0.078 (0.292)
Males	-0.183 (0.091)	-0.059 (0.59)	-0.046 (0.675)	-0.349 (0.001)	0.102 (0.349)	0.013 (0.908)	0.205 (0.058)	-0.028 (0.799)	0.084 (0.443)	0.028 (0.797)	0.063 (0.565)	0.030 (0.783)	0.019 (0.863)	-0.043 (0.694)	0.063 (0.566)	-0.066 (0.549)	0.109 (0.316)	0.031 (0.780)	-0.051 (0.639)	0.190 (0.079)
Females	-0.304 (0.002)	-0.207 (0.04)	-0.179 (0.077)	-0.307 (0.002)	0.301 (0.002)	-0.239 (0.017)	-0.066 (0.514)	-0.238 (0.018)	0.028 (0.782)	-0.103 (0.310)	-0.117 (0.247)	-0.253 (0.011)	-0.203 (0.044)	0.051 (0.616)	-0.204 (0.043)	-0.170 (0.093)	-0.120 (0.236)	0.039 (0.701)	-0.096 (0.343)	0.010 (0.919)
										Germany										
MEQ (Overall)	-0.299 (<0.001)	-0.129 (0.062)	-0.234 (<0.001)	-0.276 (<0.001)	0.049 (0.485)	-0.206 (0.003)	-0.113 (0.102)	-0.302 (<0.001)	-0.075 (0.282)	-0.132 (0.057)	-0.147 (0.033)	0.159 (0.022)	0.049 (0.481)	0.007 (0.925)	-0.096 (0.167)	-0.068 (0.328)	-0.007 (0.923)	0.097 (0.163)	0.008 (0.906)	0.101 (0.145)
Males	-0.270 (0.027)	-0.139 (0.262)	-.0324 (0.008)	-0.227 (0.067)	0.154 (0.214)	-0.220 (0.073)	-0.099 (0.424)	-0.342 (0.005)	-0.193 (0.119)	-0.141 (0.255)	-0.162 (0.191)	0.213 (0.084)	-0.043 (0.727)	0.048 (0.700)	-0.292 (0.016)	-0.079 (0.526)	-0.150 (0.228)	-0.039 (0.752)	0.025 (0.842)	0.231 (0.060)
Females	-0.317 (<0.001)	-0.131 (0.119)	-0.200 (0.017)	-0.320 (<0.001)	-0.004 (0.966)	-0.225 (0.007)	-0.130 (0.124)	-0.303 (<0.001)	-0.012 (0.888)	-0.125 (0.137)	-0.150 (0.076)	0.130 (0.124)	0.101 (0.233)	-0.003 (0.967)	0.026 (0.756)	-0.073 (0.389)	0.026 (0.761)	0.135 (0.109)	-0.002 (0.982)	0.041 (0.631)

Abbreviations: MEQ, Morningness-Eveningness Questionnaire; D, Depression; A, Anxiety; S, Stress; DASS-21, Depression Anxiety and Stress Scale-21 Items; PSQI, Pittsburgh Sleep Quality Index; E, Extraversion; N, Neuroticism; EPQ-SF, Eysenck Personality Questionnaire-Revised; UE, Unusual Experience; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; NU, Negative Urgency; LP, Lack of Perseverance; LPr, Lack of Premeditation; SS, Sensation Seeking; PU, Positive Urgency; S-UPPS-P, Impulsive Behaviour Scale-Short Version; EA, Emotional Abuse; PA, Physical Abuse; SA, Sexual Abuse; EN, Emotional Neglect; PN, Physical Neglect; CTQ-SF, short form of Childhood Trauma Questionnaire.

Table 6.4 *Correlations (Pearson's r) between measures of mental health, sleep quality, personality traits and childhood trauma in the UK sample.*

	Mental Health			Sleep Quality	Personality Traits															Childhood Trauma		
	DASS-21				EPQ-SF		s-OLIFE					S-UPPS-P								CTQ-SF		
	D	A	S	PSQI	E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN		
D	1	0.712 (<0.001)	0.656 (<0.001)	0.565 (<0.001)	-0.249 (<0.001)	0.478 (<0.001)	0.370 (<0.001)	0.443 (<0.001)	0.358 (<0.001)	0.238 (0.001)	0.365 (<0.001)	0.063 (0.397)	0.122 (0.097)	-0.114 (0.121)	0.271 (<0.001)	0.413 (<0.001)	0.199 (0.007)	0.204 (0.005)	0.214 (0.003)	0.183 (0.013)		
A		1	0.769 (<0.001)	0.535 (<0.001)	-0.113 (0.127)	0.570 (<0.001)	0.478 (<0.001)	0.517 (<0.001)	0.314 (<0.001)	0.333 (<0.001)	0.319 (<0.001)	0.059 (0.422)	0.194 (0.008)	-0.166 (0.024)	0.265 (<0.001)	0.444 (<0.001)	0.285 (<0.001)	0.322 (<0.001)	0.217 (0.003)	0.291 (<0.001)		
S			1	0.510 (<0.001)	-0.071 (0.335)	0.598 (<0.001)	0.403 (<0.001)	0.506 (<0.001)	0.331 (<0.001)	0.324 (<0.001)	0.361 (<0.001)	-0.001 (0.993)	0.213 (0.004)	-0.175 (0.017)	0.269 (<0.001)	0.406 (<0.001)	0.120 (0.104)	0.268 (<0.001)	0.142 (0.054)	0.135 (0.067)		
PSQI				1	-0.102 (0.169)	0.379 (<0.001)	0.236 (0.001)	0.363 (<0.001)	0.175 (0.017)	0.203 (0.006)	0.315 (<0.001)	0.046 (0.536)	0.136 (0.066)	-0.070 (0.345)	0.175 (0.017)	0.422 (<0.001)	0.118 (0.109)	0.230 (0.002)	0.141 (0.056)	0.061 (0.408)		
E					1	-0.161 (0.029)	-0.082 (0.268)	-0.274 (<0.001)	-0.442 (<0.001)	0.018 (0.811)	0.060 (0.418)	-0.216 (0.003)	0.004 (0.952)	0.172 (0.019)	0.085 (0.249)	0.020 (0.791)	-0.020 (0.788)	0.159 (0.030)	-0.037 (0.614)	-0.005 (0.944)		
N						1	0.524 (<0.001)	0.707 (<0.001)	0.293 (<0.001)	0.335 (<0.001)	0.523 (<0.001)	-0.018 (0.809)	0.037 (0.619)	-0.235 (0.001)	0.362 (<0.001)	0.247 (<0.001)	0.080 (0.281)	0.147 (0.046)	0.109 (0.138)	0.126 (0.086)		
UE							1	0.615 (<0.001)	0.410 (<0.001)	0.500 (<0.001)	0.442 (<0.001)	-0.061 (0.411)	-0.028 (0.710)	0.033 (0.659)	0.444 (<0.001)	0.230 (0.002)	0.167 (0.023)	0.211 (0.004)	0.145 (0.050)	0.243 (<0.001)		
CD								1	0.362 (<0.001)	0.431 (<0.001)	0.480 (<0.001)	0.109 (0.139)	0.202 (0.006)	-0.103 (0.163)	0.427 (<0.001)	0.253 (<0.001)	0.056 (0.449)	0.089 (0.226)	0.184 (0.012)	0.125 (0.089)		
IA									1	0.263 (<0.001)	0.166 (0.024)	0.007 (0.929)	0 (0.999)	-0.179 (0.015)	0.174 (0.018)	0.178 (0.016)	0.128 (0.083)	0.135 (0.067)	0.153 (0.038)	0.170 (0.021)		
IN										1	0.362 (<0.001)	0.085 (0.251)	0.223 (0.002)	0.113 (0.127)	0.439 (<0.001)	0.254 (<0.001)	0.169 (0.022)	0.211 (0.004)	0.174 (0.018)	0.179 (0.015)		
NU											1	-0.057 (0.438)	0.119 (0.108)	0.088 (0.235)	0.693 (<0.001)	0.240 (<0.001)	0.131 (0.075)	0.179 (0.015)	0.084 (0.253)	0.152 (0.039)		
LP												1	0.507 (<0.001)	-0.123 (0.095)	0.035 (0.640)	0.059 (0.427)	0.053 (0.473)	-0.072 (0.333)	0.032 (0.667)	0.056 (0.45)		
LPr													1	-0.022 (0.767)	0.217 (0.003)	0.181 (0.014)	0.119 (0.108)	0.103 (0.163)	0.093 (0.206)	0.078 (0.292)		
SS														1	0.197 (0.007)	-0.063 (0.392)	0 (0.998)	0.016 (0.828)	0.113 (0.127)	0.126 (0.087)		
PU															1	0.148 (0.045)	0.071 (0.340)	0.140 (0.057)	0.139 (0.060)	0.155 (0.035)		
EA																1	0.669 (<0.001)	0.546 (<0.001)	0.581 (<0.001)	.0432 (<0.001)		
PA																	1	0.430 (<0.001)	0.425 (<0.001)	0.489 (<0.001)		
SA																		1	0.329 (<0.001)	0.342 (<0.001)		
EN																			1	0.534 (<0.001)		
PN																				1		

Abbreviations: D, Depression; A, Anxiety; S, Stress; DASS-21, Depression Anxiety and Stress Scale-21 Items; PSQI, Pittsburgh Sleep Quality Index; E, Extraversion; N, Neuroticism; EPQ-SF, Eysenck Personality Questionnaire-Revised; UE, Unusual Experience; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; NU, Negative Urgency; LP, Lack of Perseverance; LPr, Lack of Premeditation; SS, Sensation Seeking; PU, Positive Urgency; S-UPPS-P, Impulsive Behaviour Scale-Short Version; EA, Emotional Abuse; PA, Physical Abuse; SA, Sexual Abuse; EN, Emotional Neglect; PN, Physical Neglect; CTQ-SF, short form of Childhood Trauma Questionnaire.

Table 6.5 *Correlations (Pearson's r) between measures of mental health, sleep quality, personality traits and childhood trauma in German sample.*

	Mental Health			Sleep Quality	Personality Traits															Childhood Trauma	
	DASS-21				EPQ-SF		s-OLIFE					S-UPPS-P				CTQ-SF					
	D	A	S	PSQI	E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN	
D	1	0.505 (<0.001)	0.620 (<0.001)	0.275 (<0.001)	-0.193 (0.005)	0.581 (<0.001)	0.302 (<0.001)	0.508 (<0.001)	0.382 (<0.001)	0.322 (<0.001)	0.337 (<0.001)	-0.137 (0.049)	-0.134 (0.053)	0.098 (0.160)	0.293 (<0.001)	0.188 (0.006)	0.091 (0.193)	-0.050 (0.471)	0.184 (0.008)	0.108 (0.120)	
A		1	0.557 (<0.001)	0.305 (<0.001)	-0.113 (0.104)	0.496 (<0.001)	0.535 (<0.001)	0.416 (<0.001)	0.285 (<0.001)	0.281 (<0.001)	0.224 (0.001)	-0.039 (0.571)	-0.088 (0.205)	0.019 (0.784)	0.285 (<0.001)	0.283 (<0.001)	0.189 (0.007)	0.067 (0.336)	0.134 (0.054)	0.127 (0.066)	
S			1	0.271 (<0.001)	-0.098 (0.156)	0.687 (<0.001)	0.411 (<0.001)	0.561 (<0.001)	0.190 (0.006)	0.321 (<0.001)	0.432 (<0.001)	0.002 (0.973)	-0.110 (0.113)	0.032 (0.648)	0.324 (<0.001)	0.232 (<0.001)	0.079 (0.259)	-0.082 (0.241)	0.170 (0.015)	0.087 (0.210)	
PSQI				1	-0.064 (0.360)	0.244 (<0.001)	0.308 (<0.001)	0.289 (<0.001)	0.196 (0.005	0.186 (0.007)	0.157 (0.024)	0.070 (0.318)	-0.048 (0.490)	0.043 (0.534)	0.121 (0.082)	0.261 (<0.001)	0.181 (0.010)	0.188 (0.007)	0.124 (0.076)	0.109 (0.118)	
E					1	-0.225 (0.001)	0.013 (0.855)	-0.233 (<0.001)	-0.499 (<0.001)	0.183 (0.008)	0.043 (0.539)	0.045 (0.522)	-0.211 (0.002)	0.356 (<0.001)	0.153 (0.027)	-0.027 (0.693)	0.011 (0.876)	-0.048 (0.494)	-0.134 (0.054)	-0.010 (0.885)	
N						1	0.402 (<0.001)	0.652 (<0.001)	0.282 (<0.001)	0.288 (<0.001)	0.461 (<0.001)	-0.070 (0.314)	-0.114 (0.100)	-0.135 (0.051)	0.235 (<0.001)	0.213 (0.002)	-0.005 (0.947)	-0.025 (0.715)	0.166 (0.017)	0.004 (0.949)	
UE							1	0.423 (<0.001)	0.182 0.008	0.343 (<0.001)	0.340 (<0.001)	-0.060 (0.391)	-0.159 (0.022)	0.117 (0.092)	0.414 (<0.001)	0.271 (<0.001)	0.160 (0.023)	0.098 (0.159)	0.117 (0.095)	0.131 (0.059)	
CD								1	0.312 (<0.001)	0.396 (<0.001)	0.470 (<0.001)	-0.225 (0.001)	-0.227 (<0.001)	-0.003 (0.969)	0.276 (<0.001)	0.180 (0.009)	0.068 (0.337)	0.040 (0.570)	0.166 (0.017)	0.079 (0.258)	
IA									1	0.083 (0.231)	0.076 (0.273)	-0.052 (0.457)	0.083 (0.231)	-0.088 (0.207)	0.124 (0.075)	0.034 (0.625)	-0.006 (0.927)	-0.012 (0.867)	0.175 (0.012)	0.206 (0.003)	
IN										1	0.444 (<0.001)	-0.089 (0.199)	-0.336 (<0.001)	0.298 (<0.001)	0.386 (<0.001)	0.165 (0.017)	0.046 (0.513)	0.064 (0.356)	0.023 (0.742)	0.119 (0.085)	
NU											1	-0.138 (0.046)	-0.325 (<0.001)	0.158 (0.022)	0.511 (<0.001)	0.260 (<0.001)	0.026 (0.717)	0.019 (0.784)	0.166 (0.017)	0.060 (0.388)	
LP												1	0.291 (<0.001)	-0.052 (0.453)	-0.044 (0.524)	0.004 (0.956)	0.091 (0.194)	-0.028 (0.692)	-0.036 (0.608)	-0.103 (0.139)	
LPr													1	-0.211 (0.002)	-0.210 (0.002)	-0.121 (0.080)	0.058 (0.407)	-0.042 (0.550)	-0.051 (0.463)	-0.027 (0.699)	
SS														1	0.273 (<0.001)	0.062 (0.374)	0.025 (0.722)	-0.008 (0.903)	-0.015 (0.827)	-0.008 (0.904)	
PU															1	0.093 (0.179)	0.059 (0.402)	0.047 (0.503)	0.049 (0.484)	0.075 (0.279)	
EA																1	0.592 (<0.001)	0.280 (<0.001)	0.644 (<0.001)	0.313 (<0.001)	
PA																	1	0.255 (<0.001)	0.419 (<0.001)	0.348 (<0.001)	
SA																		1	0.290 (<0.001)	0.263 (<0.001)	
EN																			1	0.537 (<0.001)	
PN																				1	

Abbreviations: D, Depression; A, Anxiety; S, Stress; DASS-21, Depression Anxiety and Stress Scale-21 Items; PSQI, Pittsburgh Sleep Quality Index; E, Extraversion; N, Neuroticism; EPQ-SF, Eysenck Personality Questionnaire-Revised; UE, Unusual Experience; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; NU, Negative Urgency; LP, Lack of Perseverance; LPr, Lack of Premeditation; SS, Sensation Seeking; PU, Positive Urgency; S-UPPS-P, Impulsive Behaviour Scale-Short Version; EA, Emotional Abuse; PA, Physical Abuse; SA, Sexual Abuse; EN, Emotional Neglect; PN, Physical Neglect; CTQ-SF, short form of Childhood Trauma Questionnaire.

6.5.3 The Mediating Role of Sleep Quality: SEM Analysis

6.5.3.1 UK

Our proposed model (Figure 6.2) had a good fit to the data (χ^2/df=1.13, p<0.001; RMSEA=0.01; GFI=0.96; AGFI=0.90; CFI=0.99) but had a poor local fit. We therefore revised it by removing non-significant paths to reach our final model (χ^2/df=0.99; GFI=0.97; TLI=1; CFI=1; RMSEA=0.000) (see Figure 6.3). As evident in Figure 6.3, there was no significant direct influence of chronotype on mental health; instead, the chronotype–mental health relationship was fully mediated by poor sleep quality. The mental health relationship with Neuroticism and Cognitive Disorganisation was also partially mediated by poor sleep quality. Lastly, we found no sex-related influence in the final model, as indicated by non-significant differences [$\Delta\chi^2(8)$=4.68, p=0.791; ΔCFI=0; ΔRMSEA=0.008] when comparing the model fit of the unconstrained model with that of the structural-weight-constrained model.

Figure 6.2 *Results of the initial SEM analyses in the UK-based sample. Solid lines denote significant paths (** p<0.001, *p<0.005) and dotted lines denote non-significant paths.*

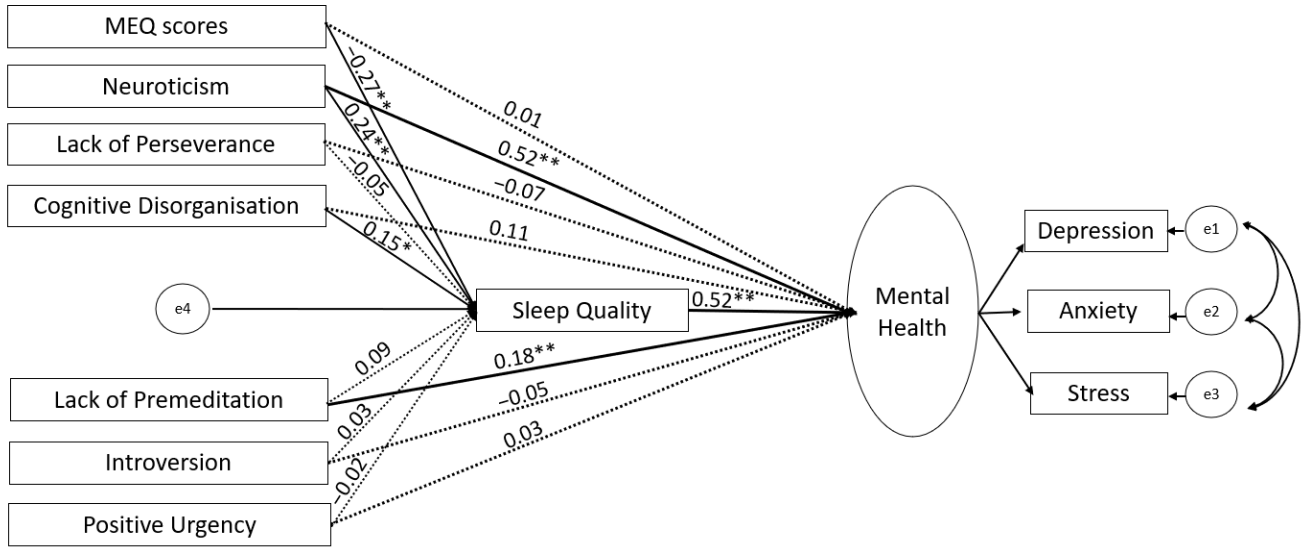
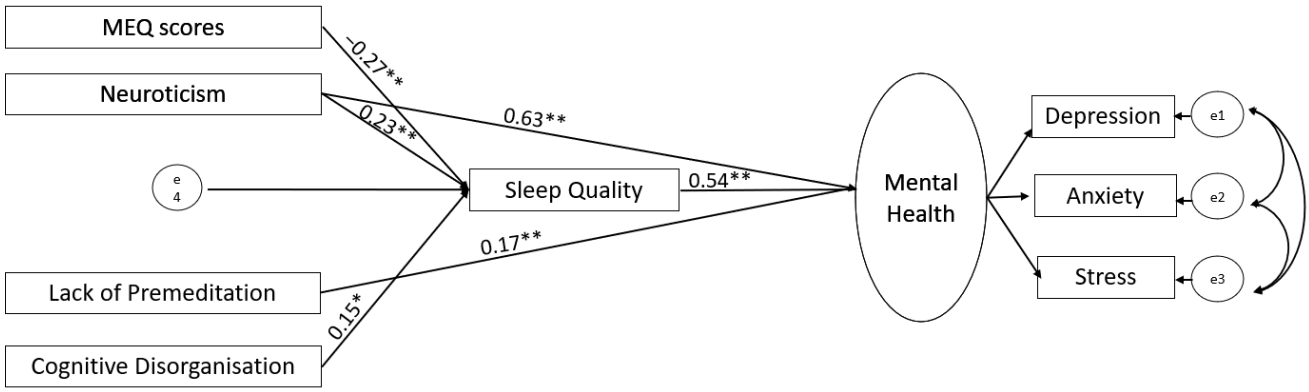


Figure 6.3 *Revised (final) model displaying significant paths (**p<0.001, *p<0.005) in the UK-based sample.*



6.5.3.2 Germany

In line with the UK findings, our proposed model (Figure 6.4) had an acceptable fit (χ^2/df = 4.38, p<0.001; RMSEA=0.12; GFI=0.94; AGFI=0.78; CFI=0.92) to the data, but it was revised, due to poor local fit, to remove the non-significant paths (model fit indices: χ^2/df=3.72; GFI=0.93; TLI=0.82; CFI=0.91; RMSEA=0.11) (see Figure 6.5). As depicted in Figure 6.5, we found no direct effect of chronotype on mental health and observed that its relationship with mental health was fully mediated by poor sleep quality. We also found that sleep quality partially mediated the association of mental health with Cognitive Disorganisation and Lack of Perseverance. While exploring sex differences, we found that the comparison of the unconstrained model with the structural-weight-constrained model showed a non-significant chi-square difference $\Delta\chi^2(9)=16.44$, p=0.058 and RMSEA (ΔRMSEA=0.003) but a significant difference in CFI (ΔCFI=0.013). The pairwise difference in the path coefficients of the unconstrained model in males and females showed a significant difference in the path linking sleep quality with mental health [Critical ratio=2.04; stronger in females (β=0.252) than males (β=0.028)], and the path linking Cognitive Disorganisation with sleep quality [Critical ratio=2.10; stronger in males (β=0.485) than females (β=0.128)], suggesting a partial variance in the model.

Figure 6.4 *Results of the initial SEM analyses in the Germany-based sample. Solid lines denote significant paths (**p< 0.001, *p< 0.005) and dotted lines denote non-significant paths.*

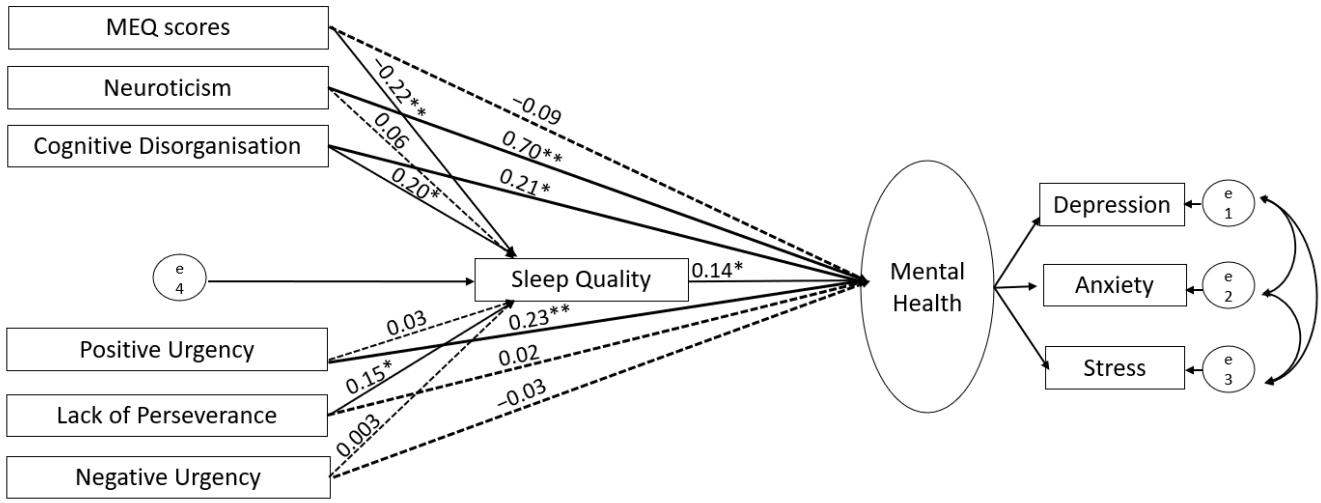
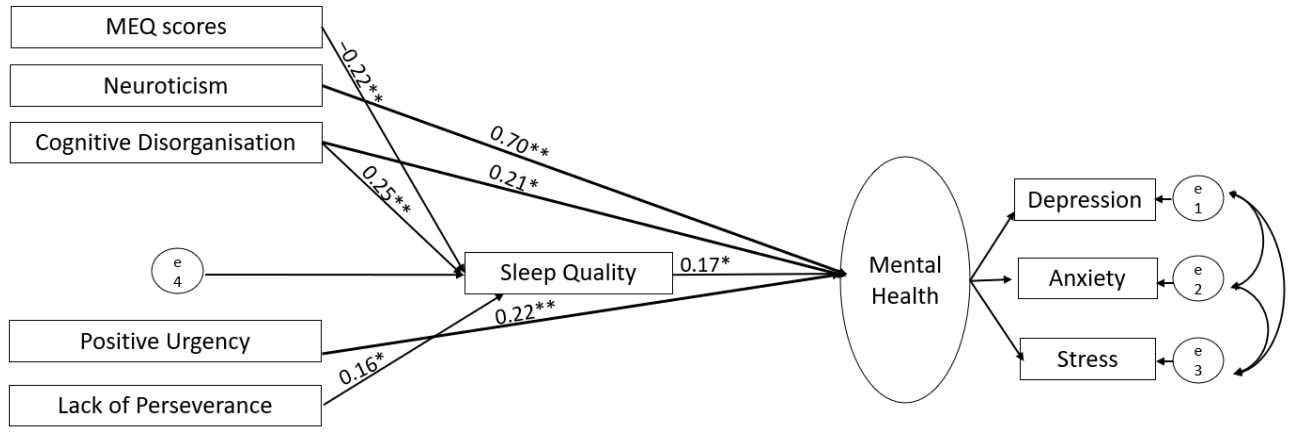


Figure 6.5 *Revised (final) model displaying significant paths (**p<0.001, *p<0.005) in the Germany-based sample.*



6.5.3.3 Chronotype, Sleep Quality, and Mental Health Associations: UK versus Germany

When exploring the possible invariance of the path model across the UK and Germany-based samples, we found the measurement model of mental health to be variant [$\Delta\chi^2(2)=11.22$, $p=0.004$; ΔCFI=0.008; ΔRMSEA=0.013]. The factor loading of anxiety in the UK ($\beta=0.675$) and Germany ($\beta=0.531$) was found to be significantly different (Critical ratio=3.36). Additionally, compared to the measurement-weight-constrained model, the structural-weight-constrained model also differed [$\Delta\chi^2(6)=18.73$, $p=0.005$; ΔCFI=0.011] although with a non-

significant RMSEA (ΔRMSEA=0.005). The pairwise difference in the path coefficients of the measurement-weight-constrained model showed a difference in the path linking sleep quality to mental health (CR=3.84), this being stronger in the UK (β=0.55) than Germany (β=0.16).

6.6 Discussion

The present study aimed to further examine our recent finding of sleep quality as a mediating factor in the chronotype–mental health relationship in young non-clinical (healthy) adults residing in North India (Chauhan et al., 2024a) in a sample of young non-clinical adults residing in the UK or Germany while also quantifying the role of psychopathology-related personality traits and childhood trauma in this relationship. Unexpectedly, our UK (London)-based participants, on average, were found to have, higher levels of depression, anxiety, and stress, as well as poor sleep quality, compared to those who were residing in Germany (Bonn). This may be related to a difference in the recruitment strategy used in the UK and Germany. In the UK, each recruited participant received GBP 5 for their participation, while those recruited in Germany were enrolled in a lottery system to win EUR 50. A small but guaranteed financial incentive that was offered to each participant in the UK might have attracted more participants belonging to a lower socioeconomic background which is known to be associated with poor mental health and reduced psychological well-being (Ibrahim et al., 2013; Hao & Farah, 2020; Papadopoulos & Etindele, 2023).

In relation to our study hypothesis, the key findings of the present study were: (i) EC had small-to-medium-sized associations with metal health outcomes (UK and Germany, *r* values: 0.20-0.30), (ii) Poor sleep quality had large associations with mental health outcomes in the UK-based sample (*r* values: 0.51-0.56), while small-to-medium-sized associations were observed in Germany-based sample (*r* values: 0.27-0.30), and (iii) Sleep quality fully mediated the chronotype–mental health relationship, with no significant direct effect of EC on mental health outcomes in either the UK- or Germany-based samples. EC had significant but mostly small-to-medium-sized (*r* values, 0.14-0.34) associations with psychopathology-relevant personality traits in both samples. The association between EC and severity of childhood emotional maltreatment, although in line with our earlier findings in the North Indian sample (Chauhan et al., 2024a), was not formally significant in the UK- or Germany-based samples.

In the present study, we employed same methods and replicated our previous findings in a North Indian sample (Chauhan et al., 2024a) in showing that sleep quality fully mediated the chronotype-mental health association in non-clinical young UK and Germany-based samples, though this effect was weaker in Germany-based sample, possibly due to a limited range of scores on measures of both mental health and sleep (Table 6.2) as well as a possible difference between the UK and Germany-based samples in resilience that was recently reported to impact both chronotype–mental health and sleep–mental health associations (Poon et al., 2024). Nonetheless, our findings across India, the UK, and Germany are generally in line with previous correlational studies that have consistently found an association between EC and depressive symptoms (Au & Reece, 2017; Norbury, 2021) as well as general mental health (Cheung et al., 2023). Some longitudinal studies show that the prevalence of higher levels of depression predicts EC, especially in adolescents (Haraden et al., 2017, 2019), but there are also some longitudinal studies, using actigraphy, that failed to detect an association between depression and EC in adolescents (Bai et al., 2021; Karan et al., 2021). These studies, however, did not consider sleep-related disturbances, including poor sleep latency, quality, and duration, all of which are known to be more common in ECs (Chauhan et al., 2024a; Ma et al., 2022; Muzni et al., 2021; Poon et al., 2024), as also shown in the current study. The mediating role of sleep quality in the chronotype–mental health relationship is also visible in clinically depressed individuals (Merikanto & Partonen, 2021). Further support for the mediating role of sleep quality in the chronotype–poor mental health link comes from recent findings suggesting that this link is either attenuated or absent in the presence of sufficient and good quality sleep (for example, in individuals who can work remotely) in ECs (Salfi et al., 2022).

In the modern world, humans realistically rely less on their internal clock and more on the social clock to sleep, which disrupts and shifts their circadian rhythms (Czeisler et al., 1990; Roenneberg et al., 2003) of melatonin and cortisol secretions (Gooley et al., 2011; Zeitzer et al., 2000), both linked with psychiatric illnesses such as schizophrenia and depression (Chauhan et al., 2023; Rahman et al., 2010). One of the most noticeable forms of circadian disruption is sleep disturbance and social jetlag, commonly found in ECs (Roenneberg et al., 2003; Tan et al., 2022) due to their natural tendency to be awake at later hours, which causes difficulties in sleep restoration and falling asleep (Randler et al., 2017; Tutek et al., 2019). Not surprisingly, studies have reported insomnia severity (β=−0.14) as a significant moderator of the chronotype–mental health relationship (Cheung et al., 2023). Taken together, non-restoration of sleep and/or poor sleep habits as a result of disrupted CRs may explain previously

observed positive associations between EC and adverse mental health outcomes. The prevalence of poor sleep quality may render ECs more susceptible to developing mental health issues. This may be especially true for people who have lower resilience (Poon et al., 2024; Zhou et al., 2021), though such a possibility was not directly addressed in the current study.

While investigating the influence of psychopathology-related traits, we found a small-sized positive association between EC and neuroticism in female participants of both the UK and Germany-based samples. This is consistent with previous findings on this topic (Adan et al., 2012; Chauhan et al., 2023; Muzni et al., 2021; Randler et al., 2017). Interestingly, this relationship was somewhat weaker and non-significant for males, who also scored, on average, lower than females, which is not surprising given known sex differences in neuroticism (females>males) across countries and cultures (Jorm, 1987). Extraversion had a small association with MC in the UK, which is also consistent with the previous literature (Chauhan et al., 2024a; Muzni et al., 2021; Randler et al., 2017). This relationship, however, was not found in Germany-based sample for reasons that we do not fully understand. There are some other studies that have found no significant associations between extraversion and MC (Adan et al., 2012). We found a small correlation between EC and impulsivity both in the UK and German-based samples. This has also been seen in previous studies (Chauhan et al., 2024a; McCarthy et al., 2023). Impulsivity as a personality trait has been linked with impulsive behaviour in healthy and clinical populations (Whiteside & Lynam, 2001) and might explain why ECs may be more likely to engage in substance abuse and addiction (Adan et al., 2012). Interestingly, we also replicated our previous findings of a small but significant association between cognitive disorganisation aspect of schizotypy and EC in both UK (females) and German (all) participants. Individuals scoring high on schizotypy share some characteristics with schizophrenia patients (Nelson et al., 2013), including higher stress-reactivity and anxiety (Premkumar et al., 2020, 2021; Stelton & Ferraro, 2008), which disrupts sleep cycles (Kalmbach et al., 2018), and sleep deprivation in turn can induce psychosis-like symptoms in healthy adults (Bliss et al., 1959; Kumari & Ettinger, 2020; Petrovsky et al., 2014).

6.6.1 Limitations and Future Directions

The study had some limitations. First, we used self-report questionnaires and did not control for light exposure, and menstrual cycle phase in females, both of which may influence sleep and mental health (Adan et al., 2012; Manber & Bootzin, 1997). Second, we restricted our

sample to young adults (≤40 years), and thus the findings cannot be generalised to adolescents (≤17 years) or older adults (>40 years). Third, our study used chronotype as continuous variable and employed a cross-sectional design; therefore, it cannot speak of causation. Fourth, we did not collect data on nationality. Further studies employing objective measures of circadian rhythm alongside relevant self-report measures in a longitudinal design and different age groups are needed to substantiate and refine the present findings.

6.6.2 Conclusions

To conclude, we did not observe any direct impact of chronotype on mental health; instead, this association was found to be fully mediated by poor sleep quality in young adults living in the UK or Germany. These and our previous findings (Chauhan et al., 2024a) argue against the independent role of chronotype as a transdiagnostic risk factor for mental health problems in non-clinical young adults and highlight sleep disruption and circadian misalignment as important therapeutic targets for improving mental health outcomes. Intervening early on to ensure good sleep quality may be a preventive strategy in combination with attempts to shift circadian preference towards morning.

Chapter 7: Influence of Chronotype and Sleep Quality in Verbal Learning and Memory: An Experimental Study

Abstract

Previous research has highlighted the limited-to-no effect of chronotype (on its own) on verbal learning and memory while the findings in relation to ToD and/or synchrony effect on verbal memory and learning in young healthy adults have been mixed. The majority of previous research, however, has not considered sleep-related disturbances or relevant personality traits while assessing chronobiological influences in cognitive function. This study examined potential chronotype, ToD and synchrony effects on verbal learning and memory while also taking sleep quality (sleep quality, latency, efficiency, duration, disturbance, daytime dysfunction, medication use) and relevant personality traits (schizotypy, impulsivity) into account. Sixty-three young non-clinical adults (18-40 years), selected from a larger participant pool to represent morning (N=21), intermediate (N=22), and evening (N=20) chronotypes, were assessed on the Hopkins Verbal Learning Test (HVLT) on two separate occasions one week apart: once in the morning (8:00-10:00) and once during the late afternoon (16:00-18:00). The results showed no main effect of chronotype in any memory variables but MCs performed better (delayed recall) at their optimal ToD. Daytime dysfunction (a poor sleep quality dimension) was negatively associated with learning slope and cumulative word learning. Any ToD-related influence on delayed recall (episodic memory) or strategy formation was explained by daytime dysfunction and Introvertive Anhedonia (a facet of schizotypy). Overall, these findings suggest a synchrony effect and sleep-related disturbances in episodic memory and related processes.

7.1 Chapter Aims and Overview

This chapter reports an empirical study conducted to examine the effect of chronobiological variables on verbal learning and memory while also taking possible roles of sleep quality and personality variables into account.

7.2 Introduction

Verbal learning and memory typically involve encoding, storing, and retrieving of verbally presented items (e.g., list of words) (Tatsumi & Watanabe, 2009). The item information is encoded via the associations between phonological and lexical representation of the stimuli (i.e., words) while the sequence is coded through the connections between lexical representation and the timing of presented stimuli. These connections can be altered or strengthened in the short-term (i.e., temporary limited capacity storage; Baddeley & Hitch, 1974) and long-term memory (Burgess, 1995). Verbal long-term memory has been characterised as an episodic long-term memory, which refers to the declarative/explicit memory of past events and occurrences (Tatsumi & Watanabe, 2009). Capacity for both short-term and long-term memory capacity declines with ageing (Luo & Craik, 2008) and may be particularly impaired in psychiatric disorders (e.g., schizophrenia; Coffman et al., 2020; Seabury & Cannon, 2020) and neurodegenerative diseases (e.g., dementia; Mollers et al., 2022).

There is considerable evidence showing no associations between chronotype and verbal learning and memory (Adan, 1991; Bennetts et al., 2008; Evansova et al., 2022), but there some reports of chronotype effect on short- and long-term verbal memory (Lehmann et al., 2013; Petros et al., 1990; Anderson et al., 1991). The role of ToD is also well established in influencing short-term memory (Drust et al., 2005), immediate and delayed recall (Evansova et al., 2022; Hidalgo et al., 2004), with typically better performance in the evening hours. As discussed in Chapter 3, there is considerable evidence for a synchrony effect in memory but these studies have not considered or controlled for sleep-related disturbance and personality-related traits (e.g., schizotypy) prior to testing, all known to influence memory (Carlson et al., 2023; Luchetti et al., 2021).

The role of sleep disruption is widely reported in memory impairment (Carlson et al., 2023; Diekelmann et al., 2010). A large body of evidence has shown improved encoding, consolidation, and recall of various types of information as a result of adequate overnight sleep (Carlson et al., 2023; Gilley, 2023; Newbury et al., 2021; Paller et al., 2021) in non-clinical adults (Mednick et al., 2013) and also in psychiatric patients (Goder et al., 2008). Subjective poor sleep quality has also been reported to severely impact verbal learning and memory in healthy adults (Carlson et al., 2023) as well as in individuals with insomnia (Chen et al., 2020), schizophrenia (Bian et al., 2021), and Alzheimer's disease (Balouch et al., 2022) though not consistently so (Exalto et al., 2022; Stiver et al., 2021). These differences could be attributed to differences in the study design or approach, as much of the previous work has been centred towards sleep deprivation, duration, and/or global sleep quality score on its own (without chronotype) and also not examined the potential role of individual sleep dimensions.

The primary aim of the present study, therefore, was to investigate, the effects of chronotype, ToD, and synchrony effect on verbal learning and memory, and to explore possible associations between memory performance and global sleep quality as well as specific sleep dimensions (i.e., sleep quality, duration, latency, efficiency, disturbance, medication, and dysfunction) and personality-related traits (i.e., schizotypy, impulsivity) in young healthy adults. Based on previous research (May et al., 1993), superior verbal performance at optimal ToD for both MCs and ECs and no significant change in ICs' performance was hypothesised. It was further hypothesised that sleep dimensions especially sleep quality, duration, and day time dysfunction will be negatively associated with verbal memory performance, especially in the morning session.

7.3 Methods

7.3.1 Participants and Study Design

The study involved 63 healthy adults (18-40 years) who were carefully screened and selected from a larger pool of sample (N=213; Chauhan et a., 2024b) who had completed an online survey to ensure they met the study inclusion criteria of (i) being aged between 18-40 years and living in the UK, (ii) being fluent in English, (iii) not doing shift work, (iv) not being on any regular medication (except multivitamins and contraceptives), (v) and not having a diagnosis of any mental disorders or drug abuse. As part of the screening survey, all potential participants completed the MEQ (Horne & Östberg, 1976) so that the most representative MCs,

ICs, and ECs could be selected based on their MEQ score. Of the initial 213 participants, 63 participants who met the additional study criteria for being MCs (MEQ scores between 54-86; N=21), ICs (MEQ scores between 42-53; N=22) or ECs (MEQ scores between 16-41; N=20) were invited to partake in two identical experimental sessions once in the morning between 8:00-10:00 hours and another in the late afternoon between 16:00-18:00 hours, a week apart (mean difference between session 1 and 2: 12.98±12.32). Of 63 participants, 36 attended the morning session first and 27 attended the late afternoon session first.

The study was approved by College of Health, Medicine and Life Science Research Ethics Committee, Brunel University of London (ref no. 36745-A-Jan/2023- 43031-3). Participants were compensated with a £20 Amazon gift card for their participation in two experimental sessions and, in addition, all potential participants received £5 for completing the screening survey.

7.3.2 General Procedure

Participants were told that the study aimed to investigate potential ToD effects on learning and memory. Participants were administered two parallel versions of HVLT (Form A and B) in the morning and later afternoon sessions to eliminate any learning effect, with about 50% of the sample in each chronotype group receiving Form A and the remaining Form B in their first session. All participants were asked to refrain from smoking for 2 hours, drinking caffeine for 3 hours, and consuming alcohol for 24 hours prior to their scheduled testing sessions.

7.3.2.1 Self-Report Measures

As described earlier, during the screening session, all participants completed self-report measures of chronotype, sleep quality (over the past month), schizotypy and impulsivity; all of these measures have already been described in detail in Chapters 5 and 6. In addition, all participants completed the self-report measure of sleep quality (over the previous week) prior to both experimental sessions.

7.3.2.1.1 Chronotype

Chronotype was assessed using the 19-item MEQ (Horne & Östberg, 1976). As described in previous chapters (Chapters 5 and 6), higher MEQ scores indicate morningness, and lower

scores indicate eveningness, and the scale has high reliability (*a*=0.83, Horne & Östberg, 1976; 0.86 in the current sample).

7.3.2.1.2 Sleep Quality

Sleep quality was assessed using the 19-item PSQI (Buysse et al., 1989). The PSQI assesses *daytime dysfunction, use of sleeping medication, sleep disturbances, habitual sleep efficiency, sleep duration, sleep latency, and subjective sleep score*. Higher scores indicate poor sleep quality. Prior to the experimental sessions, the PSQI was administered with a slight modification, i.e., to assess sleep quality over the past week. Cronbach's alpha coefficients in the current sample were: screening session: *a*=0.70, morning session: *a*=0.73, late afternoon session: *a*=0.74.

7.3.2.1.3 Personality Traits

Schizotypal personality traits were assessed using the short version of the 43-item s-OLIFE (Mason et al., 2005). s-OLIFE assesses *Unusual Experiences*, *Cognitive Disorganization*, *Introvertive Anhedonia*, and *Impulsive Non-conformity*. Higher scores indicate higher levels of schizotypy. Cronbach's alpha in the current sample for Unusual Experiences, Cognitive Disorganisation, Introvertive Anhedonia, and Impulsive Nonconformity were 0.74, 0.83, 0.51, and 0.61, respectively.

Impulsivity was assessed using the 20-item S-UPPS-P (Cyders et al., 2014). There are five (5-item) sub-scales: *Lack of Perseverance*, *Lack of Premeditation*, *Sensation Seeking*, *Negative Urgency*, and *Positive Urgency*. Higher scores indicate higher levels of impulsivity. Cronbach's alpha in the current sample for Positive Urgency, Negative Urgency, Sensation Seeking, Lack of Perseverance, and Lack of Premeditation were 0.79, 0.72, 0.67, 0.61 and 0.77, respectively.

7.3.2.2 Hopkins Verbal Learning Test (HVLT)

Verbal learning and memory performance was assessed using the HVLT test (Benedict et al., 1998), which consists of a 12-item word list, with words from three different semantic categories (i.e., four words in each category). The three categories in the HVLT Form A are jewels, animals, and dwellings; and in the HVLT Form B they are weapons, kitchen utensils, and alcoholic beverages. In total, there are three immediate recall trials and, on each trial, the list of words is verbally presented to the participant with an inter-item interval of 2 seconds.

After presenting the final word in each trial, the participant is asked to freely recall as many words as possible and the number of correct responses, as well as the sequence of the recalled words, is recorded for each trial. The total number of words recalled over the three trials (possible range 0 to 36) is used to assess immediate recall. The three immediate recall trials are followed by an assessment of recognition memory in which 12 old and 12 new words (6 semantically related and 6 unrelated to the old words) are verbally presented, and the participant is asked to respond 'yes' if the word belongs to the list presented earlier and 'no' for a new word. The resulting true-positive (possible range 0 to 12) and false-positive responses (possible range 0 to 12) are then subtracted to calculate the discrimination index, which measures recognition memory. The task ends with a delayed recall trial. After 20 minutes of initial administration (without any warning to prevent sub-vocal rehearsal), the participant is asked to freely recall as many words as possible from the earlier presented list. The number of words recalled accurately provided a measure of delayed recall (episodic memory). For this study, the experimenter pre-recorded both versions A and B in native British English speaker voices, with separate male and female recordings, to ensure standardised presentation and correct inter-item-intervals across participants and sessions. All male participants were assessed with the male audio clips and females with the female audio clips.

7.3.3 Statistical Analysis

All analyses were performed using the Statistical Package for Social Sciences (for Windows, version 29; IBM, New York, USA). Alpha level for testing significance of effects was maintained at $p<0.05$ unless stated otherwise.

The data on all self-report measures were examined for normalcy, followed by reliability assessments. Since sleep medication use scores were found to be skewed, non-parametric statistical approach was used in all analyses involving this variable.

Group differences (MCs, ICs, ECs) in age and various self-report measures were explored using one-way analysis of variance (ANOVA), with chronotype or sex (in separate analyses to allow power) as a between-subject factor. Group differences in sleep quality (global score) were assessed using a 3 (Group; MCs, ICs, ECs) x 3 (Session; screening, morning, late afternoon) ANOVA with Group as a between-subjects factor, and Session as a within-subjects factor.

On HVTL-R, the following variables were computed: a) *immediate recall* (sum of correct words recalled in trials 1-3), b) *delayed recall* (number of correct words recalled during trial four), c) *discrimination index* (true-positive score *minus* false-positive score), d) *learning slope* (highest score on trial 2 or 3 minus by trial 1), e) *cumulative word learning* (learning slope multiplied by total immediate recall), f) and *semantic clustering* (number of times a word is recalled by another correct word from the same category divided by number of total correct words recalled across all trials; Echemendia et al., 2001).

The main and interactive effects of Group and ToD in each of the HVLT variables were examined using a 3 (Group: MCs, ICs, ECs) x 2 (ToD: morning, late afternoon) ANOVA, with Group as a between-subjects factor and ToD as a within-subjects factor. Given that daytime dysfunction (a poor sleep quality dimension) was associated with learning slope and cumulative word learning (see Table 7.3) and the groups differed on Introvertive Anhedonia (see Section 7.4.1), any significant effects from ANOVA on HVLT variables were re-evaluated after covarying for daytime dysfunction and Introvertive Anhedonia. Post-hoc *t*-tests followed significant main effects and interaction effects as appropriate. Effect sizes, where reported, are partial eta squared (ηp2; the proportion of variance associated with a factor).

Lastly, correlational analyses (Pearson's *r* or Spearman rho as appropriate) were performed to examine the relationship of sleep quality dimensions (obtained on morning and late afternoon session) with HVLT performance indices. Correlational analyses (Pearson's *r*) were also conducted to explore possible relationships between schizotypy and impulsivity dimensions and HVLT performance. All non-hypothesised correlations were re-evaluated by applying Bonferroni corrections to control for type-I error. Effect sizes for correlation coefficients were interpreted based on Cohen (1988) (*r* value +/-0.1 to +/-0.29 as small; +/-0.3 to +/-0.49 as medium; and +/- 0.5 to +/- 1 as large).

7.4 Results

7.4.1 Sample Characterisation

The demographic information about the sample is presented in Table 7.1. As expected (by design), results confirmed a significant difference in MEQ scores of the three study groups [$F_{(2,60)}$=144.16, p<0.001, η^2=0.828]. A significant group differences in Introvertive Anhedonia

[($F_{(2,60)}$=3.55, p=0.035, η^2=0.106), with MCs scoring lower than ICs (p=0.040) was also observed. Group effects for all other personality measures were not significant.

For sleep quality, no main effect of Group [$F_{(2,57)}$=0.792, p=0.458, η^2=0.027], Session [$F_{(2,114)}$=0.441, p=0.644, η^2=0.008], or Group × Session interaction [$F_{(4,114)}$=0.615, p=0.653, η^2=0.021] was found.

Table 7.1 *Demographic characteristics of the study sample.*

Demographic Characteristics		Frequency (%) of N=63
Sex	Male	42.9%
	Female	57.1%
Ethnicity	White European	33.3%
	South Asian	44.4%
	East Asian	4.8%
	Mixed	7.9%
	Black	3.2%
	Other Ethnicities	6.3%
Body Mass Index	<18.5	43.3%
	18.5-24.9	48.3%
	25-29.9	6.7%
	30 and above	1.7%
Occupation	Student	79.4%
	Full-time Work	20.6%

Note: All participants had a minimum qualification of an undergraduate degree or were studying for an undergraduate degree; Body mass index categories: underweight (<18.5), normal weight (18.5–24.9), overweight (25–24.9), obese (>30).

Table 7.2 *Descriptive statistics for chronotype, sleep and personality measures.*

			Chronotype Groups							
			MCs (n=21, 6M/15F)		ICs (n=22, 11M/11F)		ECs (n=20, 10M/10F)		Overall (n=63, 27M/36F)	
			Mean±SD	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Age			26±3.52	21-36	22.86±2.62	18-29	25.9±5.94	18-39	24.87±4.4	18-39
Chronotype	**MEQ**		59.09±4.5	54-68	48.45±3.46	42-53	35.45±5.31	21-41	47.87±10.57	21-68
Sleep Quality	**PSQI (Screening)**	Sleep Quality	1.04±0.49	0-2	1.13±0.63	0-2	1.35±0.48	1-2	1.17±0.55	0-2
		Sleep Latency	1.42±0.87	0-3	1.27±0.98	0-3	1.70±0.92	0-3	1.46±0.93	0-3
		Sleep Duration	0.47±0.60	0-2	0.68±0.83	0-3	1±0.79	0-3	0.71±0.77	0-3
		Sleep Efficiency	0.47±0.74	0-3	0.68±1.21	0-3	0.55±0.75	0-3	0.57±0.92	0-3
		Sleep Disturbance	1.23±0.62	0-2	1.31±0.47	1-2	1.10±0.55	0-2	1.22±0.55	0-2
		Sleep Medication	0.28±0.71	0-3	0.09±0.42	0-2	0.10±0.44	0-2	0.15±0.54	0-3
		Sleep Dysfunction	0.76±0.70	0-2	1.50±0.80	0-3	1.50±0.60	1-3	1.25±0.78	0-3
		PSQI Global	5.23±2.27	2-11	6±2.41	1-10	6.75±1.80	4-10	5.98±2.23	1-11
	PSQI (Morning session)	Sleep Quality	1.14±0.79	0-3	1.13±0.63	0-3	1.31±0.58	0-2	1.19±0.67	0-3
		Sleep Latency	1.14±0.96	0-3	1.22±0.86	0-3	1.47±0.96	0-3	1.27±0.92	0-3
		Sleep Duration	0.57±1.02	0-3	0.54±0.91	0-3	0.78±1.08	0-3	0.62±0.99	0-3
		Sleep Efficiency	0.76±0.94	0-3	0.72±0.88	0-3	0.52±0.84	0-3	0.67±0.88	0-3
		Sleep Disturbance	1.19±0.51	0-2	1.09±0.42	0-2	1.15±0.60	0-2	1.14±0.50	0-2
		Sleep Medication	0.00±0.00	0-0	0.00±0.00	0-0	0.10±0.31	0-1	0.03±0.17	0-1
		Sleep Dysfunction	0.95±0.66	0-2	1.09±0.52	0-2	1.21±0.63	0-2	1.08±0.60	0-2
		PSQI Global[a]	5.76±3.37	2-15	5.81±2.78	3-13	6.57±2.77	2-13	6.03±2.96	2-15
	PSQI (Late afternoon session)	Sleep Quality	1.33±0.85	0-3	1.23±0.43	1-2	1.21±0.41	1-2	1.26±0.60	0-3
		Sleep Latency	0.95±0.92	0-3	1.38±0.92	0-3	1.36±0.76	0-3	1.22±0.88	0-3
		Sleep Duration	0.66±1.01	0-3	0.57±0.81	0-3	0.52±0.77	0-3	0.59±0.86	0-3
		Sleep Efficiency	0.66±0.91	0-3	0.71±1.00	0-3	0.73±1.09	0-3	0.70±0.98	0-3
		Sleep Disturbance	0.80±0.60	0-2	1.14±0.57	0-2	0.94±0.52	0-2	0.96±0.57	0-2
		Sleep Medication	0.00±0.00	0-0	0.00±0.00	0-0	0.05±0.22	0-1	0.01±0.12	0-1
		Sleep Dysfunction	0.76±0.62	0-2	1.04±0.58	0-2	1.21±0.63	0-2	1±0.63	0-2
		PSQI Global[b]	5.19±3.64	1-14	6.09±2.96	2-13	6.05±2.46	2-11	5.77±3.05	1-14
Schizotypy (Screening)	**s-OLIFE**	Unusual Experiences	4.66±2.68	0-9	5.18±3	0-11	4.8±3.03	0-10	4.88±2.87	0-11
		Cognitive Disorganisation	5.04±3.51	0-11	7.04±2.98	3-11	6.45±3.36	0-11	6.19±3.34	0-11
		Introvertive Anhedonia	2.33±1.71	0-7	3.81±2.1	1-8	3.5±1.87	0-7	3.22±1.98	0-8
		Impulsive Nonconformity	2.19±1.93	0-8	3.13±2.16	0-8	2.75±1.97	0-6	2.69±2.03	0-8

		Positive Urgency	6.90±2.40	4-12	8.54±3.46	4-16	8.25±2.82	4-15	7.90±2.98	4-16
		Negative Urgency	8.42±2.54	4-12	9.09±3.11	4-16	9.05±2.66	5-16	8.85±2.76	4-16
Impulsivity (Screening)	**UPPS-P**	Sensation Seeking	11.85±2.49	5-16	11±2.69	5-15	11.05±3.26	5-16	11.30±2.80	5-16
		Lack of Perseverance	6.28±1.73	4-9	7±1.77	4-11	6.9±1.94	4-11	6.73±1.81	4-11
		Lack of Premeditation	6.85±2.28	4-11	7.09±2.04	4-11	6.8±1.88	4-10	6.92±2.05	4-11

Note: [a]PSQI data missing for one participant; [b]PSQI data missing for two participants.

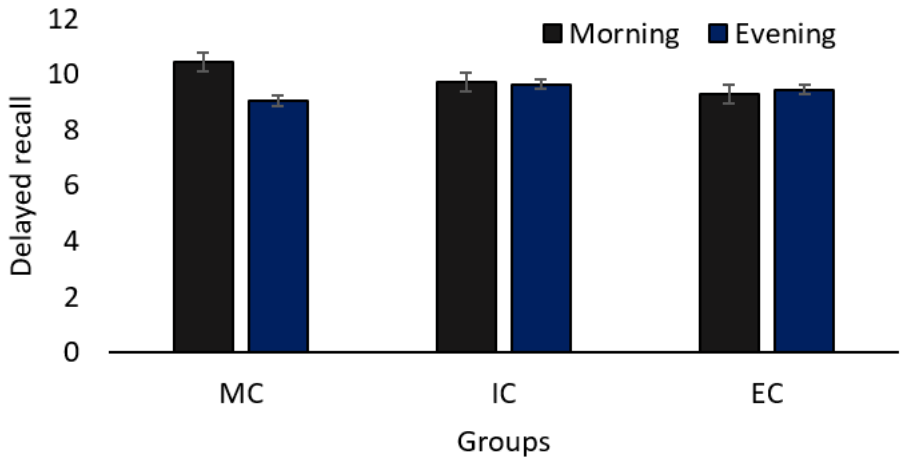
Abbreviations: ECs, Evening Chronotypes; ICs, Intermediate Chronotypes; MCs, Morning Chronotypes; MEQ, Morningness-Eveningness Questionnaire; PSQI, Pittsburgh Sleep Quality Index; s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions; UPPS-P, Impulsive Behaviour Scale-Short Version.

7.4.2 Group and ToD Effects in HVLT Performance

For immediate recall, no main effect of Group [$F_{(2,56)}$=0.93, p=0.912, η^2=0.003], ToD [$F_{(1,56)}$=2.88, p=0.095, η^2=0.49], or a Group × ToD interaction [$F_{(2,56)}$=0.300, p=0.742, η^2=0.011] was found. Similarly, no significant main or interaction effects were observed for discrimination index, learning slope, cumulative word learning, or organisation strategy (semantic clustering) scores (p>0.05).

For delayed recall, a marginally significant effect of ToD was found [$F_{(2,60)}$=4.08, p=0.048, η^2=0.064] showing better performance in the morning than late afternoon session (9.81±.25 vs 9.37±.27). This effect, however, was no longer significant after covarying for daytime dysfunction [$F_{(1,59)}$=1.69, p=0.199, η^2=0.028] and Introvertive Anhedonia [$F_{(1,59)}$=1.97, p=0.166, η^2=0.032]. A significant Group × ToD interaction was also observed [$F_{(2,60)}$=4.72, p=0.012, η^2=0.136] with MCs recalling more words at their optimal ToD [$t_{(20)}$=3.56, p=0.002, η^2=0.778] (Figure 7.1). This effect remained significant after covarying for daytime dysfunction [$F_{(2,59)}$=3.30, p=0.044, η^2=0.101] or Introvertive Anhedonia [$F_{(2,59)}$=3.82, p=0.027, η^2=0.115]. No other main effects or interactions were significant (p>0.05).

Figure 7.1 *Delayed recall in three groups (MCs, ICs, ECs) when tested in the morning and later afternoon. Error bars represent ±1 standard error of mean (SEM).*



Regarding memory organisation strategies for delayed recall, a significant main effect of ToD was found [$F_{(2,60)}$=5.74, p=0.020, η^2=0.087] with more usage of semantic clustering strategy in the late afternoon than morning session [$t_{(62)}$=2.41, p=0.009, η^2=0.226], but it became non-significant after covarying for daytime dysfunction [$F_{(1,59)}$=1.53, p=0.220, η^2=0.025] or

Introvertive Anhedonia [$F_{(1,59)}$=0.226, p=0.636, η^2=0.004]. No other main effects and interactions were significant.

7.4.4 Associations of Sleep Quality with HVLT Performance Indices

For the morning session, higher daytime dysfunction was negatively associated with learning slope (r=-0.339, p=0.007) and cumulative word learning (r=-0.343, p=0.006). No other correlations were significant (Table 7.3).

7.4.5 Associations of Personality Traits with HVLT Performance Indices

In the morning session, higher level of Sensation Seeking was negatively associated with immediate recall (r=-0.284, p=0.024) and poor use of semantic clustering strategy on immediate recall (r=-0.310, p=0.013). Lack of Perseverance was positively associated with use of semantic clustering strategy on immediate recall (r=0.257, p=0.042). Lastly, Lack of Premeditation was positively associated with immediate recall (r=0.284, p=0.024), delayed recall (r=0.338, p=0.007), and use of semantic clustering strategy on immediate recall (r=0.317, p=0.011). (Table 7.4). In the late afternoon session, higher level of Cognitive Disorganisation was associated with higher discrimination index (r=0.255, p=0.044). Higher level of Sensation Seeking was also associated with poor use of semantic clustering strategy on immediate recall (r=-0.307, p=0.015).

Overall, the personality and memory variables did not show a clear pattern of relationships for the morning or late afternoon sessions (Table 7.4), and none of the correlations was strong enough to survive a Bonferroni correction for multiple comparisons (p>0.0031).

Table 7.3 *Correlations between sleep and HVLT components in the morning and late afternoon sessions.*

	IR (M)	**DR (M)**	**DI (M)**	**IRsem (M)**	**DRsem (M)**	**LS (M)**	**CWL (M)**
Sleep Quality (M)	0.028	0.067	-0.175	0.033	-0.013	-0.108	-0.15
	(0.826)	(0.608)	(0.173)	(0.801)	(0.921)	(0.404)	(0.243)
Sleep Latency (M)	0.105	0.026	-0.073	0.112	0.203	-0.096	-0.056
	(0.417)	(0.839)	(0.572)	(0.384)	(0.113)	(0.458)	(0.667)
Sleep Duration (M)	0.012	-0.064	0.035	-0.210	-0.203	-0.206	-0.237
	(0.928)	(0.622)	(0.788)	(0.101)	(0.113)	(0.108)	(0.063)
Sleep Efficiency (M)	-0.097	-0.164	-0.137	-0.135	-0.143	0.010	-0.023
	(0.453)	(0.204)	(0.289)	(0.296)	(0.269)	(0.937)	(0.858)
Sleep Disturbance (M)	0.142	0.066	0.153	-0.03	0.069	0.053	0.111
	(0.272)	(0.609)	(0.235)	(0.817)	(0.594)	(0.684)	(0.392)
Sleep Medication (M)	0.028	0.153	-0.075	0.189	0.204	0.016	0.046
	(0.828)	(0.234)	(0.565)	(0.142)	(0.111)	(0.904)	(0.723)
Daytime Dysfunction (M)	0.027	-0.075	0.004	0.086	-0.048	**-0.339**	**-0.343**
	(0.836)	(0.564)	(0.978)	(0.508)	(0.709)	**(0.007)**	**(0.006)**
PSQI Global (M)	0.046	-0.042	-0.068	-0.046	-0.036	-0.179	-0.186
	(0.720)	(0.748)	(0.598)	(0.721)	(0.781)	(0.163)	(0.147)
	IR (LA)	**DR (LA)**	**DI (LA)**	**IRsem (LA)**	**DRsem (LA)**	**LS (LA)**	**CWL (LA)**
Sleep Quality (LA)	0.024	0.016	-0.022	0.223	-0.013	-0.096	-0.086
	(0.856)	(0.905)	(0.869)	(0.084)	(0.918)	(0.461)	(0.509)
Sleep Latency (LA)	0.009	-0.018	0.030	0.033	-0.062	0.036	0.059
	(0.943)	(0.892)	(0.821)	(0.799)	(0.632)	(0.782)	(0.651)
Sleep Duration (LA)	-0.033	0.089	0.060	0.068	-0.056	0.153	0.130
	(0.802)	(0.495)	(0.644)	(0.605)	(0.670)	(0.240)	(0.318)
Sleep Efficiency (LA)	-0.036	0.022	-0.013	0.206	-0.027	0.081	0.058
	(0.782)	(0.869)	(0.920)	(0.111)	(0.834)	(0.536)	(0.659)
Sleep Disturbance (LA)	0.043	0.219	0.023	0.066	0.074	0.038	0.093
	(0.744)	(0.090)	(0.863)	(0.613)	(0.571)	(0.772)	(0.477)
Sleep Medication (LA)	0.217	0.178	0.137	0.205	0.143	-0.220	-0.216
	(0.093)	(0.170)	(0.292)	(0.112)	(0.271)	(0.088)	(0.094)
Daytime Dysfunction (LA)	0.134	0.201	0.124	0.116	0.019	0.015	0.076
	(0.305)	(0.120)	(0.342)	(0.375)	(0.885)	(0.906)	(0.560)
PSQI Global (LA)	0.034	0.120	0.051	0.189	-0.021	0.060	0.077
	(0.796)	(0.358)	(0.695)	(0.144)	(0.873)	(0.649)	(0.555)

Abbreviation: M, Morning; LA; Late Afternoon; IR, Immediate Recall; DR, Delayed Recall; DI, Discrimination Index; IRsem, Immediate Recall Sematic Clustering; DRsem, Delayed Recall Sematic Clustering; LS, Learning Slope; CWL, Cumulative Word Learning.

Table 7.4 *Correlation (Pearson's r) between personality traits and verbal memory components in morning and late afternoon session.*

	IR (M)	**DR (M)**	**DI (M)**	**IRsem (M)**	**DRsem (M)**	**LS (M)**	**CWL (M)**
Unusual Experiences	0.014	-0.001	-0.019	-0.064	-0.011	-0.019	0.024
	(0.914)	(0.996)	(0.880)	(0.616)	(0.934)	(0.883)	(0.849)
Cognitive Disorganisation	-0.011	-0.009	-0.071	0.166	0.074	-0.101	-0.032
	(0.929)	(0.942)	(0.583)	(0.193)	(0.563)	(0.429)	(0.804)
Introvertive Anhedonia	-0.077	-0.095	0.108	0.047	0.074	-0.035	-0.055
	(0.549)	(0.457)	(0.400)	(0.714)	(0.564)	(0.787)	(0.670)
Impulsive Nonconformity	-0.077	0.015	0.034	0.189	0.147	-0.029	-0.021
	(0.550)	(0.910)	(0.792)	(0.137)	(0.250)	(0.823)	(0.870)
Positive Urgency	-0.030	-0.014	-0.062	0.165	0.023	-0.094	-0.061
	(0.815)	(0.916)	(0.631)	(0.197)	(0.856)	(0.465)	(0.636)
Negative Urgency	0.086	0.083	0.050	-0.030	-0.006	0.075	0.123
	(0.504)	(0.519)	(0.699)	(0.817)	(0.960)	(0.559)	(0.337)
Sensation Seeking	**-0.284**	-0.079	-0.073	**-0.310**	-0.145	0.167	0.057
	(0.024)	(0.537)	(0.571)	**(0.013)**	(0.256)	(0.191)	(0.658)
Lack of Perseverance	0.062	0.107	-0.099	**0.257**	0.226	0.031	0.064
	(0.629)	(0.406)	(0.441)	**(0.042)**	(0.075)	(0.808)	(0.616)
Lack of Premeditation	**0.284**	**0.338**	0.134	**0.317**	0.147	-0.149	-0.049
	(0.024)	**(0.007)**	(0.293)	**(0.011)**	(0.250)	(0.245)	(0.704)
	IR (LA)	**DR (LA)**	**DI (LA)**	**IRsem (LA)**	**DRsem (LA)**	**LS (LA)**	**CWL (LA)**
Unusual Experiences	0.045	0.112	0.174	-0.126	-0.194	0.043	0.073
	(0.726)	(0.383)	(0.173)	(0.325)	(0.128)	(0.736)	(0.568)
Cognitive Disorganisation	0.083	0.237	**0.255**	0.002	-0.110	-0.017	0.019
	(0.516)	(0.061)	**(0.044)**	(0.988)	(0.390)	(0.894)	(0.885)
Introvertive Anhedonia	-0.072	0.052	-0.053	0.179	0.162	-0.001	0.003
	(0.574)	(0.687)	(0.681)	(0.160)	(0.204)	(0.993)	(0.984)
Impulsive Nonconformity	0.099	0.234	0.065	0.067	0.068	-0.111	-0.095
	(0.442)	(0.065)	(0.615)	(0.604)	(0.596)	(0.386)	(0.458)
Positive Urgency	-0.091	0.026	-0.089	-0.077	-0.142	0.161	0.140
	(0.478)	(0.84)	(0.486)	(0.549)	(0.268)	(0.208)	(0.274)
Negative Urgency	-0.028	0.099	-0.069	0.009	-0.107	0.032	0.064
	(0.827)	(0.439)	(0.593)	(0.946)	(0.405)	(0.804)	(0.618)
Sensation Seeking	-0.187	-0.127	-0.192	**-0.307**	-0.203	0.104	0.029
	(0.143)	(0.323)	(0.131)	**(0.015)**	(0.111)	(0.417)	(0.822)
Lack of Perseverance	-0.112	0.039	0.199	0.070	0.102	0.136	0.119
	(0.384)	(0.76)	(0.118)	(0.583)	(0.425)	(0.289)	(0.352)
Lack of Premeditation	0.119	0.242	0.144	0.061	0.194	0.078	0.078
	(0.354)	(0.056)	(0.261)	(0.634)	(0.127)	(0.542)	(0.545)

Abbreviation: M, Morning; LA; Late Afternoon; IR, Immediate Recall; DR, Delayed Recall; DI, Discrimination Index; IRsem, Immediate Recall Sematic Clustering; DRsem, Delayed Recall Sematic Clustering; LS, Learning Slope; CWL, Cumulative Word Learning.

7.5 Discussion

The study aimed to investigate the chronotype, ToD, and synchrony effects on verbal learning and memory and, in addition, any associations between sleep facets and memory variables in young adults (aged 18-40 years). The main findings showed: a) greater delayed recall in MCs at their optimal ToD but no chronotype or synchrony effects in other HVLT-based variables, and b) medium-sized negative correlations between daytime dysfunction (poor sleep quality) and learning slope and cumulative word learning in the morning. In addition, ECs scored higher than MCs on Introvertive Anhedonia (a dimension of schizotypy) and a ToD influence on delayed recall (i.e., better performance in the morning session) and semantic organisation (i.e., more semantic clustering use for delayed recall during the late afternoon session) was abolished after covarying for daytime dysfunction or Introvertive Anhedonia.

The findings of this study concerning the first hypothesis found no chronotype, ToD, and/or synchrony effect on immediate recall, recognition, learning slope, and cumulative word learning. This partially aligns with previous literature (Barbosa & Albuquerque, 2008; Evansova et al., 2020). Evansova and colleagues (2020) using the Rey Auditory Verbal Learning Test (RAVLT) to assess short- and long-term memory in young adults (20-40 years) also found no chronotype, ToD, or synchrony effect. However, Lehmann and colleagues (2013) who tested older MCs (age range: 55-71 years) and younger ECs (age range: 18-33 years) did observe a synchrony effect on immediate recall and recognition in both groups using RAVLT but they used a between-subjects design, randomly assigning the chronotype groups to a morning or evening testing session, making the findings susceptible to confounding ToD effects. Although the present study found a ToD effect with better delayed recall in the morning than in the late afternoon/evening sessions (Barner et al., 2019; Evansova et al., 2020), this was explained by daytime dysfunction. There was, however, a significant synchrony effect in that MCs (but not ECs) shower better delayed recall at their optimal ToD. This finding offers some support to the first study hypothesis and is partially aligned with previous evidence (May et al., 2005; Lehmann et al., 2013; Petros et al., 1990; Anderson et al., 1991) which suggested better performance in both chronotypes at their optimal ToD. Of note, these studies vary considerably in experimental design, time of testing, and sample selection. For example, Lehman and colleagues (2013) and May and colleagues (2005) used a between-subjects design and randomly tested older MCs vs. young ECs in the morning or evening. Furthermore, Anderson and colleagues (1991) and Petros and colleagues (1990) tested their participants at 20:00 hour,

whereas we tested between 16:00-18:00 hours, which might not be the optimal time for ECs. This discrepancy may explain the present study's lack of synchrony effects in ECs.

The study findings concerning the second hypothesis revealed a negative association only between the daytime dysfunction dimension of poor sleep quality and learning slope as well as cumulative word learning (tested in the morning). Despite the previously well-established relationship between disrupted sleep-wake cycles and impaired retrieval, encoding, consolidation, and recall (Carlson et al., 2023; Diekelmann et al., 2010; Newbury et al., 2021; Paller et al., 2021), we did not find any relationship between memory performance and sleep quality as well as sleep duration as hypothesised. While daytime dysfunction, sleep duration and quality reflect conceptually different aspects of sleep, they are well known to impair memory performance in older adults and clinical populations such as schizophrenia (Bian et al., 2021), insomnia (Chen et al., 2020), and Alzheimer's (Balouch et al., 2022). In a recent study, Stiver and colleagues (2021) also found no association between sleep quality and verbal learning and memory performance in young adults (mean age: 20.5±1.50). Similarly, we found no association between sleep quality and memory performance in either morning or late afternoon sessions. Overall, the lack of relationship between subjective sleep quality and verbal memory in our sample of young non-clinical adults can be attributed to the lower range of PSQI scores, with most participants having good sleep quality (>55% on both occasions) and sleep duration (over 80% participants slept more than 6 hours, on average, before morning and late afternoon testing sessions) and thus limiting the possibility of finding a significant relationship.

This study also found ECs scoring higher on introvertive Anhedonia (a dimension of schizotypy) than MCs which aligns with previous findings showing ECs, on average, scoring high on psychometric measure of schizotypy (Chauhan et al., 2024a, 2024b; also discussed in Chapters 5 and 6). However, any of the schizotypy or impulsivity facets did not show a clear pattern of associations with HVLT variables. It is possible that these traits have a more robust and consistent pattern of relationships with mental health outcomes (see Chapters 5 and 6) than any cognitive variable.

7.5.1 Limitations and Future Directions

This study had a number of limitations. First, since we restricted the sample age range to 18-40 years, the present findings cannot be generalised to those below 18 and over 40 years.

Second, subjective arousal and/or alertness levels during morning or late afternoon session were not measured. Third, the late afternoon testing time was between 16:00-18:00 hours which might not be optimal for ECs, potentially masking synchrony effect in this group. Further studies are needed to confirm and extend the findings of this study after addressing these limitations and employing objective measures of circadian rhythm alongside self-report measures of chronotype and sleep quality.

7.5.2 Conclusions

To conclude, this study reported in this chapter found no main effect of chronotype and ToD on verbal learning and memory in a sample of young non-clinical adults. However, a synchrony effect on delayed recall only in MCs was observed. Daytime dysfunction, a dimension of poor sleep quality, was also found to be negatively associated with learning slope and cumulative word learning in the morning. Sleep is known to improve and facilitate good cognitive performance, and the present findings also emphasise the importance of sleep-related disturbances in studies exploring circadian effects on memory. Further studies in different age groups and populations (e.g., shift workers) using both objective (e.g., actigraphy) and subjective self-report measures of sleep are needed to examine the stability and generalisability of our findings.

Chapter 8: Circadian Rhythmicity in Prepulse Inhibition of the Acoustic Startle Response: A Study of Chronotype and Time-of-Day Effects in Young Healthy Adults

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Abstract

PPI of the acoustically-elicited startle response is a widely used cross-species measure of sensorimotor gating. PPI refers to the reliable reduction in startle amplitude to a strong auditory stimulus (i.e., pulse) when it is preceded briefly (30-500 ms) by a weaker stimulus (i.e., prepulse). PPI is found to be reduced in various psychiatric disorders and has also been used as a biomarker to discover potential new pharmacological treatments for schizophrenia. Given the utility of PPI as a neurophysiological biomarker aiding antipsychotic drug development, and possible links between EC and poor mental health, this study investigated chronotype, ToD, and synchrony effects in PPI of the acoustic startle response in young healthy adults. Thirty-six adults (age range: 18-40 years), selected from a larger pool of potential participants to represent MCs (N=8), ICs (N=15) or ECs (N=13), were assessed on PPI (prepulse-to-pulse intervals: 30, 60 and 120 ms) on two separate occasions, one week apart: once in the morning (8:00-10:00) and once during the late afternoon (16:00-18:00). There were no significant chronotype or synchrony effects on PPI, although there was greater startle amplitude on pulse-alone trials, and marginally greater PPI on 120-ms (but not 30-ms or 60-ms) prepulse-to-pulse interval PPI trials, in the late afternoon compared to the morning session. These findings provide further support to PPI, especially with short-to-medium prepulse-to-pulse intervals, to be a stable biomarker and not significantly modulated by chronotype in healthy young adults.

8.1 Chapter Aims and Overview

This chapter reports an empirical study conducted to examine the effect of chronobiological variables on PPI of the acoustic startle response (a measure of sensorimotor gating) while also taking possible roles of sleep quality and personality variables into account.

8.2 Introduction

CRs cause considerable inter-individual differences in various mechanisms, including sleeping patterns and alertness/arousal levels, known as chronotype (Adan et al., 2012). Chronotype is a multidimensional construct (Chauhan et al., 2023) that classifies individuals as MCs (i.e., circadian peak arousal in the morning), ECs (i.e., circadian peak arousal in the evening), and ICs (i.e., no fixed circadian peak arousal). Given these inter-individual differences, it is possible to expect some variation in cognitive performance, including on tasks assessing attention and inhibition, in association with chronotype and/or ToD (Schmidt et al., 2007). When an individual's performance is synchronised with their circadian arousal peak (May et al., 2023), it may result in a synchrony effect, i.e., superior performance at optimal ToD. There is evidence that chronobiological variables influence performance on cognitive tasks requiring controlled processing of information (e.g., response inhibition; Lara et al., 2014; Martínez-Pérez et al., 2020), although not consistently so (Schmidt et al., 2012, 2015; Song et al., 2018). There are also suggestions that tasks requiring higher cognitive control may be more vulnerable to ToD and/or synchrony effects than those which primarily involve automatic processing (Yang et al., 2007), for example, sensory or sensorimotor gating (Braff et al., 1978, 1992; Geyer & Braff, 1987).

PPI of the startle response is a widely-used cross-species measure of sensorimotor gating (Braff et al., 2001). It refers to a reliable reduction in startle response to a strong sensory stimulus (i.e., pulse) when preceded briefly (by 30-500 ms) by a weaker subthreshold stimulus (i.e., prepulse) (Graham, 1975). Reduced PPI has been found in various psychiatric and neurodevelopmental disorders (Santos-Carrasco & De la Casa, 2023). Overnight sleep deprivation (SD) has been reported to disrupt PPI when young healthy participants are tested in the morning following overnight SD (Petrovsky et al., 2014; Meyhofer et al., 2019). Interestingly, no PPI disruption was seen in a recent study where participants were tested in the evening following 36-hour SD (Vizeli et al., 2023). Furthermore, in one study of female rats (Adam et al., 2008) ToD was reported to influence PPI selectively with intense 86-dB prepulses

(no effect on 74-82dB prepulses) with lower PPI in the morning (light phase) relative to the evening (dark phase). No study has yet investigated chronobiological influences on human PPI. Given previous reports of disrupted sleep-wake cycles being more common in ECs than MCs (Chauhan et al., 2024a; Muzni et al., 2021), it is possible that there are chronobiological influences in human PPI. This is an important area of enquiry since the PPI model has been widely utilised not only to study various human psychopathologies (San-Martin et al., 2020; Sun et al., 2024) but also to discover potential new treatments for schizophrenia (Geyer, 2006; Light & Swerdlow, 2020).

The primary aim of this study therefore was to investigate, for the first time, the effects of chronotype, ToD, and synchrony on PPI of the acoustic startle response in young healthy adults, as well as any associations between PPI and sleep quality over the past week. We tentatively hypothesised greater PPI at optimal ToD in all chronotypes (i.e., synchrony effect), based on evidence of such effects in some cognitive tasks (executive function) that show a positive association with PPI (e.g., Giakoumaki et al., 2008; Kumari et al., 2007) and a negative association between morning PPI and poor sleep quality, given previous reports of PPI disruption following SD when tested in the morning (Petrovsky et al., 2014; Meyhofer et al., 2019). A secondary aim, given previous reports of a negative association between PPI and schizotypy (Giakoumaki et al., 2020) and impulsivity (Gee et al., 2015), was to explore possible associations between psychometric measures of schizotypy and impulsivity and PPI in the morning and late afternoon assessments, expecting the same pattern of associations in both sessions.

8.3 Methods

8.3.1 Participants and Design

A sub-sample of the UK-based healthy adults (age 18-40 years) (N=45), described in Chapter 7 (N=63) was invited to partake in this study. Of the 45 selected participants, 14 were MCs (MEQ scores: 54-86), 17 ICs (MEQ scores: 42-53), 14 were ECs (MEQ scores:16-41). All included participants also met the general study inclusion criteria of: (i) age between 18-40 years, (ii) resident in the UK, (iii) native/proficient English speaker, (iii) no hearing impairment, and (iv) no current diagnosis of any mental disorders or drug abuse. Although previous literature shows sex differences in PPI of healthy young men and women, (reviews, Kumari, 2011; Hantsoo et al., 2018), young women using hormonal contraceptives are found

to not differ from healthy young men (Naysmith et al., 2022). We thus selected only those females who were taking hormonal contraceptives to minimise sex-related differences in PPI (Naysmith et al., 2022).

All participants took part in two identical sessions, one week apart: once in the morning between 8:00-10:00 hour and once in the late afternoon between 16:00-18:00 hour. Of the initial 45 participants, 9 participants were excluded due to noise/artifact contamination in startle assessments in one or both sessions, leaving a final sample of 36 participants (8 morning, 15 intermediates, 13 evening chronotypes). Of these 36, 19 participants attended the morning session first, and the remaining 17 participants attended the evening session first.

The study was approved by College of Health, Medicine and Life Science Research Ethics Committee, Brunel University of London (ref no. 36745-A-Jan/2023- 43031-3). All participants signed a consent form and were compensated with a £20 Amazon gift card for their participation in two experimental sessions.

8.3.2 Self-Report Measures

As mentioned in the previous chapter (Chater 7), all participants completed self-reported measures of chronotype, sleep quality (over the past month), schizotypy and impulsivity; all of these measures have already been described in details in Chapters 5 and 6. In addition, all participants completed the self-report measure of sleep quality (over the past week) prior to both PPI sessions.

8.3.2.1 Chronotype

The MEQ (Horne & Östberg, 1976) was used to assess chronotype. As described in previous chapters, higher scores indicate higher morningness. This scale has high reliability (a=0.83, Horne & Östberg, 1976; in the current sample, a=0.87).

8.3.2.2 Sleep Quality

The PSQI (Buysse et al., 1989) was used to assess sleep quality. Higher scores indicate poor sleep quality. This scale has high internal consistency (a=0.83, Buysse et al., 1989; current sample, screening session: a=0.71, morning session, a=0.74, evening session a=0.73). Prior to both PPI sessions, the PSQI was administered with a slight modification, i.e., to assess sleep quality over the past week. Higher scores indicate poor sleep quality.

8.3.2.3 Schizotypy

The s-OLIFE (Mason et al., 2005) was used to assess schizotypy. s-OLIFE has four sub-scales: *Unusual Experiences, Cognitive Disorganisation*, *Introvertive Anhedonia*, and *Impulsive Non-conformity*. Higher scores indicate higher levels of schizotypy. This scale has high reliability (total scale, *a*=0.78-0.87; Fonseca-Pedrero et al., 2015). Cronbach's alpha coefficients in the current sample for Unusual Experiences, Cognitive Disorganisation, Introvertive Anhedonia, and Impulsive Nonconformity were 0.78, 0.83, 0.53, and 0.58 respectively.

8.3.2.4 Impulsivity

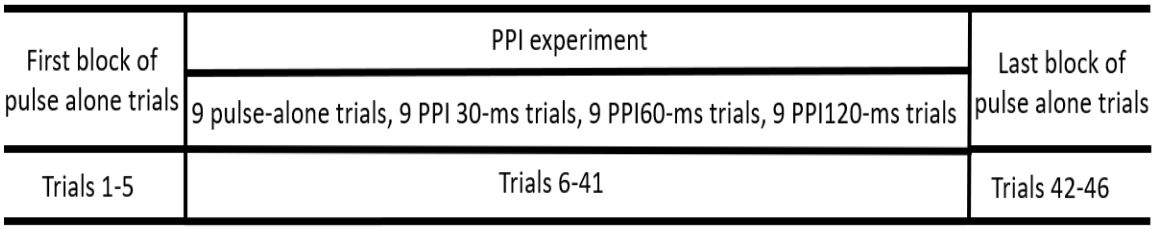
The S-UPPS-P (Cyders et al., 2014) was used to assess impulsivity. There are five (5-item) sub-scales: *Positive Urgency, Negative Urgency, Sensation Seeking, Lack of Perseverance*, and *Lack of Premeditation*. Higher scores indicate higher levels of impulsivity. This scale has high reliability (total scale, *a*=0.74-0.88; Cyders et al., 2014). Cronbach's alpha in the current sample for Positive Urgency, Negative Urgency, Sensation Seeking, Lack of Perseverance, and Lack of Premeditation were 0.75, 0.72, 0.71, 0.59, and 0.78 respectively.

8.4 PPI Assessment: Startle Paradigm and Procedure

A commercially available computerised human startle response monitoring system (SR-Lab, San Diego, California) was used to generate and deliver the acoustic stimuli through headphones (binaurally) and record the EMG activity (sample interval 1 ms).

The session started with a 2-minute acclimatisation period during which all participants were exposed via headphones to 70-dB (A) continuous white noise. The pulse-alone stimulus was a 40-ms presentation of 114-dB (A) white noise, and the prepulse stimulus was a 20-ms presentation of 84-dB (A) white noise, both over 70-dB (A) continuous background noise (Kumari et al., 2024). In total, the participants received 46 startle-eliciting stimuli. Of these 46 trials, the first five and the last 5 were the pulse-alone stimuli. The remaining 36 trials were arranged in three blocks of 12 trials each. Each of the three blocks included: three pulse-alone trials, three PPI trials (PPI30) where the prepulse (onset) to pulse (onset) interval was 30 ms, three PPI trials (PPI60) where the prepulse (onset) to pulse (onset) interval was 60 ms, and three PPI trials (PPI120) where the prepulse (onset) to pulse (onset) interval was 120 ms (Figure 8.1).

Figure 8.1 *Schematic representation of the startle experiment showing arrangement of pulse-alone trial and prepulse inhibition (PPI: 30-ms, 60-ms and 120-ms prepulse-to-pulse intervals) trials.*



The eye blink component of the startle response was measured by recording EMG activity of the orbicularis oculi muscle underneath the right eye by placing two miniature silver/silver chloride electrodes filled with Dracard electrolyte paste (SLE, Croydon, UK) and a ground electrode on the mastoid behind the right ear. The amplification gain control for the EMG signal was kept constant for all participants and all sessions. During the testing session, participants were seated comfortably in a chair. They were told that the study aimed to investigate their reactivity to various noises played through headphones at different ToD and that they should neither ignore nor try to attend these noises. They were requested to remain relaxed but stay awake with eyes kept open throughout the experiment. Participants had been asked to refrain from smoking for 2 hours given the widely-reported influence of nicotine in PPI (Kumari et al., 1997; Kumari and Postma, 2005; Hong et al., 2008), and also from drinking caffeine for 3 hours, and consuming alcohol for 24 hours prior to their scheduled testing sessions.

Scoring criteria were identical to those reported by Kumari et al. (2023, 2024). Briefly stated, recorded EMG activity was band-pass filtered, as recommended by the SR-Lab. Analogue band-pass filtering occurred before digitising. The high-pass and low-pass cut-off frequencies were 50 and 1000 Hz, respectively. EMG data were processed off-line, blind to self-report data, using the analytic programme of the SR-Lab for response amplitude [in arbitrary Analog-to-Digit (A/D) units; 1 unit=2.62μV]. The scoring programme contained a rolling average routine, which smoothed the rectified EMG response. The onset of the startle response was defined by a shift of 10 A/D units from the baseline value occurring within 20-120 ms from the startle stimulus onset.

8.5 Statistical Analysis

All analyses were performed using the Statistical Package for Social Sciences (for Windows, version 29; IBM, New York, USA). Alpha level for testing significance was maintained at $p<0.05$ unless stated otherwise. The data properties of all measures were examined and found suitable for parametric data analysis methods.

8.5.1 Sample Characteristics

Possible group differences in age and various self-report measures, except sleep quality, were explored using one-way analysis of variance (ANOVA) with chronotype as a between-subject factor. Group differences in sleep quality were assessed using a 3 (Group; MCs, ICs, ECs) x 3 (Session: screening, morning, late afternoon) ANOVA with Group as a between-subjects factor, and Session as a within-subjects factor.

8.5.2 Chronotype and ToD Influences in Startle Measures

PPI was calculated as ([a-b]/a)] × 100, where ‘‘a’’=pulse-alone amplitude (mean amplitude response on nine pulse-alone trials during the three middle blocks; see Figure 8.1) and ‘‘b’’= amplitude over PPI trials. Before examining possible Chronotype and ToD effects in PPI, we analysed average startle amplitudes on the first and last block of five pulse-alone trials using a 3 (Group: MCs, ICs, ECs) x 2 (ToD: morning, late afternoon) x 2 (first block, last block) ANOVA, with Group as a between-subjects factor, and ToD and Block as within-subjects factors. Habituation was also calculated (% reduction in average amplitude from the first block of five pulse-alone trials to the last block of five pulse-alone trials) and analysed using a 2 (Group) x 2 (ToD) ANOVA, with repeated measure on ToD.

PPI scores were examined using a 3 (Group: MCs, ICs, ECs) x 2 (ToD: morning, late afternoon) x 3 (PPI Trial Type: 30-ms, 60-ms, 120-ms) x ANOVA, with Group as a between-subjects factor, and ToD and PPI Trial Type as within-subjects factors. Given a significant ToD effect in amplitude on the first and last block of five pulse-alone trials (see Results), a 3 (Group) x 2 (ToD) ANOVA was also run-on mean startle amplitude on pulse-alone trials that were presented mixed with the PPI trials, and any significant effects from ANOVA on PPI scores were re-evaluated after covarying for mean amplitude on these pulse-alone trials.

Prior to these analyses, Sex (male, female) and Experimental Order (morning first, late afternoon first) were examined (separately to allow power) as additional between-group factors in all ANOVAs and not found to have any main or interactive effects in PPI, amplitude or habituation (thus not considered further). The assumption of sphericity was assessed using Mauchly's test in all ANOVAs for factors involving a repeated measure. If the assumption of sphericity was found to be violated, the Greenhouse-Geisser correction was applied to adjust for potential violations of sphericity. Effect sizes, where reported, are partial eta squared (ηp^2; the proportion of variance associated with a factor).

8.5.3 Self-report and Startle Measures: Inter-relationships

Correlational analyses (Pearson's *r*) were used to examine the relationship of sleep quality (global scores), schizotypy and impulsivity with PPI and startle habituation (% response reduction). Significant correlations ($p<0.05$) that had not hypothesised *a priori* were re-evaluated after applying Bonferroni correction to control family-wise Type 1 error.

8.6. Results

8.6.1 Sample Characteristics

Demographic characteristics are presented in Table 8.1. There was a main effect of Group in the total MEQ scores, as expected by design [$F_{(2,33)}=60.46$, $p<0.001$, $\eta p^2=0.786$]. The main effect of Group was also present for cognitive disorganisation [$F_{(2,33)}=3.93$, $p=0.029$, $\eta p^2=0.192$; MCs scoring lower than ICs ($p=0.009$)], introvertive anhedonia [$F_{(2,33)}=5.43$, $p=0.009$, $\eta p^2=0.248$; MCs scoring lower than ICs ($p=0.003$) and ECs ($p=0.015$)], impulsive nonconformity [$F_{(2,33)}=4.98$, $p=0.013$, $\eta p^2=0.232$; MCs scoring lower than ICs ($p=0.003$) and ECs ($p=0.040$)]; no other personality measure showed a significant group difference ($p>0.05$). For sleep quality, no main effect of Group [$F_{(2,31)}=0.866$, $p=0.430$, $\eta p^2=0.053$], Session [$F_{(2,62)}=1.05$, $p=0.353$, $\eta p^2=0.033$] or Group × Session interaction [$F_{(4,62)}=1.69$, $p=0.164$, $\eta p^2=0.098$] was found.

Table 8.1 *Sample Characterisation Measures.*

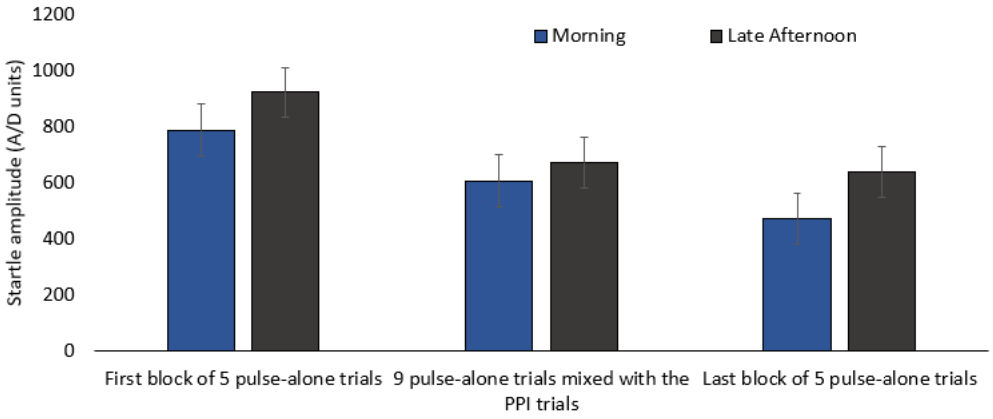
	Morning Types (N=8)		Intermediate Types (N=15)		Evening Types (N=13)		Total (N=36)	
	Mean±SD	**Range**	**Mean**	**Range**	**Mean±SD**	**Range**	**Mean±SD**	**Range**
Age	27.5±4.78	21-36	22.73±2.46	18-27	27.07±6.18	18-39	25.36±5.02	18-39
Chronotype								
MEQ	58.5±4.62	54-67	48.20±3.98	42-53	34.30±6.26	21-41	45.47±10.60	21-67
Sleep Quality								
PSQI (S)	4.75±2.31	2-8	6.33±2.52	1-10	7.15±1.90	4-10	6.27±2.38	1-10
PSQI (M)	6.25±3.49	3-13	6.06±3.15	3-13	6.91±3.31	2-13	6.4±3.21	2-13
PSQI (E)	4.50±3.46	1-11	6.40±2.92	2-13	6.41±0.60	3-11	5.97±2.97	1-13
Schizotypy								
UE	3.5±2.92	0-8	5.73±3.15	0-11	4.61±2.95	0-10	4.83±3.07	0-11
CD	4.25±3.19	1-9	7.93±2.73	3-11	6.38±3.20	1-11	6.55±3.25	1-11
IA	1.62±1.18	0-4	4.26±1.98	1-8	3.76±2.04	0-7	3.5±2.09	0-8
IN	1.12±0.83	0-2	3.6±2.06	0-8	2.84±1.86	0-6	2.77±1.98	0-8
Impulsivity								
PU	7±2.26	4-11	9.26±3.30	4-16	8.76±2.97	4-15	8.58±3.03	4-16
NU	7.37±2.06	5-11	9.46±3.11	5-16	9.61±2.81	5-16	9.05±2.87	5-16
SS	11.25±2.81	5-14	11.6±2.19	8-15	10.53±3.66	5-16	11.13±2.88	5-16
LP	6.75±1.98	4-9	7.53±1.76	5-11	7.07±2.10	4-11	7.19±1.90	4-11
LPre	7.5±2.87	4-11	7.33±2.05	5-11	6.84±2.07	5-10	7.19±2.21	4-11

Abbreviation: MEQ, Morningness-Eveningness Questionnaire; Pittsburgh Sleep Quality Index (Evening); PSQI (M), Pittsburgh Sleep Quality Index (Morning); PSQI (E); PSQI (S), Pittsburgh Sleep Quality Index (Screening); UE, Unusual Experiences; CD, Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; PU, Positive Urgency; NU, Negative Urgency; SS, Sensation Seeking; LP, Lack of Perseverance; LPre, Lack of Premeditation.

8.6.2 Chronotype and ToD Influences in Startle Amplitude, Habituation and PPI

Group x ToD x Block ANOVA on startle amplitude over the first and last block of pulse alone trials showed significant main effects of Block [$F_{(1,32)}$=49.99, p<0.001, ηp^2=0.610] indicating higher amplitude on the first block (828.72±86.70), compared to the last block of trials (530.33±65.35), and also of ToD [$F_{(1,32)}$=6.38, p=0.017, ηp^2=0.166] indicating generally lower amplitudes in the morning (605.37±74.89) than in the late afternoon (753.68±83.72) (Figure 8.2); there was no interaction involving Group, Block or ToD factors (p>0.05). Group x ToD ANOVA on habituation scores (% reduction in amplitude from the first to the last block of pulse-alone trials) also revealed no effect of Group [$F_{(2,32)}$=2.57, p=0.092, ηp^2=0.138], ToD [$F_{(1,32)}$=0.027, p=0.870, ηp^2=0.001] or a Group x ToD interaction [$F_{(2,32)}$=0.299, p=0.744, ηp^2=0.018].

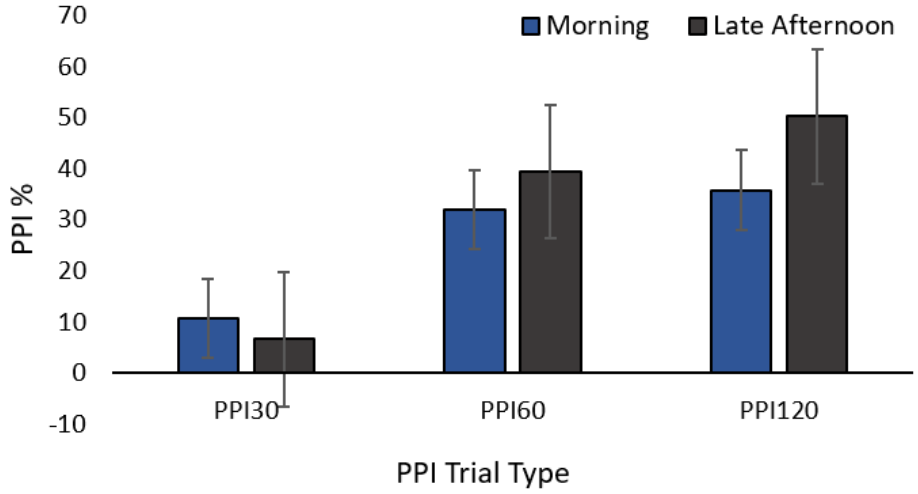
Figure 8.2 *Mean startle amplitude in analogue-to-digit (A/D) units on the first and last block of pulse-alone trials (5 trials each) and 9 pulse-alone trials during the PPI experiment (middle) in the morning and late afternoon session. Error bars represent ±1 standard error of the mean (SEM).*



The Group x ToD ANOVA on amplitude over pulse-alone trials that were presented interspersed with the PPI trials revealed no effect of Group [$F_{(2,33)}$=1.98, p=0.153, ηp^2=0.108], ToD [$F_{(1,33)}$=1.34, p=0.255, ηp^2=0.039] or a Group x ToD interaction [$F_{(2,33)}$=0.06, p=0.939, ηp^2=0.004].

Group x ToD x PPI Trial Type ANOVA on PPI scores revealed a significant main effect of Trial Type [$F_{(2,66)}$=29.12, p<0.001, ηp^2=0.469], with a linear increase in PPI from 30-ms through 60-ms to 120-ms PPI trials [linear $F_{(1,33)}$=28.38, p<0.001, ηp^2=0.462]. There was also a significant PPI Trial Type x ToD interaction [$F_{(1.70, 56.06)}$=3.88, p=0.03, ηp^2=0.105], explained by significantly lower PPI on 120-ms (but not 60-ms or 30-ms) PPI trials in the morning session, compared to the late afternoon session (t_{35}=2.25, p=0.015) (Figure 8.3). There was no main effect or any interaction involving Group (all p values>0.05). The ToD x Trial Type interaction became marginally significant after co-varying for pulse-alone amplitude [$F_{(1.64,51.03)}$=3.49, p=0.047, ηp^2=0.101].

Figure 8.3 *PPI in the morning and late afternoon sessions. Error bars represent ±1 SEM.*



8.6.3 Self-report and Startle measures: Inter-relationships

Of the hypothesised correlations, only Positive Urgency was associated with less 30-ms PPI30 (r=-0.354, p=0.034) and 60-ms PPI60 (r=-0.372, p=0.026) in the morning session. Sleep quality (over the past week) was not significantly associated with any startle measures (see Table 8.2).

In exploratory correlational analyses, MC did not show significant association with any startle measure except a negative correlation with amplitude on the last block of pulse-alone trials in the late afternoon session (r=-0.344, p=0.040). Sensation Seeking was associated with higher amplitude on the first block of pulse-alone trials (r=0.354, p=0.037) and more habituation (r=-0.375, p=0.026) in the morning session (Table 2). Impulsive Nonconformity was associated with higher amplitude on pulse-alone trials (r values 0.228 to -0.471) and a weaker habituation from the first block to the last block of pulse-alone trials (r=-0.336, p=0.045) in the late afternoon session (Table 8.2). None of these correlations were strong enough to survive Bonferroni correction for multiple correlations.

Table 8.2 *Self-report and startle measures: Inter-relationships.*

Variables	CT	PSQI		s-OLIFE				UPPS-P				
	MEQ	M	LA	UE	CD	IA	IN	PU	NU	SS	LP	LPre
Morning (M) Session	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**
Pulse-alone Amplitude - First Block	-0.235	-0.170	0.114	-0.280	-0.133	0.022	0.112	0.156	0.045	**0.354**	0.029	-0.030
	(0.175)	(0.336)	(0.522)	(0.103)	(0.447)	(0.899)	(0.520)	(0.371)	(0.796)	**(0.037)**	(0.868)	(0.864)
Pulse-alone Amplitude - Last Bloc	-0.240	-0.109	0.119	-0.189	0.034	0.056	0.190	0.200	0.206	0.135	-0.121	-0.056
	(0.159)	(0.534)	(0.495)	(0.270)	(0.842)	(0.746)	(0.266)	(0.241)	(0.227)	(0.432)	(0.484)	(0.744)
Habituation: Reduction from First to Last Block	0.108	-0.254	-0.134	0.023	-0.171	-0.044	-0.131	-0.095	-0.189	**0.375**	0.214	0.032
	(0.535)	(0.148)	(0.449)	(0.898)	(0.326)	(0.800)	(0.453)	(0.589)	(0.276)	**(0.026)**	(0.216)	(0.857)
Pulse-alone Amplitude - PPI Experiment	-0.228	-0.105	0.136	-0.161	0.030	0.045	0.204	0.192	0.169	0.166	0.024	-0.006
	(0.181)	(0.548)	(0.435)	(0.348)	(0.860)	(0.796)	(0.234)	(0.263)	(0.324)	(0.334)	(0.888)	(0.971)
PPI30 (M)	-0.183	-0.053	0.085	-0.121	-0.055	0.273	-0.155	**-0.354**	-0.096	0.039	-0.132	-0.108
	(0.286)	(0.761)	(0.628)	(0.482)	(0.748)	(0.107)	(0.366)	**(0.034)**	(0.579)	(0.822)	(0.442)	(0.530)
PPI60 (M)	-0.048	-0.093	0.022	-0.118	-0.104	0.183	-0.009	**-0.372**	0.045	-0.096	-0.035	-0.066
	(0.782)	(0.594)	(0.899)	(0.494)	(0.545)	(0.286)	(0.959)	**(0.026)**	(0.793)	(0.576)	(0.841)	(0.703)
PPI120 (M)	-0.065	-0.105	0.214	0.171	0.144	0.217	0.124	-0.039	0.037	-0.023	0.018	-0.131
	(0.706)	(0.548)	(0.218)	(0.319)	(0.403)	(0.205)	(0.470)	(0.821)	(0.832)	(0.895)	(0.917)	(0.448)
Late afternoon (LA) Session	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**	***r*(*p*)**
Pulse-alone Amplitude - First Block	-0.229	-0.101	0.164	0.042	0.128	0.012	0.228	0.231	0.149	0.114	0.025	-0.050
	(0.179)	(0.562)	(0.345)	(0.807)	(0.455)	(0.945)	(0.181)	(0.175)	(0.387)	(0.506)	(0.885)	(0.770)
Pulse-alone Amplitude - Last Block	**-0.344**	-0.129	0.103	-0.126	0.143	-0.008	**0.351**	0.283	0.229	0.276	0.011	0.025
	(0.040)	(0.461)	(0.556)	(0.465)	(0.405)	(0.963)	**(0.036)**	(0.094)	(0.180)	(0.103)	(0.948)	(0.884)
Habituation: Reduction from First to Last Block	0.291	-0.004	-0.074	0.232	-0.121	-0.062	**-0.336**	-0.139	-0.159	-0.199	-0.026	-0.084
	(0.086)	(0.982)	(0.673)	(0.174)	(0.482)	(0.721)	**(0.045)**	(0.419)	(0.356)	(0.245)	(0.880)	(0.627)
Pulse-alone Amplitude - PPI Experiment	-0.262	-0.150	0.034	-0.044	0.258	-0.054	**0.471**	0.274	0.311	0.062	0.094	0.037
	(0.123)	(0.390)	(0.846)	(0.800)	(0.129)	(0.754)	**(0.004)**	(0.105)	(0.065)	(0.718)	(0.584)	(0.830)
PPI3	-0.048	-0.106	-0.059	-0.202	-0.164	-0.212	0.150	-0.097	0.086	0.196	-0.124	0.007
	(0.781)	(0.544)	(0.737)	(0.237)	(0.339)	(0.215)	(0.382)	(0.572)	(0.619)	(0.251)	(0.469)	(0.968)
PPI60	0.047	-0.188	-0.130	-0.040	0.140	-0.141	0.312	-0.196	0.266	-0.177	0.116	0.031
	(0.784)	(0.279)	(0.455)	(0.817)	(0.416)	(0.411)	(0.064)	(0.252)	(0.116)	(0.303)	(0.499)	(0.857)
PPI120	-0.278	-0.068	0.102	-0.058	-0.035	-0.113	0.236	-0.030	0.256	0.143	-0.054	-0.195
	(0.100)	(0.696)	(0.560)	(0.735)	(0.840)	(0.510)	(0.165)	(0.861)	(0.132)	(0.405)	(0.756)	(0.255)

Abbreviation: CT, Chronotype; MEQ, Morningness-Eveningness Questionnaire; M, Morning; LA, Late-Afternoon; PPI, Prepulse Inhibition; PSQI, Pittsburgh Sleep Quality Index; s-OLIFE: short Oxford-Liverpool Inventory of Feelings Experiences; UE, Unusual Experiences; CD,

Cognitive Disorganisation; IA, Introvertive Anhedonia; IN, Impulsive Nonconformity; UPPS-P; PU, Positive Urgency; NU, Negative Urgency; SS, Sensation Seeking; LP, Lack of Perseverance; LPre, Lack of Premeditation.

Table 8.3 *Correlations between startle amplitude, habituation, and PPI.*

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Morning (M) Session														
(1) Pulse-alone Amplitude - First Block	1	**0.708 (<0.001)**	0.217 (0.210)	**0.826 (<0.001)**	0.260 (0.131)	0.262 (0.128)	**0.452 (0.006)**	**0.610 (<0.001)**	**0.645 (<0.001)**	**-0.418 (0.012)**	**0.502 (0.002)**	0.083 (0.636)	-0.034 (0.848)	**0.345 (0.042)**
(2) Pulse-alone Amplitude - Last Block		1	**-0.382 (0.023)**	**0.927 (<0.001)**	0.251 (0.139)	0.127 (0.459)	**0.445 (0.007)**	**0.747 (<0.001)**	**0.739 (<0.001)**	**-0.400 (0.016)**	**0.761 (<0.001)**	0.045 (0.793)	-0.091 (0.596)	0.318 (0.059)
(3) Habituation: Reduction from First to Last Block			1	-0.118 (0.501)	0.056 (0.747	0.115 (0.509)	0.248 (0.152)	-0.135 (0.438)	-0.058 (0.743)	-0.030 (0.863)	-0.191 (0.273)	0.060 (0.730)	0.066 (0.708)	0.122 (0.487)
(4) Pulse-alone Amplitude - PPI Experiment				1	**0.352 (0.035**	0.208 (0.224)	**0.579 (<0.001)**	**0.774 (<0.001)**	**0.798 (<0.001)**	**-0.482 (0.003)**	**0.765 (<0.001)**	0.106 (0.539)	-0.079 (0.647)	**0.378 (0.023)**
(5) PPI30					1	**0.427 (0.009)**	**0.651 (<0.001)**	0.299 (0.077)	0.292 (0.084)	-0.054 (0.753)	0.210 (0.218)	-0.003 (0.984)	0.003 (0.985)	0.093 (0.589)
(6) PPI60						1	**0.418 (0.011)**	-0.132 (0.444)	-0.105 (0.541)	0.003 (0.986)	-0.063 (0.714)	0.160 (0.351)	**0.530 (<0.001)**	**0.344 (0.040)**
(7) PPI120							1	**0.551 (<0.001)**	**0.482 (0.003)**	-0.138 (0.422)	**0.464 (0.004)**	-0.036 (0.835)	0.150 (0.382)	**0.378 (0.023)**
Late afternoon (LA) Session														
(8) Pulse-alone Amplitude - First Block								1	**0.884 (<0.001)**	-0.236 (0.166)	**0.759 (<0.001)**	0.047 (0.788)	-0.116 (0.499)	**0.420 (0.011)**
(9) Pulse-alone Amplitude - Last Block									1	**-0.621 (<0.001)**	**0.812 (<0.001)**	0.177 (0.301)	-0.094 (0.585)	**0.433 (0.008)**
(10) Habituation: Reduction from First to Last Block										1	**-0.540 (<0.001)**	-0.261 (0.125)	-0.036 (0.836)	-0.233 (0.171)
(11) Pulse-alone Amplitude - PPI Experiment											1	0.175 (0.308)	0.208 (0.223)	**0.432 (0.009)**
(12) PPI30												1	**0.345 (0.039)**	**0.574 (<0.001)**
(13) PPI60													1	**0.497 (0.002)**
(14) PPI120														1

Abbreviation: PPI, Prepulse Inhibition.

8.7 Discussion

The primary aim of the present study was to investigate possible effects of chronotype, ToD, and synchrony on PPI of the acoustic startle response in young healthy adults. The main findings indicated i) no chronotype or synchrony effects on startle amplitude, habituation or PPI, ii) marginally greater PPI on 120-ms prepulse-to-pulse interval trials during the late afternoon, compared to the morning session, iii) no association of sleep quality with startle amplitude, habituation or PPI, iv) medium-sized negative association between a psychometric measure of Positive Urgency (impulsivity) and PPI during the morning session (with weaker and non-significant negative association with late afternoon PPI).

The failure to observe chronotype or synchrony effects on PPI or any startle measure offers no support for first tentative hypothesis. This finding, however, provides further empirical support for Yang and colleagues' (2007) suggestion of no chronotype effect on tasks where performance relies mainly on automatic processing and does not require conscious effort on part of the participant. Some studies in rodents have shown higher startle amplitude and PPI during the dark, relative to the light phase (Adams et al., 2008; Chabot & Taylor, 1992; Davis & Sollberger, 1971) while others reported no effects of circadian time on habituation and PPI and attributed any effects, where found, to lighting conditions and sex-related influences (Weiss et al., 1999). Our findings cannot be directly compared to the findings of these rodent studies, as we tested our participants in the morning (8:00-10:00 hour) and late afternoon (16:00-18:00 hour) in laboratory conditions with natural light. Nonetheless, we did observe a significant a ToD effect in startle amplitude and 120-ms PPI, both being higher in the late afternoon session, compared to the morning session. Higher startle amplitude in the afternoon may be related to increased arousal levels during late afternoon session, which has been referred to as the ‘wakeful maintenance zone’ (WMZ; i.e., 2-3 hours window of increased alertness levels prior to melatonin secretion onset in the evening; Dijk et al., 1992). WMZ is known to facilitate attentional network and reduce the effect of SD in cognitive performance (McMahon et al., 2021). This would also explain our finding of greater PPI on trials with 120-ms (but not 30-ms or 60-ms) prepulse-to-pulse intervals in the late afternoon compared to the morning session. PPI with short-to-medium (30-60 ms) lead intervals mainly involves automatic processes, whereas PPI with longer lead intervals may, in addition to automatic stimulus detection, also involve controlled processes. For example, PPI enhancement has been observed when participants are required to pay attention to the prepulses (Schell et al., 2000).

In general, our findings, especially for 30-ms and 60-ms PPI, are consistent with previous studies (Abel et al., 1998; Freudenberg et al., 2023; Ludewig et al., 2002) demonstrating stability of PPI in healthy young adults and add further support to its utility as a biomarker to advance schizophrenia therapeutics (Geyer, 2006; Light & Swerdlow, 2020).

Our finding also did not reveal any relationship between sleep quality and PPI or any startle measures. Although two previous studies have demonstrated disrupted PPI in the morning following over-night SD (Petrovsky et al., 2014; Meyhofer et al., 2019), SD and poor sleep quality are conceptually very different and affect cognitive performance differently. Whilst acute SD has been consistently shown to influence cognitive functions (e.g., inhibition, working memory; Krause et al., 2017; Kumari and Ettinger, 2020), poor sleep quality may or may not have similar effects in young healthy adults when tested between 11:00-15:00 hour (Zavecz et al., 2020). As discussed earlier, these wakeful maintenance hours may facilitate performance due to increased vigilance and arousal levels at this ToD (McMahon et al., 2021) Of note, our sample also consisted predominantly of good sleepers who are known to have higher melatonin secretion (Fatemeh et al., 2022). Lastly, as expected, we found a negative correlation between a measure of impulsivity and PPI (Gee et al., 2015) which was significant only for the morning session, and weaker and non-significant in the late afternoon session possibly due to the WMZ-related influences described earlier. As there is no other study investigating ToD influences in association of PPI with psychopathology-related traits, further work is needed to explore this possibility. Lastly, schizotypy did not show a significant association with PPI in this study, although ECs did score higher than MCs on some schizotypy measures in line with our earlier findings in an independent sample (Chauhan et a. 2024a, 2024b).

8.7.1 Limitations and Future Directions

The present study had some limitations. First, we did not measure subjective or objective arousal levels. Second, we restricted our sample to 18-40 years to ensure chronotype stability in this age range (Roenneberg et al., 2007) but it also means that our findings cannot be generalised to those <18 and >40 years of age. Third, although we had enough power to examine ToD effects, there was limited power to examine Chronotype x ToD interaction. Further studies with a larger sample are needed to confirm our findings while accounting for these limitations.

8.7.2 Conclusions

To conclude, the present study showed no significant chronotype or synchrony effects on PPI, although there was greater startle amplitude on pulse-alone trials, and marginally greater PPI on 120-ms (but not 30-ms or 60-ms) prepulse-to-pulse interval PPI trials, possibly explained by greater arousal and alertness levels, in the late afternoon compared to the morning session. Furthermore, there was no significant association between PPI and sleep quality in our sample of young healthy adult who, on average, were fairly good sleepers. Taken together, our findings suggest that PPI, especially with short-to-medium prepulse-to-pulse intervals, is a fairly stable biomarker and not significantly modulated by chronotype or ToD in healthy young adults.

PART III

Chapter 9: General Discussion

Chapter 9: General Discussion

9.1 Chapter Aims and Overview

This chapter will first summarise the key findings derived from the four empirical studies. It will then present the objectives/original hypotheses of the empirical studies, followed by a synthesis of the observed findings. Finally, this chapter will discuss the implications of the findings, strengths and limitations of the studies conducted, and offer suggestions for future research.

9.2 Summary of Thesis Findings

The findings presented in Chapters 5-8 contribute to the overarching research aims to: a) examine the inter-relationships of chronotype, mental health, sleep quality, psychopathology-related personality traits and childhood trauma, b) examine the role of sleep quality in chronotype-mental health relationship, and c) investigate how and to what extent chronobiological variables (i.e., chronotype, ToD, and synchrony effect) may influence memory (requiring mainly controlled processing) and sensorimotor gating (requiring mainly automatic processing). In this thesis, chronotype was used both as a continuous (assessed via self-report measure; Chapters 5 and 6) and a categorical variable (comparing MCs, ICs, and ECs; Chapters 7 and 8). Sleep quality was assessed as a continuous variable (assessed via self-report measure; Chapters 5-8). The research question, objectives/hypotheses, methodology, and key findings are summarised in Table 9.1.

Chronotype was found to be associated with poor mental health and various psychopathology-related personality traits (e.g., neuroticism, schizotypy, impulsivity) in young non-clinical adults residing in north India, the UK, and Germany (Chapters 5 and 6). The findings of the investigation presented within this thesis showed no direct effect of chronotype on mental health. Instead, poor sleep quality fully mediated the chronotype-mental health relationship (Chapters 5 and 6). Similar to Muzni and colleagues' findings (2021), poor sleep quality, rather than chronotype, was consistently found to have a stronger association with mental health outcomes (Chapters 5 and 6). Furthermore, EC was found to be associated with various psychopathology-related personality traits, namely neuroticism, cognitive disorganisation, lack of perseverance and premeditation and sensation seeking (Chapters 5 and 6), broadly in line previous literature on this topic (Chapter 1; Section 1.7.2.3). While emotional neglect and abuse

were associated with EC in a North Indian sample (Chapter 5), this was not found in the UK and Germany-based samples (Chapter 6).

Chronotype was found to have no direct role in influencing verbal learning and memory (immediate or delayed recall) (Chapter 7) or sensorimotor gating (PPI) (Chapter 8). In line with previous research (Schmidt et al., 2007), a trend of ToD influencing delayed recall and organisation strategy was found, although as shown in Chapter 7 (Section 7.4.2) this was explained via independent effects of daytime dysfunction and introvertive anhedonia. While synchrony effect modulated episodic memory selectively in MCs, this effect remained significant after covarying for daytime dysfunction or introvertive anhedonia (Chapter 7). Daytime dysfunction of all sleep facets appeared to be significantly (negatively) associated with poor learning slope and cumulative word learning in the morning session (Chapter 7). Marginally higher PPI was observed at longer (120-ms), but not short-to-medium (30-ms, 60-ms) prepulse-to-pulse intervals in the late afternoon, compared to the morning session (Chapter 8). PPI was not found to be modulated by synchrony effect and was also not associated with sleep quality (Chapter 8). The findings presented in this thesis indicate that chronotype itself does not affect either mental health or cognitive performance; instead, any effects of chronotype are likely to be explained by sleep-related disturbance (mental health, memory) or ToD (PPI).

Table 9.1 *Research question, hypotheses, methodology, and key findings reported in Chapters 3, and 5-8.*

Chapter	Research Question	Objectives/Hypotheses	Methodology	Key Findings
3	Do chronobiological factors influence cognitive functions?	Investigate the extent to which chronotype and synchrony effect influence general and specific cognitive domains in healthy adults.	Systematic review (k=65); 53 studies assessing chronotype influence on various cognitive functions, 11 comparing young ECs vs older MCs adults, and remaining one involving older MCs adults).	No main effect of chronotype on any cognitive function in most (>80%) studies. Around 45% of the studies involving adults aged 18-45 years reported a synchrony effect in MCs and/or ECs, mainly but not exclusively in attention, inhibition, and memory. Majority of the studies in older adults (>83%) reported a synchrony effect on tasks involving fluid abilities. Limited evidence also suggested higher activation of inhibition-related brain regions at optimal ToD in both chronotypes, and synchrony effects being impacted by some exogenous factors known to affect arousal and performance (e.g., task characteristics and complexity, sleep, lighting conditions).
Chapter	**Research Question**	**Objectives/Hypotheses**	**Methodology**	**Key Findings**
5	Is chronotype linked to mental health (depression, anxiety, stress), sleep quality, psychopathology-related personality traits of neuroticism, extraversion,	EC and sleep quality will be associated with higher levels of depression, anxiety, and stress, with these associations being stronger for sleep quality than EC.	Examined associations between self-report measures of chronotype, mental health, sleep quality, psychopathology-related personality traits and childhood trauma as well as explored the role of sleep quality in chronotype-mental relationship in	Chronotype had small-to-medium sized associations (*r*: 0.20-0.30), while sleep quality had medium-to-large sized associations (*r*: 0.47-0.52) with mental health outcomes.

	schizotypy, impulsivity and childhood trauma? Does sleep quality mediates chronotype-mental health relationship?		young, non-clinical North Indian sample (N=313). The mediating role of sleep quality was assessed using SEM. The model included: eight predictors (chronotype, neuroticism, extraversion, cognitive disorganisation, sensation seeking, lack of perseverance, emotional abuse and neglect), one mediator (sleep quality), and one outcome (mental health indicated via depression, anxiety, stress).	No direct effect of chronotype on mental health outcomes, instead it was fully mediated by poor sleep quality. Chronotype had small-sized associations (*r*: >0.30), while Sleep quality had small-to-medium sized associations (*r*: 0.12-0.43) with psychopathology-related personality traits and childhood trauma.
Chapter	**Research Question**	**Objectives/Hypotheses**	**Methodology**	**Key Findings**
6	Does sleep quality mediate the chronotype-mental health relationship in individuals residing in the UK and Germany as found in a North Indian sample? Does psychopathology-related personality-traits and childhood trauma influence chronotype-mental health relationship?	There will be a stronger relationship between sleep quality and mental health than between chronotype and mental health. Any relationship between chronotype and mental health will be mediated via sleep quality.	Repeated the approach employed in Chapter 5 and examined the independent associations between self-report measures of chronotype and sleep quality with mental health, psychopathology-related personality traits and childhood trauma as well as investigated the role of sleep quality in chronotype-mental relationship in young, non-clinical UK-based sample (N=213) and Germany (N=247). As in Chapter 5, SEM approach was used to examine the mediating role of sleep quality. The model included: eight predictors (chronotype,	UK-based sample scored higher, on average, on levels of depression, anxiety, stress, certain psychopathology-related personality traits (unusual experiences, cognitive disorganisation, introvertive anhedonia, negative and positive urgency, sensation seeking) and childhood trauma as well as reported poorer sleep quality than Germany-based sample. Chronotype had small-to-medium sized associations (UK and Germany, *r*: 0.20-0.30), while sleep quality had medium-to-large sized associations (*r*: UK, 0.51-0.56; Germany, 0.27-0.30) with mental health outcomes.

			neuroticism, extraversion, cognitive disorganisation, positive and negative urgency, and lack of perseverance and premeditation), one mediator (sleep quality), and one outcome (mental health).	No direct effect of chronotype on mental health outcomes; instead, it was fully mediated by poor sleep quality in both the UK and Germany-based samples. Sleep quality had small-to-medium sized associations with certain (*r*: 0.12-0.43) personality traits and childhood trauma (*r*: UK, 0.23-0.42; Germany, 0.10-0.30).
Chapter	**Research Question**	**Objectives/Hypotheses**	**Methodology**	**Key Findings**
7	How do chronobiological factors and/or sleep quality influence verbal learning and memory performance?	Superior verbal memory and learning performance at optimal ToD for both MCs and ECs and no change in performance in ICs. Sleep dimensions especially sleep quality, duration, and dysfunction will be negatively associated with poor verbal memory performance, especially in the morning session.	Tested a sub-sample of UK-based sample (N=63), described in chapter 6 (N=213), and assessed verbal learning and memory performance using HVLT. Employed categorical approach to chronotype and assessed 22 MCs, 21 ICs, and 20 ECs in the morning (8:00-10:00) and late afternoon session (16:00-18:00), a week apart. Sleep quality was assessed on both testing sessions.	No effect of chronotype on verbal learning and memory. Greater delayed recall in MCs at their optimal ToD. ToD modulation on delayed recall and organisation strategy was explained via independent effects of daytime dysfunction and introvertive anhedonia. No association between sleep quality and duration and verbal learning and memory. No association between personality traits and verbal learning and memory. Daytime dysfunction had medium-sized correlations (*r*: 0.33-0.34) with learning slope and cumulative word learning in the morning.
Chapter	**Research Question**	**Objectives/Hypotheses**	**Methodology**	**Key Findings**

8	Do chronobiological factors and/or sleep quality influence sensorimotor gating, as assessed with PPI of the acoustic startle response?	Greater PPI at optimal times in all chronotypes (i.e., synchrony effect). Negative associations between sleep quality and PPI assessed in the morning. Possible negative associations also between the measures of schizotypy and impulsivity and PPI, expecting the same pattern of associations in both testing sessions.	Tested a sub-sample of UK-based sample (N=45), described in Chapter 7 (N=63) on an acoustic PPI paradigm Similar to Chapter 7, a categorical approach to chronotype was used and compared 14 MCs, 17 ICs, and 14 ECs in the morning (8:00-10:00) and late afternoon session (16:00-18:00), a week apart. Sleep quality was assessed on both testing sessions.	No chronotype or synchrony effect on PPI. More PPI with 120 ms (but not 30-ms or 60-ms) prepulse-to-pulse interval trials in the late afternoon session, compared to the morning session. No association between sleep quality and startle habituation and PPI.

Note: ECs, Evening chronotypes; HVLT, Hopkins Verbal Learning Test; ICs, Intermediate Chronotypes; MCs, Morning Chronotypes; MS, Milliseconds; PPI, Prepulse Inhibition; SEM, Structural Equation Modelling; UK, United Kingdom; ToD, Time of Day.

9.3 Interpretation of the Findings

The findings reported in Chapters 5 and 6 consistently showed that sleep quality is a key determinant of poor mental health and a mediator of chronotype-mental health relationship in young non-clinical adults (age range: 18-40 years) (Table 9.1). A recent genome-wide study involving 697,828 individuals in the UK has shown that genetic variants linked with chronotype are associated with depression and schizophrenia. (Jones et al., 2019). While these findings may not align with those of this thesis, it is important to recognise that chronotype is shaped by CRs but is also influenced by various environmental, social, and individual factors (Chauhan et al., 2023).

Higher prevalence of mental health issues in association with poor sleep quality in India-based sample (Chapter 5), followed by the UK and Germany-based samples (Chapter 6), can be understood via the complex interaction and inter-relationships or poor sleep, psychopathology-related personality traits (i.e., neuroticism, schizotypy, impulsivity), and childhood maltreatment. Psychopathology-related traits of neuroticism and schizotypy, as well as childhood trauma and abuse, are well known as risk factors for poor mental health outcomes (Stephan et al., 2018). Individuals scoring high on these psychopathology-related personality traits experience higher distress, anxiety, and sleep-related disturbances, as also demonstrated in Chapter 5 and 6. Despite the differences in magnitude of the association between sleep quality and mental health in the UK, India, and Germany-based samples, sleep quality consistently mediated the chronotype-mental health relationship in three culturally and geographically different countries. These consistent findings from different parts of the world provide substantial support to the sleep hypothesis as a predisposing, precipitating, and perpetuating risk factor for poor mental health and reject the widely reported role of chronotype as an independent risk factor of mental health.

The findings from Chapters 7 and 8 also provided a consistent picture that chronotype does not have a main effect on verbal learning and memory or prepulse inhibition (sensorimotor gating) in young non-clinical adults. This finding generally aligns with literature examining the chronotype effect in young healthy adults on memory (Barbosa & Albuquerque, 2008; Evansova et al., 2022) and inhibition (Carlson et al., 2023; Facer-Childs et al., 2019; Martínez-Pérez et al., 2020; Schmidt et al., 2012a; Song et al., 2018). A systematic synthesis of the existing literature (Chapter 3, Section 3.4.1) also highlighted a limited-to-no role of chronotype

in performance across various cognitive domains, including memory and inhibition (Table 9.1). It could be assumed that individuals often overestimate their objective performance based on subjective feelings (i.e., metacognition) which may not be significantly associated with their expectations of higher (objective) cognitive performance (Hourihan & Benjamin, 2014). The findings reported in this thesis also suggested no differences in objective performance on memory and prepulse inhibition tasks; however, subjective feelings about cognitive performance were not assessed in any of the empirical investigations reported in this thesis.

The findings concerning ToD and synchrony effect partially align with previous literature supporting the role of ToD/synchrony in influencing various cognitive functions, including memory and inhibition (Schmidt et al., 2007; May et al., 2023). As also highlighted in Chapter 3, higher-order cognitive functions are more sensitive to ToD (optimal) modulations. A trend for ToD influence on episodic memory and organisation strategy was observed but was entirely explained via independent effects of daytime dysfunction and introvertive anhedonia. This could be understood in the context of sleep-related disturbances. Overnight SD has been found to elicit more use of organisation strategy to facilitate recall of words (Takeuchi et al., 2014), typically suggesting that more use of organisation strategy reflects poor memory. These disrupted sleep-wake cycles, including difficulty falling/maintaining asleep, excessive daytime sleepiness, and nocturnal waking, are commonly present in patients with depression and schizophrenia (review, Scott et al., 2021) who have also been found to rely on strategy formation and organisation to facilitate free recall (Tsuno et al., 2005; Murty et al., 2018; Zarcone, 1979). It could also be argued that circadian fluctuations in cognitive performance are a by-product of lower alertness/arousal levels (Czeisler et al., 1985), given previous reports of higher body temperature and lower melatonin secretion resulting in higher cognitive performance (Kleitman et al., 1938). However, some studies have also reported that enhanced cognitive performance is not univocally determined via physiological parameters (e.g., body temperature, melatonin secretion) (West et al., 2002; Blatter et al., 2005) but is also dependent on task characteristics and complexity as also discussed in Chapter 3 (Section 3.5.3). This explains why MCs were found to perform better at their optimal ToD selectively on episodic memory while immediate recall and recognition index remain unaffected. Studies have also shown that individuals experience a 2–3-hour window of increased alertness levels prior to melatonin secretion onset in the evening (Dijk et al., 1992), which may explain the marginally significant ToD modulation at longer (120-ms) prepulse-to-pulse intervals reported in this thesis. Nonetheless, these findings provide further support to the influence of circadian

functions on episodic memory (requiring mainly controlled processing) and sensorimotor gating (requiring mainly automatic processing) remained unaffected.

As previously discussed in Chapter 2, ECs generally experience higher sleep-related disturbances (Adan et al., 2012; Muzni et al., 2021; Randler et al., 2017; Ronneberg et al., 2007) and both acute and chronic sleep disruptions are known to be significant risk factors for cognitive decline (Carlson et al., 2023; Gilley, 2023; Newbury et al., 2021; Paller et al., 2021). Against the well-established sleep literature, Chapters 7 and 8 findings suggested no associations of poor sleep quality as indexed by the PSQI global score with memory or PPI. The nature of the assessment and sample itself could explain these findings. The PSQI assesses poor sleep quality on different dimensions (e.g., sleep dysfunction, duration, use of medication) based on an individual's past month experience, while in Chapter 7 and 8 PSQI was administered twice a week apart asking participants to rate their subjective sleep quality based on their past week's sleep. Over 50% of participants, on both occasions, reported good sleep quality, and over 80% had good sleep duration (>6 hours). Participants might have benefited from good sleep quality, masking the hypothesised sleep relationship with poor cognitive performance in Chapters 7 and 8. However, daytime dysfunction was linked to poor learning slope and cumulative word learning. Daytime dysfunction reflects persistent daytime sleepiness, reduced responsiveness, and higher sleep inertia, which maybe conceptually different to sleep quality. Daytime dysfunction is also linked to insomnia, which is known to negatively affect executive functioning (Kong et al., 2023). While insomnia was not examined in this thesis in relation to mental health or cognitive functions, the findings do reflect the universal nature of poor sleep-related impairments on cognitive measures, although the magnitude of different sleep facets on cognitive function (e.g., sleep deprivation, sleep quality, duration, and dysfunction) may or may not be similar.

9.4 Implications and Considerations

The findings presented in this thesis highlight sleep, rather than chronotype, as a key determinant in mental health outcomes, emphasising the need for sleep-centred interventions in clinical practices and public health initiatives. First, since no direct effect of chronotype was observed on mental health outcomes in three different countries, a chronotype-centred approach to therapies might not be optimal. Instead of focusing on shifting circadian preference from eveningness to morningness, sleep-related disturbances should be identified and

considered important therapeutic targets for improving mental health in the general population and those at high risk (individuals with a history of trauma/abuse or scoring high on neuroticism and schizotypy). Second, including a sleep assessment and introducing sleep-hygiene awareness in cognitive therapies and educational settings for individuals with existing mental health conditions, learning or memory-related difficulties might result in a better lifestyle and improved cognitive health. Children at schools and universities might benefit from these public health campaigns advocating good sleep practices and hygiene to support mental well-being and optimise cognitive performance. To date, there are no standard guidelines to assist individuals working in educational, hospitality, hospitals, corporate, or other industry settings to achieve optimal performance, proficient work, and higher productivity. Considering the findings of the systematic review showing a synchrony effect on higher-order cognitive tasks especially in individuals aged ≥50 years (Chapter 3), though not robustly observed in the two investigations involving a young non-clinical sample mostly with ≥6 hours of sleep on a regular basis (Chapters 7 and 8), attention to an individual's optimal timing in these workspaces, especially while planning tasks that require higher cognitive load, use of cognitive reserves, strategic thinking and planning, will achieve the overarching goal of higher productivity. Furthermore, failure to account for the ToD/synchrony effect may result in exaggerated cognitive deficits in the elderly, especially those at risk of developing dementia or psychosis. Lastly, advancement in science comes from building on the previous work of other researchers, for which reproducibility is essential though hard to achieve given various methodological and sometimes unspecified variations (e.g., different tasks employed, study methods and procedures). In this context, failure to account for ToD/synchrony effect may further aid to replication crisis.

9.5 Strengths, Limitations, and Future Directions

The empirical studies reported in this thesis included young, non-clinical adults from the general population and had specific methodological strengths and weaknesses.

First, a comprehensive SEM model was used to understand the role of chronotype in mental health by quantifying the role of sleep quality, psychopathology-related personality traits, and childhood trauma in three independent samples (Chapters 5 and 6). Second, the use of a between-within-subjects design in young adults allowed repeated testing and a direct comparison of MCs, ICs, and ECs in the morning and late afternoon sessions when examining

chronobiological influences on memory and sensorimotor gating measures (Chapters 7 and 8). This approach ruled out the possibility of random, practice, or age-related effects as well as time-of-testing-related confounders (Chapters 7 and 8). As highlighted in Chapter 3, majority of the previously reported studies on memory and inhibition had either used a between-subject design for comparing young ECs vs old MCs and also randomly assigned either a morning or evening testing session (Hasher et al., 2002; Lehman et al., 2013; May et al., 1999; 2005; May & Hasher, 2017) or tested participants in bigger testing blocks exceeding 24-hour cycle (Iskander et al., 2016; Schmidt et al., 2012b; West et al., 2002). Second, the use of validated and reliable HVLT and PPI experiments could be considered a strength. Two alternative versions (Form A and B) of HVLT were used to eliminate known practice effects of HVLT (Stout et al., 2014) during morning and late afternoon testing sessions (Chapters 7). Lastly, to control for sleep-related changes between the two testing sessions, sleep quality was assessed in both testing sessions which could be a strength. Fourth, since sex and hormonal fluctuations in females are known to influence sleep and mood (Morssinkhof et al., 2020), as well as cognitive performance (Kilpi e al., 2020; Naysmith et al., 2022; Santhi et al., 2016), the strict criteria for only inviting females on contraceptives in the experimental studies could also be considered a strength (Chapters 7 and 8). However, females not using contraceptives are equally important in research, as they provide a more representative sample of the general population compared to those using contraceptives and also enable examination of menstrual cycle related hormonal fluctuations in relation to sleep, chronotype, mental health and cognitive function.

The empirical studies reported in this thesis also have some notable limitations. Despite using validated self-report measures of chronotype (MEQ) and sleep quality (PSQI), it is essential to highlight the absence of objective measures (actigraphy) and markers (e.g., melatonin or cortisol) of chronotype and sleep (Chapters 5-8). Second, the subjective or objective levels of arousal/vigilance and sleep fragmentation were not recorded. This limits the understanding of the true extent of chronotype on PPI. On average, lower PPI was observed in the morning session which could potentially be attributed to sleep inertia or simply lower arousal levels (Chapter 8). Future studies should employ objective markers of chronotype, sleep, and arousal levels as they can further validate the findings based on subjective measures. Furthermore, the limited final sample size in Chapter 8 should also be acknowledged. This was due to the removal of noisy psychophysiological signals in one or both sessions. Another reason for a smaller than anticipated sample size was a higher dropout rate because of study timings:

morning (8:00-10:00) and late afternoon sessions (16:00-18:00). Although Chapter 7 had a modest sample size, the late afternoon session might not be optimal for ECs as previous work has shown young ECs perform better at their optimal ToD (20:00). As highlighted in Chapter 3, this is a general problem in chronobiology literature as there is no standard optimal time for either MCs or ECs to examine the true magnitude of synchrony effect.

Regarding the nature of the sample, it was predominantly recruited from the general population aged between 18-40 years. However, over 80% of the participants happened to be students (Chapters 5-8). Given the restricted age range, it was considerably difficult to recruit MCs participants (specifically males) (Roenneberg et al., 2007). Furthermore, over 50% of participants were also good sleepers (Chapters 7 and 8), which could have masked the effect of any sleep-related disturbance on memory and PPI.

Taken together, further research is needed to conclusively determine the optimal ToD for MCs and ECs to examine the magnitude of the synchrony effect employing a) appropriate research designs, b) both objective and subjective measures of chronotype, sleep, and arousal to further replicate and validate the findings presented in this thesis, and c) sufficiently large samples with different age groups.

9.6 Conclusions

Despite some methodological limitations, the finding of the studies reported in this thesis provide substantial support for the following:

- Chronotype is not an independent risk factor for poor mental or cognitive health outcomes.
- Sleep quality mediates chronotype-mental health relationship in young non-clinical populations.
- There is no effect of chronotype or ToD (on its own), but synchrony effect may modulate episodic memory and semantic clustering strategy in young non-clinical adults.
- Chronotype does not influence sensorimotor gating in young non-clinical adults.

Appendices

Appendix 1: Ethical Approval (Chapter 5)

Appendix 2: Participant Information Sheet (Chapter 5)

Appendix 3: Consent Form (Chapter 5)

Appendix 4: Debrief Form (Chapter 5)

Appendix 5: Ethical Approval (Chapters 6-8)

Appendix 6: Participant Information Sheet (Chapter 6-8)

Appendix 7: Consent Form (Chapter 6-8)

Appendix 8: Debrief Form (Chapter 6-8)

Appendix 9: Published Paper

Appendix 1: Ethical Approval (Chapter 5)

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15 March 2023

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 15/03/2023 AND 30/09/2024

Applicant (s): Mr Satyam Chauhan Dr Ray Norbury, Ms Kaja Faßbender, Prof Ulrich Ettinger , Prof Rakesh Pandey

Project Title: Happy larks and lonesome owls: Association between chronotype and psychopathology-related traits in Indian population.

Reference: 41125-MHR-Mar/2023- 44225-4

Dear Mr Satyam Chauhan

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- Please use your approved study dates (above) in all your study documents (eg Advert, PIS, Debrief, Consent form).
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to any conditions that may appear above.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.
- You may not undertake any research activity if you are not a registered student of Brunel University or if you cease to become registered, including abeyance or temporary withdrawal. As a deregistered student you would not be insured to undertake research activity. Research activity includes the recruitment of participants, undertaking consent procedures and collection of data. Breach of this requirement constitutes research misconduct and is a disciplinary offence.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DLS)

Brunel University London

Appendix 2: Participant Information Sheet (Chapter 5)

College of Health, Medicine and Life Sciences
Department of Life Sciences

Psychological Wellbeing in Larks and Owls

PARTICIPANT INFORMATION SHEET

Invitation Paragraph
You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?
The purpose of this study is to investigate how chronotype (i.e., preference for being awake or asleep at certain times) may impact psychological wellbeing in healthy adults.

Why have I been invited to participate?
We are inviting people from the general population to participate in this study. You can participate if you are: (i) aged between 18-40 years and live in India, (ii) fluent in English, (iii) not be on any regular medical prescription, (iv) not have a history of any diagnosed mental disorders or drug abuse (any past or current use of non-prescribed drugs), (v) able to provide a written informed consent.

Do I have to take part?
As participation is entirely voluntary, it is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign an online consent form. You are still free to withdraw from the study. This can be done by closing the browser before completing the survey. Your withdrawal from the project will not adversely affect you. If you decide to participate in this study, you will not be able to withdraw your data after submitting your responses as we are not collecting any identifiable information and cannot link you to your responses.

What will happen to me if I take part?
The study involves taking part in an online session, taking approx. 30 minutes. During this session, you will be asked about your personality, habits and experiences, sleep quality, general mental and physical health, childhood experiences, as well as basic demographic information. Please be assured that you are free to not answer any of the questions that you do not wish to answer.

Are there any lifestyle restrictions?
There are no lifestyle restrictions.

What are the possible disadvantages and risks of taking part?
There are no disadvantages or risks in the taking part of this study that exceed those present in everyday life. If you find some of the questions personal, you are free to not answer those questions. The study does not seek to uncover any mental disorders.

What are the possible benefits of taking part?

There are no possible benefits in the taking part of this study. The completed research will help us to investigate how chronotype (i.e., preference for being awake or asleep at certain times) may impact mental health in healthy adults.

What if something goes wrong?
If something goes wrong during this study, complaints will be assessed by Professor Louise Mansfield (Chair of College of Health, Medicine and Life Sciences Research Ethics Committee; Email: Louise.mansfield@brunel.ac.uk).

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential and stored on a secure password protected Brunel University server for a period of 10 years after the completion of the study.

What will happen to the results of the research study?
The anonymised research data will be analysed by the researcher(s) before being reported. The results will be disseminated, for instance at public talks, conferences, in scientific journals, and/or social media. The anonymised research data may be analysed and reported for purposes not related to this study. The anonymised research data may also be shared with other researchers, and/or made available as "open data". This means the data will be publicly available and may be used for purposes not related to this study. Since, we are not collecting any unique identifiable data, it will not be possible to identify you from these data. The data will be stored by the lead researcher for a period of at least ten years from completion of the project (subject to any legal, ethical or other requirements of the funding body). After the study completion, should you wish it, we will send you a summary describing the findings of the current study and alerting you to any research publication we have generated from the project.

Will I be recorded, and how will the recording be used?
No, there will be no personal audio or video recording of you at any time for this research study.

Who is organising and funding the research?
This research is organised by Satyam Chauhan, Division of Psychology, Department of Life Science, Brunel University London (Email: satyam.chauhan2@brunel.ac.uk) under the supervision of Professor Veena Kumari, in conjunction with Brunel University London.

What are the indemnity arrangements?
Brunel University London provides appropriate insurance cover for research which has received ethical approval.

Who has reviewed the study?
This study has been reviewed by the College of Health, Medicine and Life Sciences Research Ethics Committee, Brunel University London (Reference: 41125-MHR-Mar/2023- 44225-4).

Brunel University's commitment to the UK Concordat on Research Integrity
Brunel University is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from our researchers during the course of their research.

Contact for further information and complaints

For general information

- Mr Satyam Chauhan, Division of Psychology, Department of Life Sciences, Brunel University London. (Email: satyam.chauhan2@brunel.ac.uk).
- Professor Veena Kumari, Division of Psychology, Department of Life Sciences, Brunel University London. (Email: veena.kumari@brunel.ac.uk).

For complaints and questions about the conduct of the research
Professor Louise Mansfield (Chair of College of Health, Medicine and Life Sciences Research Ethics Committee; Email: Louise.mansfield@brunel.ac.uk).

Thank you for taking the time to read this information sheet and considering taking part in the research study.

Appendix 3: Consent Form (Chapter 5)

College of Health, Medicine and Life Sciences
Department of Life Sciences

CONSENT FORM

Psychological Wellbeing in Larks and Owls

Principal Investigator: Mr Satyam Chauhan

Ethical approval has been obtained for this study by the College of Health, Medicine and Life Sciences Research Ethics Committee for this study to be carried out between 15.03.2023 to 30.09.2024.

The participant should complete the whole of this sheet		
	Please tick the appropriate box	
	YES	NO
Have you read the Research Participant Information Sheet included in this questionnaire?		
I am over the age of 18.		
Have you had an opportunity to ask questions and discuss this study?		
Have you received satisfactory answers to all your questions?		
Do you understand that you will not be referred to by name in any report concerning the study?		
Do you understand that no personal identifying data will be collected in this study, therefore once you have submitted your answers you are unable to withdraw the data from the study?		
Do you understand that your data will be anonymised, stored, and used in future research in line with Brunel University's data retention policies?		
Would you like to receive a lay summary of the findings of this study, and a copy of related publications?		
Do you agree to be contacted about participation in future research studies?		

Appendix 4: Debrief Form (Chapter 5)

College of Health, Medicine and Life Sciences
Department of Life Sciences

Psychological Wellbeing in Larks and Owls

Ethical approval has been obtained for this study by the College of Health, Medicine and Life Sciences Research Ethics Committee for this study to run from 15.03.2023 to 30.09.2024.

Debrief form

We would like to take this opportunity to say **Thank You** for participating in this study. Your contribution is much appreciated. The completed research will help us to investigate how chronotype (i.e., preference for being awake or asleep at certain times) may impact mental health in healthy adults.

Please be assured, all data collected will be treated in the strictest confidence. You are free to discuss this research by contacting one of the research team members: Mr Satyam Chauhan (Email: satyam.chauhan2@brunel.ac.uk), Dr Ray Norbury (Email: ray.norbury@brunel.ac.uk) or Professor Veena Kumari (Email: veena.kumari@brunel.ac.uk). Please let one of the research team members know if you would like to be kept up to date with the progress of the study and if you would like to know the overall results. We have tried to ensure that this study does not cause any distress. However, if you were unduly or unexpectedly affected by taking part in the study, please feel free to feed it back to the research team. If you feel unable, for whatever reason what-so-ever to talk with the researchers, then please contact the Division of Psychology Research ethics coordinators led by Dr Justin O'Brien (justin.obrien@brunel.ac.uk).

Once again, thank you for your participation in this study.

The following support services may be of interest to you.

Kiran (Indian government initiate)
Helpline: 1800-599-0019
24/7 available
Languages: English & Hindi

Samaritans Mumbai
Website: http://samaritansmumbai.org/
Helpline: +91 84229 84528 /84229 84529/84229 84530

Mann Talks
Helpline: +918686139139
Email: counselling@manntalks.org
Timings: Monday till Sunday between 09:00AM - 6:00 PM

Appendix 5: Ethical Approval (Chapters 6-8)

College of Health, Medicine and Life Sciences Research Ethics Committee (DLS)
Brunel University London
Kingston Lane
Uxbridge
UB8 3PH
United Kingdom

www.brunel.ac.uk

10 June 2022

LETTER OF APPROVAL

APPROVAL HAS BEEN GRANTED FOR THIS STUDY TO BE CARRIED OUT BETWEEN 20/06/2022 AND 31/12/2024

Applicant (s): Mr Satyam Chauhan Dr Ray Norbury, Ms Kaja Faßbender, Professor Ulrich Ettinger

Project Title: How do chronotype and psychopathology-related traits influence cognitive function and affect processing in the general population? An experimental study

Reference: 36745-MHR-May/2022- 39617-2

Dear Mr Satyam Chauhan

The Research Ethics Committee has considered the above application recently submitted by you.

The Chair, acting under delegated authority has agreed that there is no objection on ethical grounds to the proposed study. Approval is given on the understanding that the conditions of approval set out below are followed:

- **D18 - Will you, as the researcher, have any relationship with potential participants?**
- **The agreed protocol must be followed. Any changes to the protocol will require prior approval from the Committee by way of an application for an amendment.**
- **Please ensure that you monitor and adhere to all up-to-date local and national Government health advice for the duration of your project.**

Please note that:

- Research Participant Information Sheets and (where relevant) flyers, posters, and consent forms should include a clear statement that research ethics approval has been obtained from the relevant Research Ethics Committee.
- The Research Participant Information Sheets should include a clear statement that queries should be directed, in the first instance, to the Supervisor (where relevant), or the researcher. Complaints, on the other hand, should be directed, in the first instance, to the Chair of the relevant Research Ethics Committee.
- Approval to proceed with the study is granted subject to receipt by the Committee of satisfactory responses to any conditions that may appear above, in addition to any subsequent changes to the protocol.
- The Research Ethics Committee reserves the right to sample and review documentation, including raw data, relevant to the study.
- If your project has been approved to run for a duration longer than 12 months, you will be required to submit an annual progress report to the Research Ethics Committee. You will be contacted about submission of this report before it becomes due.

Professor Louise Mansfield

Chair of the College of Health, Medicine and Life Sciences Research Ethics Committee (DLS)

Brunel University London

Appendix 6: Participant Information Sheet (Chapter 6-8)

College of Health, Medicine and Life Sciences
Department of Life Sciences

PARTICIPANT INFORMATION SHEET

How does chronotype influence cognitive function and emotion processing?

Invitation Paragraph
You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?
The purpose of this study is to investigate how chronotype (i.e., preference for being awake or asleep at certain times) may influence our cognitive functions (e.g., memory and attention) and affect processing (e.g., reaction time to happy or unhappy faces) in healthy adults.

Why have I been invited to participate?
We are inviting people from the general population and university students to participate in this study. You can participate if you are: (i) aged between 18-40 years and live in the UK, (ii) fluent in English, (iii) have normal hearing and normal or corrected vision, (iv) not be on any regular medical prescription (except for contraceptives and multivitamins), (v) not have a history of any diagnosed mental disorders or drug abuse (any past or current use of non-prescribed drugs), (vi) able to provide a written informed consent.

All participants who take part in the online study (Phase 1) will be asked to indicate whether they would like to be contacted for two further in-person study sessions (Phase 2). Of those who agree to be contacted, a similar number of people with late chronotype, early chronotype, or no preference for morningness or eveningness (three groups in total), will be invited (ensuring that the three groups, on average, match on age and sex) to take part in Phase 2 of the study.

Do I have to take part?
As participation is entirely voluntary, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw any time without giving a reason and can withdraw your data until 31/12/2023. Your withdrawal from the project will not adversely affect you.

What will happen to me if I take part?
The study first involves taking part in an online session, taking approx. 30 minutes. During this session, you will be asked about your personality, habits and experiences, sleep quality, general mental and physical health as well as basic demographic information.

A small proportion (up to 50%) of the sample (people who participated in the online session) will then be invited for two further sessions (each approx. 1 hours) that will be conducted at Brunel University London. The sessions will be scheduled in the morning (8 -10 am) and afternoon (4 - 6 pm), one week apart. In each of these two sessions:

- We will conduct an eye movement assessment. For this, you will need to sit in front of a computer screen, and we will record your eye movements while you engage in number of short tests, which may require you to look at, or away from, a small dot on the monitor. This assessment will take about 18 minutes in total and serves to measure your ability to attend and follow, or ignore, visual stimuli (dots on the monitor in this case).

- You will then undergo a brief assessment of basic cognitive function (attention and memory) and emotion processing (e.g., reaction time to happy or unhappy faces), taking about 30 minutes in total. The tasks are designed to be engaging and you will be requested to respond as fast and accurately as possible.
- Your startle reactions (eye blinks) to a number of auditory clicks will be assessed during a brief experiment, lasting for about 10 minutes. The clicks are played through earphones, which you will wear, and are no louder or unpleasant than a vacuum cleaner being switched on. The eye blink will be measured using EMG (electromyography) through two small electrodes placed on the muscle below the right eye and one behind your right ear.
- We will ask you some questions about your sleep quality, diet, drug/stimulant intake, and personal habits. This should take about 5 minutes. We will also ask you to fill a sleep journal daily, taking about 2-3 minutes of your time, per day for a period of 7 days between the two study sessions. We request that you fill the sleep journal around the same time every day.
- Lastly, we will also measure your body temperature on two different occasions using a forehead infrared thermometer. First, before, during (at 15 min interval) and after morning study session and second, before, during (at 15 min interval) and after afternoon study session. We want to examine whether and how body temperature may influence your chronotype and cognitive performance.

Brunel psychology students will have an option to either obtain course credits (3 course credits for completing the online assessment, and 4 course credits for each research session on campus) or Amazon vouchers (£5 Amazon voucher for completing the online assessment, and £10 Amazon voucher for each of the two research sessions on campus). Everyone else will receive Amazon vouchers for their participation.

COVID secure measures (for those invited to participate in research sessions on campus):

- You may be asked to wear a mask. Researchers will also wear a mask when interacting with you.
- We will ensure that the room is well ventilated during study sessions and maintain social distancing of 1 meter (or more).
- The researchers and participants will be asked to wash or sanitise their hands regularly during the experiments and when traveling to and from campus.
- All members of the research team are fully vaccinated and have also received or booked their booster vaccine doses. When combined with other safety measures, vaccination reduces the likelihood of transmission of Covid-19 and reduces the risk of serious illness.

Furthermore, any other health and safety regulations implemented at the time by Brunel University London to minimise the risk of you or others catching COVID-19 infection will be strictly followed.

What are the possible disadvantages and risks of taking part?

There are no disadvantages or risks in the taking part of this study that exceed those present in everyday life. There are no known adverse reactions to:

- EMG, though the use of non-toxic gel to attach the tiny electrodes under your eye might be somewhat unpleasant. Any such sensation will be short lived, lasting no more than a few minutes.

You may find some of the questions personal. You are free to not answer those questions. The study does not seek to uncover any mental disorders. You will be required to travel to the university campus

for the two occasions. If you need to use public transport to attend these sessions, we advise you to follow the current government mandated Covid-19 advice. Furthermore, as mentioned earlier, we will take all possible care to minimise the chances of catching COVID-19 infection for you and others involved in this research.

What if something goes wrong?
If something goes wrong during this study, complaints will be assessed by Professor Louise Mansfield (Chair of College of Health, Medicine and Life Sciences Research Ethics Committee; Email: Louise.mansfield@brunel.ac.uk).

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential and stored on a secure password protected Brunel University server for a period of 10 years after the completion of the study. Any information about you which leaves the University will be fully anonymised (i.e., it will have your personal details removed so that you cannot be identified from it).

What will happen to the results of the research study?
The research data will be coded for anonymity by 31.08.2022 and analysed by the researcher(s) before being reported. The results will be disseminated, for instance at public talks, conferences, in scientific journals, and/or social media. The anonymised research data may be analysed and reported for purposes not related to this study. The anonymised research data may also be shared with other researchers, and/or made available as "open data". This means the data will be publicly available and may be used for purposes not related to this study. However, it will not be possible to identify you from these data, which means that at no point will any uniquely identifiable data be shared. The data will be stored by the lead researcher for a period of at least ten years from completion of the project (subject to any legal, ethical or other requirements of the funding body). You may withdraw your data, without giving a reason, until the point at which your data are anonymised, the results of the study are published in any form, and/or until the point at which your data are made publicly available in an anonymised form. After the study completion, should you wish it, we will send you a summary describing the findings of the current study and alerting you to any research publication we have generated from the project.

Will I be recorded, and how will the recording be used?
No, there will be no personal audio or video recording of you at any time for this research study.

Who is organising and funding the research?
This research is organised by Satyam Chauhan, Division of Psychology, Department of Life Science, Brunel University London (Email: satyam.chauhan2@brunel.ac.uk) under the supervision of Professor Veena Kumari and Dr Ray Norbury. This research has funded by the Brunel University London.

What are the indemnity arrangements?
Brunel University London provides appropriate insurance cover for research which has received ethical approval.

Who has reviewed the study?
This study has been reviewed by the College of Health, Medicine and Life Sciences Research Ethics Committee, Brunel University London (Reference: 36745-MHR-May/2022- 39341-1).

Brunel University's commitment to the UK Concordat on Research Integrity
Brunel University is committed to compliance with the Universities UK Research Integrity Concordat. You are entitled to expect the highest level of integrity from our researchers during the course of their research.

Contact for further information and complaints

For general information

- Mr Satyam Chauhan, Division of Psychology, Department of Life Sciences, Brunel University London. (Email: satyam.chauhan2@brunel.ac.uk).
- Dr Ray Norbury, Division of Psychology, Department of Life Sciences, Brunel University London. (Email: ray.norbury@brunel.ac.uk).
- Professor Veena Kumari, Division of Psychology, Department of Life Sciences, Brunel University London. (Email: veena.kumari@brunel.ac.uk).

For complaints and questions about the conduct of the research

Professor Louise Mansfield (Chair of College of Health, Medicine and Life Sciences Research Ethics Committee; Email: Louise.mansfield@brunel.ac.uk).

Thank you for taking the time to read this information sheet and considering taking part in the research study.

Appendix 7: Consent Form (Chapter 6-8)

College of Health, Medicine and Life Sciences
Department of Life Sciences

CONSENT FORM

How does chronotype influence cognitive function and emotion processing?

Ethical approval has been obtained for this study by the College of Health, Medicine, and Life Sciences Research Ethics Committee for this study to run from 10.08.2022 to 31.12.2024.

The participant should complete the whole of this sheet		
	Please tick the appropriate box	
	YES	NO
Have you read the Research Participant Information Sheet?		
I am over the age of 18.		
Have you had an opportunity to ask questions and discuss this study?		
Have you received satisfactory answers to all your questions?		
Who have you spoken to?		
Do you understand that you will not be referred to by name in any report concerning the study?		
Do you understand that you are free to withdraw from the study		
a) without having to give a reason for withdrawing?		
b) your anonymised data from this study may be shared with other researchers for further analyses not necessarily related to this study, and/or made publicly available as “open data”.		
c) you can request for your data to be removed any time until 31.12.2023.		
Do you agree to take part in this study?		
Would you like to receive a lay summary of the findings of this study, and a copy of related publications?		
Do you agree to be contacted about participation in future research studies?		
Signature of Research Participant:		
Date:		
Name in capitals:		
Researcher name:	Signature:	

Appendix 8: Debrief Form (Chapter 6-8)

College of Health, Medicine and Life Sciences
Department of Life Sciences

How does chronotype influence cognitive function and emotion processing?'

Debrief form

We would like to take this opportunity to say **Thank You** for participating in this study. Your contribution is much appreciated. The completed research will help us to investigate how chronotype (i.e., preference for being awake or asleep at certain times) may influence our cognitive functions (e.g., memory and attention) and affect processing (e.g., reaction time to happy or unhappy faces) in healthy adults.

Please be assured, all data collected will be treated in the strictest confidence. You are free to discuss this research by contacting one of the research team members: Mr Satyam Chauhan (Email: satyam.chauhan2@brunel.ac.uk), Dr Ray Norbury (Email: ray.norbury@brunel.ac.uk) or Professor Veena Kumari (Email: veena.kumari@brunel.ac.uk). Please let one of the research team members know if you would like to be kept up to date with the progress of the study and if you would like to know the overall results.

We have tried to ensure that this study does not cause any distress. However, if you were unduly or unexpectedly affected by taking part in the study, please feel free to feed it back to the research team. If you feel unable, for whatever reason what-so-ever to talk with the researchers, then please contact the Division of Psychology Research ethics coordinators led by Dr Justin O'Brien (justin.obrien@brunel.ac.uk).

Once again, thank you for your participation in this study.

Appendix 9: Published Papers

Appendix 9.1	Chauhan, S., Norbury, R., Faßbender, K. C., Ettinger, U., & Kumari, V. (2023). Beyond sleep: A multidimensional model of chronotype. *Neuroscience & Biobehavioural Reviews*, *148*, 105114.
Appendix 9.2	Chauhan, S., Pandey, R., Vakani, K., Norbury, R., Ettinger, U., & Kumari, V. (2024). Sleep quality mediates the association between chronotype and mental health in young Indian adults. *NPJ Mental Health Research*, *3*(1), 31.
Appendix 9.3	Chauhan, S., Faßbender, K., Pandey, R., Norbury, R., Ettinger, U., & Kumari, V. (2024). Sleep matters in chronotype and mental health association: Evidence from the UK and Germany. *Brain Sciences*, *14*(10), 1020.
Appendix 9.4	Chauhan, S., Barbanta, A., Ettinger, U., & Kumari, V. (2023). Pineal abnormalities in psychosis and mood disorders: A systematic review. *Brain Sciences*, *13*(5), 827.

Appendix 9.1

Neuroscience and Biobehavioral Reviews 148 (2023) 105114

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review article

Beyond sleep: A multidimensional model of chronotype

Satyam Chauhan [a,b,*], Ray Norbury [a,b], Kaja Christina Faßbender [c], Ulrich Ettinger [c,1], Veena Kumari [a,b,*,1]

[a] Department of Psychology, College of Health, Medicine and Life Sciences, Brunel University London, London, United Kingdom
[b] Centre for Cognitive and Clinical Neuroscience, College of Health, Medicine and Life Sciences, Brunel University London, London, United Kingdom
[c] Department of Psychology, University of Bonn, Germany

ARTICLE INFO

Keywords:
Chronotype
Circadian preference
Multidimensional model
Genetics
Environment
Social factors

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.

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 and 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 and 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.

* Corresponding authors at: Department of Psychology, College of Health, Medicine and Life Sciences, Brunel University London, London, United Kingdom.
E-mail addresses: satyam.chauhan2@brunel.ac.uk (S. Chauhan), veena.kumari@brunel.ac.uk (V. Kumari).
[1] Joint senior authorship

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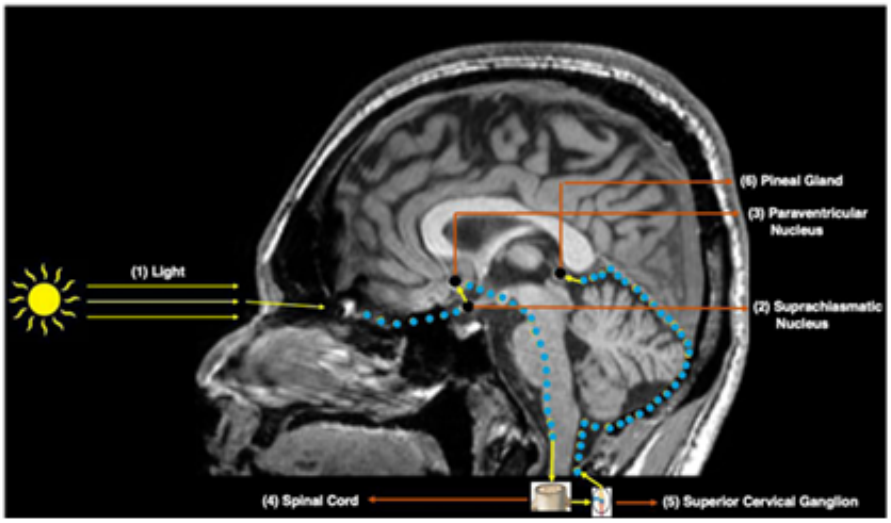


Fig. 1. The schematic representation of circadian circuits in humans according to the model proposed by Koller et al. (2020). Light signals (artificial or natural) are transduced by ipRGCs in the eye and transmitted to the following structures in order: the SCN (suprachiasmatic nucleus), the PVN (paraventricular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

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 h (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 h (e.g., biochemical, physiological, behavioural rhythms) (Fuller and Fuller, 2002). The word 'circadian' has been derived from two Latin words, 'circa' meaning 'about' and 'diem' meaning 'day or 24 h 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 and Wever, 1976; Wever, 1986). The main internal biological clock is found in the suprachiasmatic nucleus (SCN) of the hypothalamus (Moore and 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 1.1.1 *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; Nováková et al., 2013). In humans, the endogenous CRs oscillate with some periodic variation in length (Czeisler and 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 and Swaab, 1993). 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 and Robertis, 2005). 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 and Pintor, 2007), helping individuals to fall asleep (Fig. 1).

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 h. 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 and Benca, 2015; Logan & McClung, 2018; Walker et al., 2021). 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., 2020; 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-Rugerio 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 and Ostberg, 1976; Kerkhof, 1985; Benedito-Silva et al., 1998; Adan and 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 1.3.1 *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.

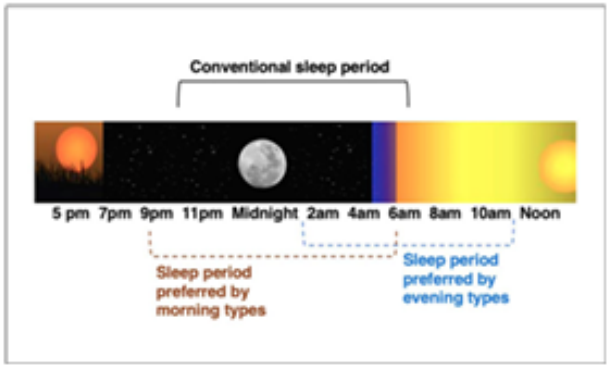


Fig. 2. The schematic representation of sleep periods preferred by morning and evening types. These periods and timings are commonly found, on average, in most populations across the world.

1.3.1. Commonly Used Self-Report Scales

1.3.1.1. Morningness-Eveningness Questionnaire (MEQ). The MEQ (Horne and 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 Fig. 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 and 58 indicating neither morning nor evening preference (intermediate type).

In the first validation study of the MEQ (Horne and 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 min earlier than evening types, 36.6% 'intermediate types', and 2.2% 'evening types' who went to bed 99 min 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 and 0.86) across different countries (Larsen, 1985; Adan and Natale, 2002; Caci et al., 2009; Lee et al., 2011) with strong split-half reliability (0.80; Adan and Natale, 2002) and test-retest reliability (coefficient range, 0.80–0.95; Larsen, 1985; Griefahn 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 and 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: 0.08–0.46; 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 and 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 ($\leq$ 22), higher scores indicating morning type ($\geq$ 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; Kühnle, 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.

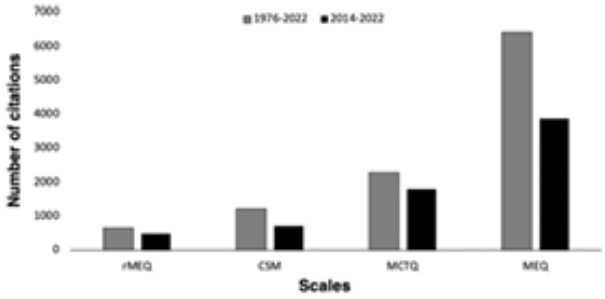


Fig. 3. Graphical representation of commonly used self-report scales cited from 1976 to 2022 (highlighted in grey) and 2014–2022 (highlighted in black) based on Google scholar search conducted on 8th November 2022. Abbreviations: rMEQ, Reduced Morningness-Eveningness Questionnaire (1991); CSM, Composite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

1.3.2. Methodological limitations

Many of the self-report measures of chronotype are well researched and widely used questionnaires (see Fig. 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.

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.

1.3.2.1.1. 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 and Natale, 2002) and have suggested two, three, and four-factor solutions (Adan and 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.

1.3.2.1.2. 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).

1.3.2.1.3. 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.

1.3.2.1.4. 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 and

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 and Czeisler, 2002; Taillard et al., 2004), 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., 2012). 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., 2016).

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

2.1. Melatonin secretion

Melatonin onset is the most reliable marker of the endogenous circadian clock (Benloucif et al., 2008). On average, melatonin levels in humans increase 2–3 h before sleep onset (Burgess and 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 h 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, 2006, 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 h) 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 (Díaz-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. 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 min 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; Wüst 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 min 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 and Robens, 2008; Oginska et al., 2010; Dockray and Steptoe, 2011). The reasons for this may include other factors that also influence cortisol levels, for example, sleep loss (Oginska et al., 2010), a prolonged exposure to environmental stressors (Lenaert et al., 2016), or presence or psychological and physical conditions associated with cortisol abnormities (Geiss et al., 1997) in their samples.

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 and a complex feedback mechanism (Hammel and 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 and 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 and 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 (Nováková 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), 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., 2018; 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 (Roenneberg 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, 2002; 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). 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 and 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 = 8972) also reported the absence of chronotype differences between the two sexes beyond the age of 55. Furthermore, Randler, N=7, 480) (2011) 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 and 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 and 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 (Eysenck, 1967), some studies using the *Eysenck Personality Inventory'* (Eysenck and Eysenck, 1965) suggested that evening types score higher on *extraversion* than morning types (Horne and Östberg, 1977; Adams et al., 1986; Neubauer, 1992; Mitchell and Redman, 1993; Tankova et al., 1994; Langford and Glendon, 2002). However, other studies did not find this (Mura and Levy, 1986; Mecacci and Rocchetti, 1998), or reported this relationship only in females (Matthews, 1988). 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 and Rocchetti, 1998; Tankova et al., 1994), while several others did not (Mitchell and Redman, 1993; Tankova et al., 1994; Langford and 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 and Redman, 1993; Tankova et al., 1994) as measured by the Psychoticism scale of the Eysenck Personality Questionnaire (Eysenck and Eysenck, 1975).

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 corelate 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 (di Milia 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 and 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 and 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 and 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; Kennaway, 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 and 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 & di Milia., 2011). Natale & di Milia (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 & di Milia, 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 is 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).

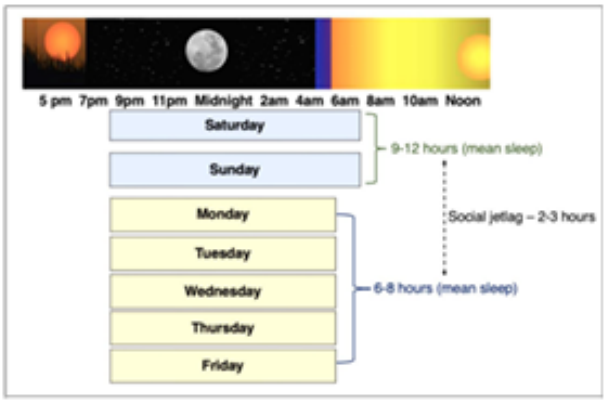


Fig. 4. Light blue bar represents 'sleep timing on free-days', light yellow bar represents 'sleep timing on workdays', and the dotted black vertical line shows social jetlag of 2–3 h.
Example of social jetlag (adapted from Taillard et al., 2021).

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.

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.

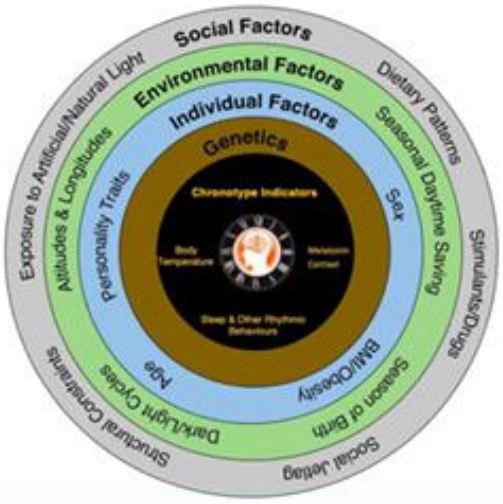
3.4.2. Exposure to artificial/natural light

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 and Smyth, 2017), 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 (Benloucif et al., 2008; Cajochen et al., 2011), and body temperature (Kräuchi 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 sedimentary 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., 2013), preference for food and beverages having higher concentrated sugar (Wilson et al., 2016; Wright and 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 (Muñoz 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.

a



b

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

c

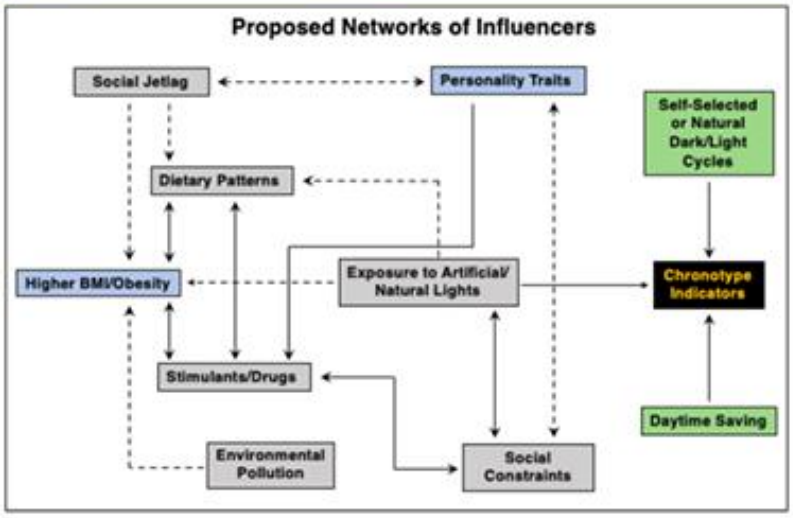


Fig. 5. The schematic representation of (5a) the proposed multidimensional model of chronotype integrating various social, environmental and individual factors (5a; the clock in the centre represents an individual's circadian preference or chronotype, and each circle represents a factor), (5b) the known 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).

3.4.4. Stimulants

The relationship between chronotypes and consumption of stimulants and other substances (e.g., caffeine, nicotine, alcohol) is well established (Singleton and 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 and 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., 2009). 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 and Malinowska-Borowska, 2021) reported that morning type individuals consume stimulants less frequently than evening type individuals, especially those above 30 years. (Fig. 4).

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 Fig. 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 (Fig. 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 (Fig. 5b), and outline various potential feedback loops between these factors (Fig. 5c). We acknowledge that directionality in some of the loops we have proposed (Fig. 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 Fig. 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.

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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Appendix 9.2

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Article

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Sleep quality mediates the association between chronotype and mental health in young Indian adults

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There is increasing recognition of 'higher preference for eveningness' as a potential independent risk factor for poor mental health. To examine the chronotype-mental health relationship while also quantifying the potential roles of poor sleep quality, relevant personality traits, and childhood trauma, we assessed 282 young adults (18–40 years; 195 females) residing in North India, between January and March 2023 (to control for seasonal variation), using self-report measures of diurnal preference, sleep patterns, mental health (depression, anxiety, and stress), personality traits (extraversion, neuroticism, schizotypy, and impulsivity), and childhood trauma. The results showed a significant association between eveningness and poor mental health but this association was fully mediated by poor sleep quality. Neuroticism, emotional abuse and cognitive disorganisation were correlated with eveningness as well as with poor mental health and sleep quality. Neuroticism and emotional abuse, but not cognitive disorganisation, also had indirect effects on mental health via sleep quality. Our findings highlight the crucial role played by sleep quality in the chronotype-mental health relationship.

Chronotype is a multidimensional construct which reflects behavioural consequences and manifestations of various circadian mechanisms[1]. It is known to exist on a continuum between two extremes, i.e., early morning and late evening chronotype. Most individuals, however, fall in the middle of this continuum and are intermediate type. There is considerable evidence that the late chronotype (i.e., eveningness) is associated with adverse mental health outcomes, such as depression[2–5], anxiety[6,7], psychosis[8,9], impulsive and maladaptive behaviour[10,11], and substance abuse[12]. Furthermore, personality traits that are known to be associated with a higher risk of developing these mental disorders or problematic behaviours, namely, neuroticism (linked to depression and anxiety disorders[13]), schizotypy (psychosis[14]) and impulsivity (substance abuse[15]) also show a positive association with eveningness in non-clinical samples in some studies[1,16]. By contrast, extraversion which is associated with a lower risk for mental disorders[1,16,17] may have a small association with the early chronotype (i.e., morningness)[18].

There are reports that individuals with a higher preference for eveningness have poor quality or altered sleep patterns[19,20], including spending less time in bed during weekdays, shorter sleep duration, daytime sleepiness and dysfunction, irregular sleep-wake cycles, and a need for more sleep on weekends[19,21–23]. Such self-reported sleep alterations are also common in various mental illnesses, for example major depression or anxiety disorders[24–27]. Furthermore, poor sleep quality has been consistently found in people with a history of childhood abuse/trauma[28–30], and childhood maltreatment is an established risk factor for many disorders, including depression, anxiety, psychosis, personality disorder, post-traumatic stress disorder, and substance abuse[31–35]. Whether and to what extent a history of childhood trauma might influence any relationship between chronotype and mental health, however, remains unclear.

Against the backdrop of previous findings supporting a direct association between eveningness and poor mental health[2,6,7], a study conducted in the UK[24] reported a positive association between eveningness and depressive symptomatology and this association was partly mediated by subjective sleep quality. A more recent UK study by Muzni and colleagues[18] involving a large non-clinical adult sample suggested a much stronger relationship between poor sleep quality and adverse mental health (with medium-to-large effect sizes), relative to that observed between eveningness and poor mental health (negligible-to-small effect sizes), especially in females. These findings raise doubts about the widely publicised association of eveningness with poor health outcomes, at least in the general population.

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There are, however, no data examining the chronotype-mental health relationship while also quantifying the influence of sleep quality, chronotype-relevant personality traits, and childhood trauma within the same homogenous sample of non-clinical adults.

The main aim of the present study, therefore, was to determine the association between chronotype and mental health (depression, anxiety, and stress) in young (18–40 years) males and females, with a particular focus on the roles of sleep quality, relevant personality traits (neuroticism, schizotypy, impulsiveness, and extraversion), and childhood trauma. We tentatively hypothesised, based on the findings of Muzni and colleagues[18], that both eveningness and poor sleep quality would be associated with higher levels of depression, anxiety, and stress, with these associations being stronger for sleep quality than for eveningness. Lastly, we explored possible associations between chronotype, sleep quality, personality traits, childhood trauma and mental health, and examined the influence of personality traits and childhood trauma, while also considering sleep quality, in the chronotype-mental health relationship.

Results

Sample characterisation

The majority of the sample comprised of Asian Indians (92.2%), pursuing a bachelor's degree or above (95.7%). Just over half (54.3%) of the sample self-reported consuming caffeine, and only 0.7% self-reported consuming alcohol (Table 1). About half of the sample (47.51) reported normal BMI, and a significant proportion (46.45%) reported being underweight (as also seen in other young North Indian cohorts[35]. Just over half of sample (55.3%) met the PSQI criteria for good sleep (score ≤ 5)

Females were younger than males ($t_{280} = 4.04$, $p < 0.001$), had significantly lower BMI ($t_{275} = 4.24$, $p < 0.001$), had a higher morning preference ($t_{280} = 4.53$, $p < 0.001$), and rated themselves as having poorer sleep quality ($t_{280} = 4.09$, $p < 0.001$). They also scored higher than males on Neuroticism ($t_{280} = 5.62$, $p < 0.001$), Depression ($t_{280} = 2.14$, $p = 0.033$), Anxiety ($t_{280} = 2.07$, $p = 0.039$), Stress ($t_{280} = 3.48$, $p < 0.001$), Cognitive Disorganisation ($t_{280} = 3.11$, $p = 0.002$), Lack of Perseverance ($t_{280} = 3.06$, $p = 0.002$), Lack of Premeditation ($t_{280} = 2.85$, $p = 0.005$), and Emotional Abuse ($t_{280} = 2.56$, $p = 0.011$) (Table 2). Males had higher scores than females for Sensation Seeking ($t_{280} = 7.30$, $p = 0.001$), Positive Urgency ($t_{280} = 3.84$, $p = 0.001$), and Physical Neglect ($t_{280} = 3.49$, $p = 0.001$) (Table 2).

Chronotype, sleep quality, mental health, personality traits and childhood trauma

Higher preference for eveningness (i.e., lower MEQ scores) correlated with higher scores on Depression ($r = -0.308$, $p = 0.001$), Anxiety ($r = -0.213$, $p = 0.001$), Stress ($r = -0.267$, $p = 0.001$) scales; higher scores on personality measures of Neuroticism ($r = -0.299$, $p = 0.001$), Cognitive Disorganisation ($r = -0.287$, $p = 0.001$), Lack of Perseverance ($r = -0.181$, $p = 0.002$), Lack of Premeditation ($r = -0.180$, $p = 0.002$), and Sensation Seeking ($r = -0.215$, $p = 0.001$); as well as Emotional Abuse ($r = -0.196$, $p = 0.001$) and Emotional Neglect ($r = -0.153$, $p = 0.001$) (Table 3). Higher preference for morningness was associated with higher Extraversion scores ($r = 0.222$, $p = 0.001$) (Table 3). Of these correlations, the correlation between eveningness and Lack of Premeditation appeared stronger in males than females (Fisher's Exact z = 2.01, $p = 0.044$) though this sex difference failed to maintain statistical significance after Bonferroni correction for multiple comparisons ($p > 0.0025$). BMI did not correlate significantly with chronotype, any personality traits, sleep quality, and mental health.

Poor sleep quality (i.e., higher PSQI scores) correlated with higher levels of Depression ($r = 0.489$, $p < 0.001$), Anxiety ($r = 0.474$, $p < 0.001$), Stress ($r = 0.518$, $p < 0.001$); higher scores on personality measures of Neuroticism (= 0.433, $p < 0.001$), Unusual Experiences ($r = 0.168$, $p = 0.001$), Cognitive Disorganisation ($r = 0.294$, $p = 0.001$), Introvertive Anhedonia ($r = 0.150$, $p = 0.012$), Impulsive Nonconformity ($r = 0.198$, $p = 0.001$), and Negative Urgency ($r = 0.141$, $p = 0.017$); and severity of self-reported Emotional Abuse ($r = 0.377$, $p = 0.001$), Emotional Neglect ($r = 0.275$, $p = 0.001$), and Physical Abuse ($r = 0.164$, $p = 0.006$). Poor sleep also correlated with lower scores on Extraversion ($r = -0.125$, $p < 0.001$). Poor sleep quality correlated with eveningness ($r = -0.389$, $p < 0.001$); although this correlation appeared stronger in females than males (Fisher's Exact $z = 2.17$, $p = 0.029$), this sex difference did not survive correction for multiple comparisons ($p > 0.0025$). Lastly, compared to eveningness, poor sleep quality showed significantly stronger correlations, as expected, with Depression (Fisher's Exact $z = 2.55$, $p = 0.01$), Anxiety (Fisher's Exact $z = 3.53$, $p < 0.001$), and Stress (Fisher's Exact z = 3.54, $p < 0.001$).

The mediating role of sleep quality in chronotype mental health relationship

Our initial model (see Statistical analysis) was found to be a very good fit [($\chi 2/df = 2.11$, $p < 0.001$), RMSEA (.06), GFI (.97), AGFI (.90), and CFI (.98)] to the data, though some direct effects (paths) were non-significant (see Fig. 1). The model was, therefore, revised because of poor local fit (i.e., presence of nonsignificant path coefficients) by removing the non-significant paths leaving us with the final model [model fit indices: $\chi 2/df = 1.18$; GFI = 0.98; TLI = 0.99; CFI = 0.99; RMSEA = 0.02)] (Fig. 2). As shown in Fig. 2, we did not find any direct effect of eveningness (MEQ scores) on mental health ($\beta = -0.001$, $p = 0.961$), and found its relationship with (poor) mental health to be fully mediated by poor sleep quality ($\beta = -0.10$, $p < 0.001$). Poor sleep quality also partially mediated the relationship between childhood emotional abuse and poor mental health ($\beta = 0.96$, $p < 0.001$), and between higher neuroticism and poor mental health ($\beta = 0.11$, $p < 0.001$), but not between Cognitive Disorganisation and poor mental health ($\beta = -0.04$, $p = 0.427$). While exploring sex differences, we observed that the comparison of model fit of unconstrained and fully constrained model revealed a non-significant chi-square difference $\Delta\chi^2(20) = 25.87$, $p = 0.156$ and a non-significant difference in CFI (ΔCFI = 0.005), suggesting the model to be invariant in males and females. However, the difference in RMSEA was found to be higher than the prescribed cut-off of .01 (ΔRSMEA = 0.02) suggesting non-invariance. Therefore, we tested pairwise difference in the path coefficients of unconstrained model in males and females and found a significant difference (stronger in females) in the direct path linking Cognitive Disorganization to mental health (Critical ratio=2.138, $p < 0.05$).

Discussion

This is the first study, to our knowledge, to investigate chronotype-mental health associations while also examining the roles of sleep quality, clinically relevant personality traits and childhood trauma in this association. The main findings were: (i) a preference for eveningness had small-to-medium correlations (r values: 0.20–0.30) while poor sleep quality had medium-to-large correlations (r values: 0.47–0.52) with mental health outcomes (depression, anxiety, and stress), (ii) eveningness had significant but mostly small-sized (r values > 0.30) associations with various personality traits and self-reported history of childhood emotional abuse and neglect, and (iii) there was no significant direct effect of eveningness on mental health outcomes, with sleep quality fully mediating the chronotype-mental health relationship. Although, on average, females displayed more morningness than males, sex did not significantly influence any chronotype-mental health associations.

The findings in relation to our first hypothesis demonstrated only small-to-medium (at best) positive associations between a preference for eveningness and poor mental health outcomes (depression, anxiety, stress) in a North Indian, young and healthy volunteer sample, as also found in previous studies of general population samples in Western countries (UK[18], $f2 = 0.024$; Canada[5], $\eta p2 = 0.02–0.04$). Our finding of relatively stronger (medium-to-large) positive associations between poor sleep quality and poor mental health outcomes, compared to those seen between eveningness and mental health outcomes, confirm our hypothesis, and offers further support to earlier findings in a non-clinical sample in the UK[18]. Furthermore, this study supports previous findings[3] in showing significant but mostly small associations between eveningness and higher scores on

Table 1 | Demographic characteristics of the study sample

Demographic characteristics	*N* = 282	Frequency (%) of *N* = 282
Ethnicity	Asian Indian	92.2%
	European White	0.8%
	Other Ethnic Groups	4.1%
	Prefer not to say	2.8%
Stimulant/Sedative Consumption	Caffeine	54.3%
	Nicotine	4.3%
	Alcohol	0.7%
	None	40.8%
Body Mass Index (BMI)[a]	Underweight (<18.5)	46.45%
	Normal (18.5–24.9)	47.51%
	Overweight (25–29.9)	4.25%
	Obese (>30)	0%
Education/Employment	Student	95.7%
	Full-time Work	4.3%
	Part-time Work	0%
Medication	Yes	0%
	No	92.6%
	Prefer not to say	7.4%
Sleep Quality[b]	Good (≤5)	55.3%
	Poor (6–15)	44.7%

[a]BMI data missing for five participants.
[b]Individuals scoring 5 or below on the PSQI were categorised as good sleepers and those scoring above 5 and below 15 (highest score in our sample) as poor sleepers.

measures of neuroticism[18,36] and impulsivity[11,37,38]. Extraversion has also been found to have a small positive association with eveningness[36], though not consistently[1,16]. Interestingly, our findings also revealed a significant positive association ($r = 0.299$) between eveningness and the cognitive disorganisation aspect of schizotypy with non-significant associations in the same direction for other aspects of schizotypy. In a previous study[39] that did not find any relationship between eveningness and schizotypy, a positive association between all schizotypy (O-LIFE) dimensions and altered biological rhythms in patients with bipolar disorder and healthy controls was observed, and it was present most strongly for Cognitive Disorganisation, although the mechanisms underlying such an association, remain unclear at present.

The findings in relation to our second hypothesis demonstrated no direct effect of eveningness on mental health outcomes, and instead showed that eveningness-poor mental health relationship was fully mediated by poor sleep quality. It is well known that numerous environmental and social factors associated with modern-day lifestyles hinder regular sleep patterns[40,41], and contribute to irregular secretion of melatonin which in turn has been linked to mental disorders, such as psychosis and major depression[42,43]. Not surprisingly, most individuals with an evening preference accumulate higher social jetlag, sleep pressure, and sleep deprivation[21,22,40]. Sleep disturbances affect the reactivity of neuroendocrine stress systems and responsivity, reducing the ability to cope with emotional dysfunction[44]. Chronic and acute sleep-related issues may fundamentally change the brain chemistry and neuroendocrine systems (e.g., altered hypothalamic pituitary adrenal axis[44]). Poor sleep may further sensitise people with high levels of neuroticism to experience negative affect and emotional (limbic) arousal[45]. Individuals with a history of emotional abuse are also reported to experience emotional dysfunction and distress, which in turn may contribute to poor sleep quality and altered circadian rhythms[46,47] and elevate risk for affective and stress-related disorders[29,32,48]. In this context, it is noteworthy that emotional abuse appeared relatively more important than other types of abuse for mental health, as also argued in the context of prevalence of mental disorders in children with a history of physical abuse[33,49]. Individuals with high levels of schizotypy also often experience low mood[50] and report social anxiety, distress as well as higher sensitivity to social rejections[51], all of which contribute to poor mental health. Therefore, prolonged and/or acute poor sleep quality, neuroticism, history of emotional abuse, and schizotypy may explain why eveningness has been associated with poor mental health, though with a marked variation in effect sizes[4,52] possibly due to its dependency on the quality of sleep.

The present study had a number of strengths. First, it used a homogenous sample of young English-speaking, healthy adults residing in North India, with <5% consuming nicotine and alcohol as self-reported. Second, all data were collected over a brief period to minimise any season-related influences. Third, chronotype was used as a continuous variable to preserve power. Our study also had a number of limitations. First, although we used validated self-report questionnaires with sensitivity ranging between 73 and 97.7%[53], there were no objective markers of chronotype. This, however, may not be a serious concern given significant correlations and overlaps between subjective and objective chronotype measures even in a clinical sample[54]. Second, we did not collect information on natural and/or artificial light exposure that causes phase delay in circadian rhythms[40,55,56]. Third, our sample was predominantly female, limiting our ability to investigate sex differences adequately. Additionally, we did not collect information on cyclic fluctuation of reproductive hormones which may act as a potential confounding variable. Fourth, we did not examine the influence of socio-economic status, family dynamics or cultural beliefs, which may also directly or indirectly influence an individuals' mental health. Fifth, our findings from a young North Indian sample may or may not generalise to non-Indian or older age-groups. Lastly, as this was a correlational study, the findings cannot conclusively speak to causation. Despite these limitations, our findings might still have important implications. Specifically, we speculate that personal and societal interventions aiming to promote good sleep, especially in high-risk groups (e.g., with high neuroticism or emotional abuse), may help to promote good mental health in the general population.

In conclusion, this study found no direct relationship between a preference for eveningness and poor mental health outcomes (depression, anxiety, and stress) in young adults. Instead, this relationship was mediated by poor sleep quality. Our findings argue against 'eveningness' as an independent risk factor for poor mental health, and indirectly suggest that promotion of good quality sleep may provide a more helpful strategy than those aiming to shift diurnal preferences towards morningness for improving mental health, especially in high-risk groups. Further studies in other cultures, settings, age groups, and using direct measures of circadian (mis)alignments and sleep quality along with self-report measures to collect data on more than one occasion within the same individuals, are needed to examine the stability and generalisability of these findings and realise their full potential for promoting mental health in the general population.

Methods

Participants and design

The data were collected from young adults ($N = 313$, age range 18–40 years) residing in different parts of Northern India between January and March 2023 with average daytime temperatures ranging between 14 and 23 °C. The age range was restricted to 18–40 years given previous evidence of age-related changes in chronotype[57].

Of 313, 31 participants had to be excluded for failing our attention check criteria (i.e., failed to enter a given response to one or more of the four catch items; $n = 20$) or due to non-completion of some measures ($n = 11$), leaving a final sample of 282 participants (195 females, 87 males) who completed all self-report measures online in a single session. The inclusion criteria required all participants to be aged between 18–40 years and living in India, be fluent in English, not be on any regular medication, not have a history of any diagnosed mental disorders or drug abuse (any past or current use of non-prescribed drugs), and be able to provide written informed consent. Their participation was voluntary, and no compensation was

Table 2 | Descriptive statistics for self-report measures (chronotype, mental health, sleep quality, personality traits and childhood trauma)

Study Variables			Males (n = 87)		Females (n = 195)		Entire Sample (N = 282)	
			Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range
Age			26.26 ± 4.80	18–40	23.98 ± 4.17	18–40	24.68 ± 4.49	18–40
Chronotype	MEQ		53.31 ± 9.05	31–77	47.98 ± 9.11	27–70	49.63 ± 9.40	27–77
		Depression	11.90 ± 10.24	0–42	14.98 ± 11.50	0–42	14.03 ± 11.20	0–42
Mental Health	DASS-21	Anxiety	11.60 + 9.33	0–42	14.28 ± 10.32	0–42	13.46 ± 10.08	0–42
		Stress	12.20 ± 8.59	0–42	16.25 ± 9.18	0–42	15.00 ± 9.18	0–42
		Sleep Quality	0.91 ± 0.66	0–3	1.22 ± 0.78	0–3	1.13 ± 0.76	0–3
		Sleep Latency	0.80 ± 0.69	0–2	1.02 ± 0.71	0–2	0.95 ± 0.71	0–2
		Sleep Duration	1.03 ± 0.78	0–3	1.03 ± 0.83	0–3	1.03 ± 0.81	0–3
Sleep Quality	PSQI	Sleep Efficiency	0.66 ± 1.01	0–3	0.80 ± 1.02	0–3	0.76 ± 1.02	0–3
		Sleep Disturbance	1.09 ± 0.49	0–3	1.29 ± 0.53	0–3	1.23 ± 0.53	0–3
		Sleep Medication	0.05 ± 0.23	0–1	0.22 ± 0.67	0–3	0.17 ± 0.58	0–3
		Daytime Dysfunction	0.75 ± 0.80	0–3	1.2 ± 0.85	0–3	1.06 ± 0.86	0–3
		Global Score	4.67 ± 2.31	0–13	6.02 ± 2.63	1–15	5.60 ± 2.61	0–15
	EPQ-S	Extraversion	7.28 ± 3.02	0–12	6.56 ± 3.52	0–12	6.79 ± 3.39	0–12
		Neuroticism	5.47 ± 3.23	0–12	7.80 ± 3.20	0–12	7.08 ± 3.38	0–12
		Unusual Experience	5.34 ± 3.172	0–12	5.43 ± 2.89	0–12	5.40 ± 2.97	0–12
		Cognitive Disorganisation	4.95 ± 3.16	0–11	6.23 ± 3.20	0–11	5.84 ± 3.24	0–11
		Introvertive Anhedonia	3.48 ± 1.80	0–8	3.66 ± 1.93	0–9	3.60 ± 1.89	0–9
Personality Traits	sO-LIFE	Impulsive Nonconformity	3.56 ± 2.03	0–9	3.54 ± 2.12	0–9	3.54 ± 2.09	0–9
		sO–LIFE Total	17.34 ± 8.05	1–36	18.87 ± 7.71	3–36	18.40 ± 7.84	1–36
		Negative Urgency	10.49 ± 2.98	4–16	9.98 ± 2.97	4–16	10.14 ± 2.98	4–16
		Lack of Perseverance	6.72 ± 1.87	4–11	7.52 ± 2.10	4–14	7.28 ± 2.06	4–14
	S-UPPS-P	Lack of Premeditation	6.27 ± 1.95	4–11	7.08 ± 2.28	4–14	6.83 ± 2.21	4–14
		Sensation Seeking	12.74 ± 2.16	7–16	10.43 ± 2.70	4–16	11.14 ± 2.76	4–16
		Positive Urgency	10.26 ± 3.21	4–16	8.75 ± 2.95	4–16	9.22 ± 3.10	4–16
		Emotional Abuse	9.56 ± 4.26	5–25	11.15 ± 5.031	5–25	10.66 ± 4.85	5–25
		Physical Abuse	8.49 ± 4.24	5–25	8.14 ± 4.58	5–25	8.25 ± 4.47	5–25
Childhood Trauma	CTQ-SF	Sexual Abuse	8.13 ± 4.31	5–21	9.04 ± 5.20	5–25	8.76 ± 4.95	5–25
		Emotional Neglect	11.55 ± 4.26	5–21	11.98 ± 4.97	5–25	11.85 ± 4.76	5–25
		Physical Neglect	9.85 ± 3.27	5–17	8.35 ± 3.22	5–19	8.81 ± 3.30	5–19
		CTQ Total	47.59 ± 16.37	25–100	48.68 ± 17.49	25–110	48.35 ± 17.13	25–110

MEQ Morningness-Eveningness Questionnaire, *PSQI* Pittsburgh Sleep Quality Index, *EPQ-SF* Eysenck Personality Questionnaire-Revised, *DASS-21* Depression Anxiety and Stress Scale-21 Items, *sO-OLIFE* short Oxford-Liverpool Inventory of Feelings and Emotions, *S-UPPS-P* Impulsive Behaviour Scale-Short Version, *CTQ-SF* Short Form of Childhood Trauma Questionnaire.

provided. This study was approved by the Research Ethics Committee, College of Health, Medicine, and Life Sciences, Brunel University London (ref no. 41125-MHR-Mar/2023- 44225-4).

Self-report measures

The *Morningness-Eveningness Questionnaire* (MEQ)[58], which is a self-report questionnaire comprising of 19 items, was used to assess diurnal preference. The questionnaire has both a Likert scale (e.g., *item 19: are you a morning or evening type?*) and time scale (e.g., *item 18: at approximately what time of the day do you usually feel your best?*). Twelve items on the Likert scale present four options, with the lowest values indicating definite eveningness. The remaining seven items on the time scale are divided into periods of 15 min, spanning a time frame of seven hours. Higher scores indicate a preference for morningness and lower scores indicate a preference for eveningness. The scale has high internal consistency ($a = 0.83$[58]; $a = 0.76$ in the current sample).

Depression, anxiety, and stress levels were assessed using the 21-item *Depression, Anxiety and Stress Scale* (DASS-21)[59]. It has three sub-scales: Depression, Anxiety, and Stress. Each sub-scale consists of seven items. The participants respond to each item based on their feelings on most days over the past week. The Depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest, anhedonia, and inertia. The Anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The Stress scale assesses difficulty relaxing, nervous arousal, getting easily upset, agitated, irritable, over-reactive, and impatient. The sub-scales are reported to have high reliability coefficients [Depression ($a = 0.83–0.94$), Anxiety ($a = 0.66–0.87$), Stress ($a = 0.79–0.91$)][60]. The Cronbach's alphas for

Table 3 | Correlations (Pearson's *r*) between chronotype and measures of mental health, sleep quality, personality traits and childhood trauma

	Mental Health			Sleep Quality	Personality Traits										Childhood Trauma				
	DASS-21			PSQI	EPQ-SF		sO-LIFE				S-UPPS-P				CTQ-SF				
	D	A	S		E	N	UE	CD	IA	IN	NU	LP	LPr	SS	PU	EA	PA	SA	EN	PN
MEQ (Overall)	−0.308 (0.001)	−0.213 (0.001)	−0.267 (0.001)	−0.389 (0.001)	0.299 (0.001)	−0.222 (0.001)	−0.078 (0.194)	−0.287 (0.001)	−0.086 (0.152)	−0.084 (0.157)	−0.067 (0.265)	−0.181 (0.002)	−0.180 (0.002)	0.215 (0.001)	0.079 (0.186)	−0.196 (0.001)	0.034 (0.567)	0.073 (0.219)	−0.153 (0.001)	0.006 (0.923)
Males	−0.204 (0.057)	−0.057 (0.597)	−0.111 (0.307)	−0.163 (0.132)	0.274 (0.01)	−0.199 (0.065)	−0.103 (0.341)	−0.267 (0.012)	−0.103 (0.343)	−0.017 (0.879)	−0.028 (0.796)	−0.288 (0.007)	−0.326 (0.002)	0.198 (0.066)	0.025 (0.817)	−0.193 (0.073)	0.012 (0.912)	0.062 (0.566)	−0.093 (0.393)	−0.106 (0.326)
Females	−0.320 (0.001)	−0.241 (0.001)	−0.274 (0.001)	−0.421 (0.001)	0.179 (0.012)	−0.252 (0.001)	−0.064 (0.376)	−0.245 (0.001)	−0.066 (0.357)	−0.119 (0.097)	−0.118 (0.099)	−0.084 (0.245)	−0.075 (0.299)	0.103 (0.151)	0.02 (0.781)	−0.153 (0.033)	0.032 (0.662)	0.113 (0.114)	−0.168 (0.019)	−0.028 (0.702)

MEQ Morningness-Eveningness Questionnaire, *D* Depression, *A* Anxiety, *S* Stress, *DASS-21* Depression Anxiety and Stress Scale-21 items, *PSQI* Pittsburgh Sleep Quality Index, *E* Extraversion, *N* Neuroticism, *EPQ-SF* Eysenck Personality Questionnaire-Revised, *UE* Unusual Experience, *CD* Cognitive Disorganisation, *IA* Introvertive Anhedonia, *IN* Impulsive Nonconformity, *sO-LIFE* short Oxford-Liverpool Inventory of Feelings and Emotions, *NU* Negative Urgency, *LP* Lack of Perseverance, *LPr* Lack of Premeditation, *SS* Sensation Seeking, *PU* Positive Urgency, *S-UPPS-P* Impulsive Behaviour Scale-Short Version, *EA* Emotional Abuse, *PA* Physical Abuse, *SA* Sexual Abuse, *EN* Emotional Neglect, *PN* Physical Neglect, *CTQ-SF* short form of Childhood Trauma Questionnaire.

Depression ($a = 0.88$), Anxiety ($a = 0.84$), and Stress ($a = 0.81$) sub-scales also indicated good internal consistency in the current sample.

Sleep quality was assessed using the *Pittsburgh Sleep Quality Index* (PSQI)[61]. The PSQI is a 19-item scale assessing daytime dysfunction, use of sleeping medication, sleep disturbances, habitual sleep efficiency, sleep duration, sleep latency, and subjective sleep score. Participants answer the PSQI questions for each of these components by relating them to their past month. Each component is scored from "No difficulty" (0) to "Severe difficulty" (3) and tallied up to yield a total score (range 0–21). Higher scores indicate poor sleep quality. The PSQI (global score) is reported to have a high internal consistency ($a = 0.83$) and test-retest reliability ($r = 0.85$), with a sensitivity of 89.6% and a specificity of 86.5%[61]. Cronbach's alpha for the PSQI (global score) in the current sample was 0.67.

Extraversion, Neuroticism, and Psychoticism were measured using the short 48-item *Eysenck Personality Questionnaire-Revised* (EPQR-S)[62]. It has three sub-scales, corresponding to the three personality dimensions in the Eysenck's model of personality, plus a lie scale[62]. Each scale contains 12 items with a binary response, 'Yes' or 'No' (scored as 1 or 0). Extraversion ($a = 0.74$–0.84) and Neuroticism scales ($a = 0.70$–0.77) are known to have good reliability but the Psychoticism scale is reported to have less-than-satisfactory reliability ($a = 0.33$–0.52[63]; as was also the case in the current sample (Extraversion, $\alpha = 0.82$; Neuroticism, $\alpha = 0.82$; Psychoticism, $\alpha = 0.27$).

Schizotypal personality traits were assessed using the short version of the *Oxford-Liverpool Inventory of Feelings and Emotions* (sO-LIFE)[64,65]. It is a 43-item questionnaire with high reliability ($a = 0.78$–0.87) as well as good convergent and discriminant validity[66]. Each item belongs to one of the four sub-scales: (i) Unusual Experiences (12 items; describing perceptual aberrations, magical thinking, and hallucinations), (ii) Cognitive Disorganization (11 items; covering aspects of poor attention, concentration, decision-making, and social anxiety), (iii) Introvertive Anhedonia (10 items; describing a lack of enjoyment from social and physical sources of pleasure as well as avoidance of intimacy), and (iv) Impulsive Non-conformity (10 items; describing impulsive, anti-social, and eccentric forms of behaviour, often suggesting a lack of self-control). All items require a Yes/No response (scored 1 or 0). Higher scores indicate higher levels of schizotypy. Cronbach's alphas in the current sample for Unusual Experiences, Cognitive Disorganisation, Introvertive Anhedonia, and Impulsive Nonconformity were 0.75, 0.81, 0.44, and 0.54, respectively.

Impulsivity was assessed using the *Impulsive Behaviour Scale-Short Version* (S-UPPS-P)[67]. It is a 20-item self-report measure with adequate reliability ($a = 0.74$–0.88)[67]. Each item is rated on a four-point Likert scale [(1) disagree strongly, (2) disagree some, (3) agree some, and (4) agree strongly]. There are five (5-item) sub-scales: Lack of Perseverance (inability to stay focused on a task), Lack of Premeditation (inability to account to the repercussions of actions), Sensation Seeking (tendency to seek unique and exciting experiences), Negative Urgency (tendency to react rashly in an intense negative mood), and Positive Urgency (tendency to react rashly in an intense positive mood). Higher scores indicate higher levels of impulsivity. Cronbach's alphas in the current sample for Negative Urgency, Lack of Perseverance, Lack of Premeditation, Sensation Seeking, Positive Urgency were 0.73, 0.55, 0.73, 0.66, and 0.78, respectively.

Childhood trauma was assessed using the short form of the *Childhood Trauma Questionnaire* (CTQ-SF)[68]. It consists of 28 items on histories of abuse and neglect. It has five 5-item sub-scales, measuring emotional, physical, and sexual abuse, and emotional and physical neglect. All items are rated from 'never true' (score 1) to 'very often true' (score 5), and after reversing seven items, the scores on all sub-scales can range between 5 and 25. The final scores are classified as 'none to minimal', 'low to moderate', 'moderate to severe', and 'severe to extreme'. Three additional items compose the minimisation/denial sub-scale for detecting socially desirable responses or false-negative trauma reports. The total CTQ score reflects the severity of multiple forms of abuse and neglect. These sub-scales are reported to have high test-retest reliability ($\alpha = 0.79$–0.86) and internal consistency ($\alpha = 0.66$–0.92[68]), though in the current sample, Cronbach's

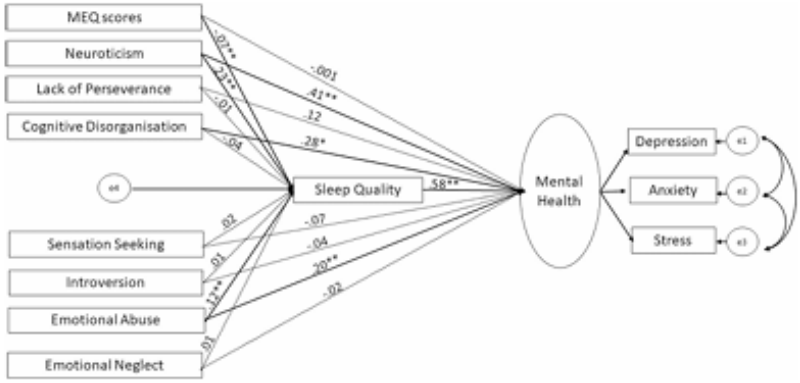

Fig. 1 | Results of the SEM analyses, with solid lines representing significant paths (**$p < 0.001$, *$p < 0.005$) and dotted lines representing non-significant paths.

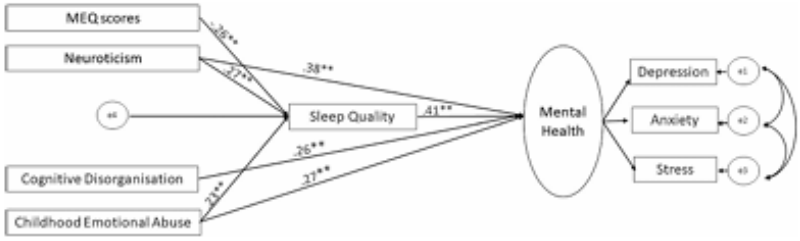

Fig. 2 | Results of the SEM analyses for the revised model showing all significant paths (** < 0.001).

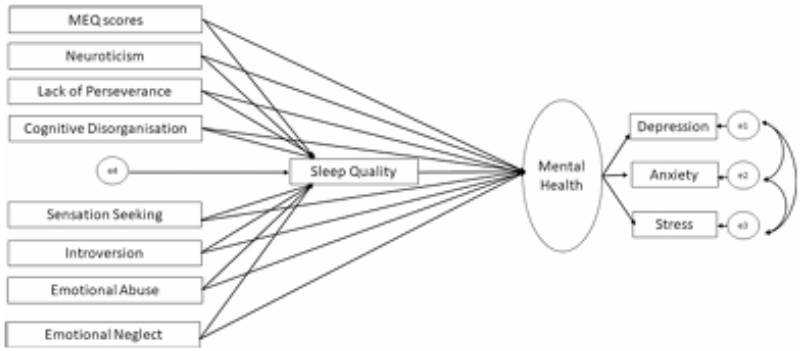

Fig. 3 | Schematic representation of proposed structural model showing the direct and indirect effects (via sleep quality) of chronotype (higher MEQ scores represent a greater preference for morningness and lower scores a greater preference for eveningness), personality traits, and childhood trauma (predictors) and mental health (outcome) relationship using SEM framework. All predictors were allowed to covary. The latent variable is indicated in an oval shape, observable variables in a rectangle shape, and e1, e2, e3, and e4 are residuals.

alphas for Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, and Physical Neglect were 0.81, 0.87, 0.89, 0.82, and 0.58, respectively.

Statistical analysis

Data were analysed using Statistical Package for Social Sciences (SPSS, for macOS, version 28; IBM, New York, United States), unless specified otherwise. Alpha level for testing the significance of effects was maintained at $p < 0.05$, unless stated.

The data on all self-report measures were examined and found to be suitable (skewness and kurtosis <±2) for parametric statistical approaches. The Psychoticism sub-scale of the EPQR-S was excluded from all analysis due to its low reliability in the current sample ($\alpha = 0.27$) (a common problem with this sub-scale, as mentioned earlier). We explored possible sex differences in various self-report measures using independent sample *t*-tests. Since we considered chronotype as a continuous variable, Pearson's *r* was used to examine the associations of chronotype (morningness-eveningness) with mental health (Depression, Anxiety, Stress), personality traits (Extraversion, Neuroticism, Schizotypy, and Impulsivity), and childhood trauma scores, followed by Fisher's Exact *z*-test to test for significant differences in chronotype-mental health and sleep-mental health correlations as well as any sex differences in these correlations. Effect sizes for correlation coefficients were interpreted based on Cohen[69] (*r* value ±0.1 to ±0.29 as small, ±0.3 to ±0.49 as medium, and ±0.5 to ±1 as large).

Given significant associations of eveningness with mental health, sleep quality, certain personality traits (Extraversion, Neuroticism, Cognitive Disorganisation, Lack of Perseverance, Lack of Premeditation, Sensation Seeking), and childhood emotional abuse and neglect (see Results), we conducted structural equation modelling (SEM) in SPSS AMOS with scores on the MEQ, personality traits, childhood emotional abuse and neglect as predictors, PSQI scores (sleep quality) as a mediator, and mental health (a latent construct, incorporating depression, anxiety, and stress) as the outcome variable (Fig. 3). All predictor, mediator, and outcome variables were checked for multicollinearity, with no significant violation (variance inflation factor <5, tolerance >0.2) found in the measured cases. The predictors were allowed to covary in the proposed model (see Fig. 3) and the maximum likelihood method was used to test the model fit and calculate the parameter estimates of path coefficients. We used the comparative fit index (CFI; >0.95 represents good model fit), root mean square of approximation (RMSEA; value >0.80 represents good fit), the ratio of maximum-likelihood chi-square to the degree of

freedom (χ^2/df; acceptable value < 5), the goodness of fit index (GFI; acceptable value >0.95), Tucker Lewis Index (TLI; >0.95), and adjusted goodness of fit index (AGFI, acceptable value >0.90) to evaluate the global fit of the model[70]. A global fitting model may have local misfit (i.e., presence of non-significant direct/indirect effects), therefore, the statistical significance of the indirect and direct effects was tested based on bias-corrected 95% bootstrap confidence intervals and associated p values. The model was then revised to exclude non-significant paths (Fig. 1; see Results) one-by-one leaving us with the significant direct or indirect paths in the final model (Fig. 1). The invariance of the model was inferred if the fully constrained model (measurement weights of measurement model of mental health as well as the structural weights, covariances and residuals were constrained to be equal in males and females) did not differ significantly from the unconstrained model. A non-significant chi-square difference ($\Delta\chi^2$ with $p > 0.05$), $\Delta CFI \leq 0.005$, and $\Delta RMSE \leq 0.01$ is considered as evidence for invariance of a given model[71,72].

Data availability

All data supporting this work are freely available via Brunel University London research repository at 10.17633/rd.brunel.25451407.

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Author contributions

S.C.: Conceptualisation, Methodology, Project administration, Formal analysis, Writing & editing. R.P.: Project administration, Formal analysis, Review & editing. K.V.: Project administration, Review & editing. R.N.: Methodology, Review & editing. U.E.: Methodology, Formal analysis, Review & editing. V.K.: Conceptualisation, Methodology, Formal analysis, Resources, Writing - review & editing, Supervision.

Competing interests

The authors declare no competing interests.

Additional information

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Appendix 9.3

brain sciences

MDPI

Article

Sleep Matters in Chronotype and Mental Health Association: Evidence from the UK and Germany

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Abstract: Background: There is considerable evidence supporting the elevated risk of mental health problems in individuals with evening chronotype relative to those with morning or intermediate chronotypes. Recent data, however, suggest that this risk may be explained, at least partially, by poor sleep quality. Methods: This study aimed to further clarify the roles of chronotype and sleep quality in mental health outcomes (depression, anxiety, stress) in young individuals (18–40 years) living in the UK (n = 185) or Germany (n = 209). Results: Consistent with our recent observations in a comparable North Indian sample, we found that poor quality of sleep had significantly positive associations with adverse mental health outcomes both in the UK and Germany-based samples. Significant associations between evening chronotype and poor mental health were also evident, but these associations were fully mediated by poor quality of sleep in both samples. Conclusions: These observations suggest that efforts to identify sleep disruption in a timely manner and promotion of good sleep may prevent mental health problems, especially in individuals with evening chronotype and other known risks for mental disorders.

Keywords: sleep; morningness–eveningness; chronotype; mental health; personality; childhood trauma; impulsivity; schizotypy

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1. Introduction

In humans, the intra-individual variation in circadian rhythms is commonly known as 'chronotype' [1]. It is a multidimensional construct [2], ranging from 'morning chronotype' to 'evening chronotype', with most individuals falling in the intermediate range, known as 'intermediate type'. Morning and evening chronotypes strongly prefer different sleep–wake timings, and the phenomenon may also impact their sleep behaviour [3]. A considerable body of evidence has shown an association between evening chronotype and various mental disorders, including depression [4,5], anxiety [6], substance-use disorder [1,7], and schizophrenia [8,9]. Of these, the most consistent association of evening chronotype has been reported to be with depression [4,5,7]. Additionally, evening chronotypes are also known to display compulsive, aggressive, and addictive behaviours, be less conscientious, have more impulsive and risky behaviour, and display negative cognitive bias, further contributing to a higher likelihood of developing mental illnesses [1,7,8].

Given that sleep timings and duration are regulated via sleep homeostatic processes [10], it is obvious to expect some form of relationship between chronotype and

sleep-related disruptions. For instance, studies have shown that evening chronotypes report poor sleep quality, latency, duration, daytime dysfunction, irregular sleep–wake cycles, accumulate higher sleep debt or social jetlag, have difficulties falling and/or maintaining sleep, build higher sleep pressures, and sleep inertia [11–16]. These disturbed sleep–wake patterns have been considered to be transdiagnostic determinants for the onset and persistence of various mental health and behavioural problems, including depression and anxiety [17], psychosis [18,19], eating disorders [20], substance abuse [21], impulsive and aggressive behaviour [22], personality disorders [23], as well as mood and emotion dysregulation [24]. Both evening chronotype and poor sleep quality are found to be linked with elevated scores on psychometric measures of certain psychopathology-related personality traits, for example, neuroticism and impulsivity [1–3], as well as with self-reported childhood maltreatment [25]. Given these findings, there is clearly a need to better understand the influence of chronotype and sleep quality in mental health outcomes.

Against the backdrop of some studies dismissing any influence of poor sleep in chronotype-mental health association [26,27], a recent study by Muzni et al. [14] observed mental health problems to be more strongly (medium-to-large effect sizes) associated with poor sleep quality than with evening chronotype (small effect sizes) in young adults recruited from the general population in the UK (n = 675). Two very recent studies, both conducted in southeast Asian non-clinical young adult populations {North India, n = 282 [25]; HongKong, n = 200 [28]}, have also shown a strong mediating influence of sleep quality in the chronotype–mental health link. Although climate may impact chronotype [1,2,29], recent findings emerging from different parts of the world [14,25,28] question the widely reported role of chronotype as an 'independent' transdiagnostic risk factor for mental disorders, at least in non-clinical young adult populations.

The present study aimed to further clarify the influence of chronotype and the extent to which it might be mediated by poor sleep quality {a modifiable risk factor [17]} in mental health outcomes in a European sample (from the UK and Germany). The methods and procedures used in this study matched closely with those employed in our recent study [25]. We hypothesised, based on our recent observations in a comparable North Indian sample [25], that there will be a stronger relationship between sleep quality and mental health than between chronotype and mental health, and that any relationship between chronotype and mental health will be mediated via sleep quality. The possible influence of neuroticism, impulsivity, schizotypal personality traits, and adverse childhood experiences [30] in the chronotype–mental health association were also explored.

2. Methodology

2.1. Participants

The study involved 460 young healthy adults (aged 18–40 years) who resided in the UK (n = 213) or Germany (n = 247) at the time of their participation. Of 460, 394 participants provided usable data (UK: 185; Germany: 209). Power analysis for multiple linear regression with eight predictors, including chronotype, quality of sleep, and relevant personality traits {as in [25]}, in G*Power [31], using an alpha of 0.01, a power of 0.90, and a medium effect size (0.15), based on our recent observations [25], indicated that we required 179 participants to test our hypothesis. We aimed to recruit a minimum of 200 participants in the UK and 200 in Germany to allow sufficient power to probe our hypothesis across and within these countries.

All included participants met the study inclusion criteria of (i) being aged between 18 and 40 years (ii) being a UK/Germany resident and a native or proficient English/German speaker, (iii) not taking any regular medication (bar contraceptives and multivitamins), and (iv) having no current or previous diagnosis of a mental disorder and/or drug abuse. Of the 213 non-clinical adults assessed in the UK, 28 were excluded because they either failed our (online) attention checks [i.e., provided an answer that differed by two or more rating points for the same (duplicated) questions; (n = 26)] or did not fully complete all study measures (n = 2). Of the 247 non-clinical adults assessed in Germany, 38 were excluded

for failing our attention checks. The final study sample consisted of 185 UK residents (86 males, 99 females) and 209 Germany residents (67 males, 142 females).

The study was approved by the College of Health, Medicine, and Life Science Research Ethics Committee, Brunel University of London (ref no. 36745-MHR-May/2022-39617-2), and the Research Ethics Committee of the Department of Psychology at the University of Bonn (ref no. 23-03-14). All participants signed an online consent form prior to their participation. All UK-based participants were compensated with a GBP 5 Amazon gift voucher for their time to complete the survey, while those recruited in Germany were enrolled in a lottery system for winning EUR 50.

2.2. Assessment of Chronotype, Mental Health, Sleep Quality, Personality Traits and Childhood Trauma

2.2.1. Chronotype

The 19-item self-report Morningness–Eveningness Questionnaire (MEQ) [32] was used to assess chronotype in the UK-based sample, and its German version [33] in Germany-based sample. The questionnaire has 12 items which are rated on a Likert scale (e.g., item 6: how hungry would you be during the first hour of waking-up?), and the remaining seven items are rated on a time scale (e.g., item 1: approximately at which hour would you wake up if you were free to plan your day?). Higher MEQ scores indicate higher preference for morningness. The MEQ has been reported to have high internal consistency {α = 0.83 [32]}, as was also the case in our study (α = 0.82 and 0.87 in the UK and German-based samples, respectively).

2.2.2. Mental Health

The Depression, Anxiety and Stress Scale (DASS-21) [34] was used to assess mental health in the UK-based sample and its German version [35] in Germany-based sample. The DASS-21 has three subscales: Depression, Anxiety, Stress. Each subscale consists of 7 items which are rated by the participants according to their feelings over the past one week (possible score range on each scale: 0–42). Higher scores indicate higher levels of Depression, Anxiety or Stress. Previous studies have indicated high internal consistency for all three DASS-21 subscales {Depression, α = 0.83–0.94; Anxiety, α = 0.66–0.87; Stress, α = 0.79–0.91 [36]}. Cronbach's alphas in the current samples for Depression (UK, α = 0.89; Germany, α = 0.85), Anxiety (UK, α = 0.83; Germany, α = 0.78), and Stress (UK, α = 0.83; Germany, α = 0.82) also indicated high reliability coefficients.

2.2.3. Sleep Quality

The Pittsburgh Sleep Quality Index [PSQI] [37] was used to assess sleep quality in the UK-based sample, and its German version [38] in Germany-based sample. The PSQI is a 19-item self-report measure assessing seven sleep facets (i.e., sleep quality, sleep efficiency, sleep disturbance, sleep dysfunction, sleep duration, daytime dysfunction, and use of sleep medication). Participants answer each item based on their sleep habits in the past month, with higher scores indicating poor sleep quality. The scale is reported to have a high internal consistency {α = 0.83 [37]}. The Cronbach's alpha coefficients in the current study were α = 0.73 (UK) and α = 0.70 (Germany).

2.2.4. Personality Traits

The Eysenck Personality Questionnaire-Revised Short Form (EPQ-RS) [39] was used to assess levels of Extraversion, Neuroticism, and Psychoticism in the UK-based sample, and its German version [40] in Germany-based sample. The EPQ-RS has four 12-item subscales: Extraversion, Neuroticism, Psychoticism, and Lie (48 items in total). Higher scores indicate higher levels of Extraversion, Neuroticism, and Psychoticism. The EPQ-RS is reported to have good internal consistency {Extraversion: α = 0.74–0.84, Neuroticism: α = 0.70–0.77; bar Psychoticism: α = 0.33–0.52 [41]}. The Cronbach's alphas in the current sample were similar to what has been reported in the literature for Extraversion (UK, α = 0.83; Germany,

α = 0.86), Neuroticism (UK, α = 0.82; Germany, α = 0.79), and Psychoticism (UK, α = 0.39; Germany, α = 0.35).

The Oxford-Liverpool Inventory of Feelings and Emotions-Short Version (s-OLIFE) [42] was used to assess schizotypy in the UK-based sample, and its German version [43] in Germany-based sample. The s-OLIFE is a 43-item self-report measure comprising four subscales assessing levels of Unusual Experiences (12 items), Cognitive Disorganisation (11 items), Introvertive Anhedonia, and Impulsive Nonconformity (10 items each), with each item rated as 'Yes' or 'No'. Higher scores indicate higher levels of schizotypy. This scale is found to have high internal consistency {α = 0.78–0.87 [44]}. The Cronbach's alpha coefficients in the current sample were acceptable-to-high for Unusual Experiences (UK, α = 0.80; Germany, α = 0.69) and Cognitive Disorganisation (UK, α = 0.82; Germany, α = 0.78) and lower for Introvertive Anhedonia (UK, α = 0.49; Germany, α = 0.53) and Impulsive Nonconformity (UK, α = 0.55; Germany, α = 0.42).

The Impulsive Behaviour Scale-Short Version [45] was used to assess impulsivity in the UK-based sample, and its German version [46], with four additional Positive Urgency items {as in Keidel et al. [47]}, in Germany-based sample. It is a 20-item self-report measure assessing levels of Lack of Perseverance, Lack of Premeditation, Positive Urgency, Negative Urgency, and Sensation Seeking, with each item rated on a four-point Likert scale in English and a five-point Likert scale in German {as in Keidel et al. [47]}. Higher scores indicate higher levels of impulsivity. This scale is reported to have a high internal consistency {α =0.74–0.88 [45]}. The Cronbach's alpha coefficients in the current sample were in the acceptable range for Lack of Perseverance (UK, α = 0.63; Germany, α = 0.58), Lack of Premeditation (UK, α = 0.76; Germany, α = 0.65), Sensation Seeking (UK, α = 0.69; Germany, α = 0.66), Negative Urgency (UK, α = 0.80; Germany, α = 0.67), and Positive Urgency (UK, α = 0.82; Germany, α = 0.79).

2.2.5. Childhood Trauma

The Childhood Trauma Questionnaire (CTQ) [48] was used to assess childhood trauma in the UK-based sample, and its German version [49] in Germany-based sample. The CTQ is a 28-item self-report measure for assessing the history and severity of Abuse (Physical, Emotional, Sexual), Neglect (i.e., Emotional, Physical), and Denial, with each item being rated on a five-point Likert scale. Higher scores indicate severity of abuse and neglect. This scale is reported to have a high internal consistency {α = 0.66–0.92 [48]}. In the current sample, the Cronbach's alpha coefficients were high for Physical Abuse (UK, α = 0.83; Germany, α = 0.83), Sexual Abuse (UK, α = 0.94; Germany, α = 0.88), Emotional Abuse (UK, α = 0.81; Germany, α = 0.83), and Emotional Neglect (UK, α = 0.83; Germany, α = 0.88), but was considerably lower for Physical Neglect (UK, α = 0.62; Germany, α = 0.42).

2.3. *Statistical Analysis*

All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) or SPSS Amos (Windows version 28; IBM, New York, NY, USA), with alpha value maintained at $p < 0.05$ unless specified otherwise.

To begin with, all data properties (skewness and kurtosis < $\pm$2) were examined, followed by a reliability assessment of the various self-report scales. Since the Psychoticism subscale of the EPQ-RS showed poor reliability (UK, α = 0.39; Germany, α = 0.35), it was not included in any further analyses. Prior to running any statistical analyses to probe our hypothesis, we conducted a series of independent sample *t*-tests to compare the UK- and Germany-based participants on mental health, sleep, chronotype, personality traits, and childhood trauma parameters to rule out any major differences between them. Given that the UK-based sample, on average, had significantly poor mental health and sleep quality scores (as well as larger range of scores on these variables) compared to the Germany-based sample (see Section 3.1), all further analyses were conducted separately for the UK- and Germany-based samples, and then significant effects were statistically evaluated for any UK versus Germany differences. Given that chronotype may be sex-dependent [1], we also

explored sex-related differences (separately in the UK- and Germany-based samples) in mental health, sleep quality, personality traits, and childhood trauma measures using a series of independent sample *t*-tests.

Pearson correlations were employed to investigate the potential relationships of chronotype (MEQ scores) with mental health, sleep quality, personality traits, and childhood trauma, as well as the relationship of sleep quality with mental health variables. We interpreted effect sizes for observed correlation coefficients (*r* values) based on the recommendations of Cohen [50] (absolute *r* value 0.1 to 0.29: small; 0.3 to 0.49: medium; 0.5 to 1: large), as in our previous study [25]. A Fisher's Exact *z*-test was used to test for statistically significant sex-related differences in these relationships.

Based on the correlations of evening chronotype with mental health, quality of sleep, and relevant personality measures (see Section 3.2), we ran structural equation modelling (SEM) using SPSS Amos (version 28; IBM, New York, NY, USA), first in the UK and then in Germany-based sample, with chronotype and personality traits as predictors (allowed to covary), sleep quality as a mediator, and mental health (a latent construct integrating depression, anxiety and stress subscales) as an outcome (Figure 1). Following our earlier study [25], we used the maximum likelihood method to assess model parameters. A good model fit was based on the following criteria: (a) comparative fit index (CFI) > 0.95, (b) root mean square error of approximation (RMSEA) < 0.08, (c) ratio of maximum-likelihood chi-square to the degree of freedom (χ^2/df) < 5, (d) goodness of fit index (GFI) > 0.95, (e) adjusted goodness of fit index (AGFI) > 0.90, (f) and Tucker–Lewis Index (TLI) > 0.95 [51]. We tested the statistical significance of direct and indirect paths using a bias-corrected 95% bootstrap confidence interval and corresponding *p* values. After testing our initially proposed model (Figure 1), first in the UK and then in Germany, we revised it by removing all non-significant paths (UK, Figures 2 and 3; Germany, Figures 4 and 5; reproduced in Microsoft Power Point, Windows version 2019 based on SPSS Amos generated outputs). Lastly, to explore any sex-related differences, we compared the fully constrained model (measurement weights of the measurement model of mental health, structural weights, covariances and residuals constrained to be equal in males and females) with the unconstrained model. A non-significant chi-square difference ($p > 0.05$), $\Delta CFI \leq 0.005$, and $\Delta RMSEA \leq 0.01$ indicated invariance [52,53]. A similar approach was taken to examine country (UK versus Germany)-related differences.

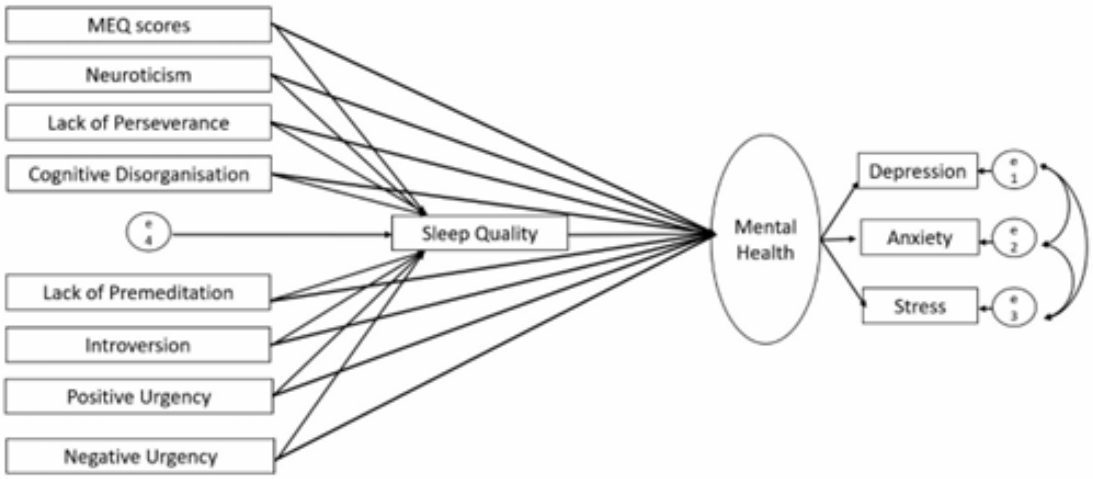

Figure 1. Proposed structural model displaying the direct and indirect (through sleep quality) influences of chronotype and personality traits (predictors; allowed to covary) on mental health (outcome).

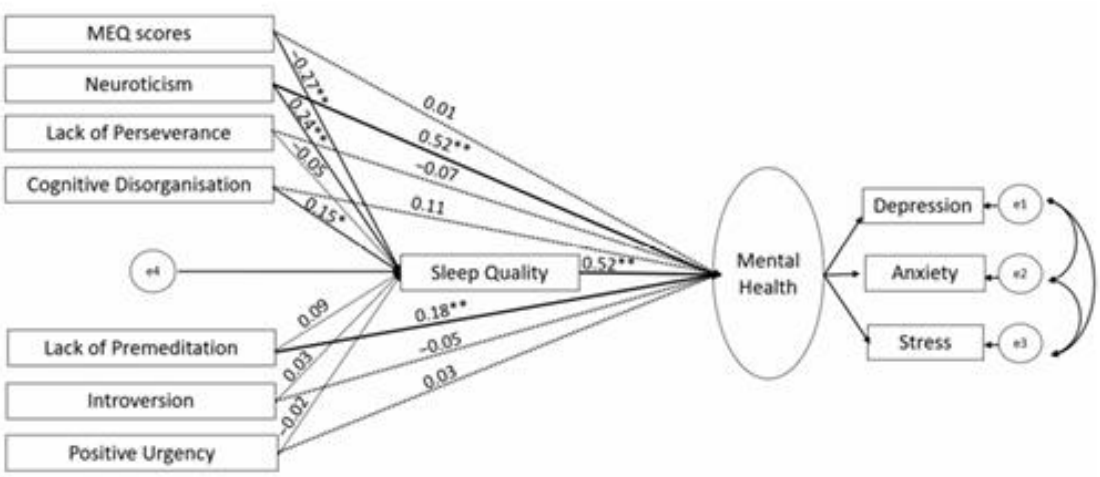

Figure 2. Results of the initial SEM analyses in the UK-based sample. Solid lines denote significant paths (** $p < 0.001$, * $p < 0.005$) and dotted lines denote non-significant paths.

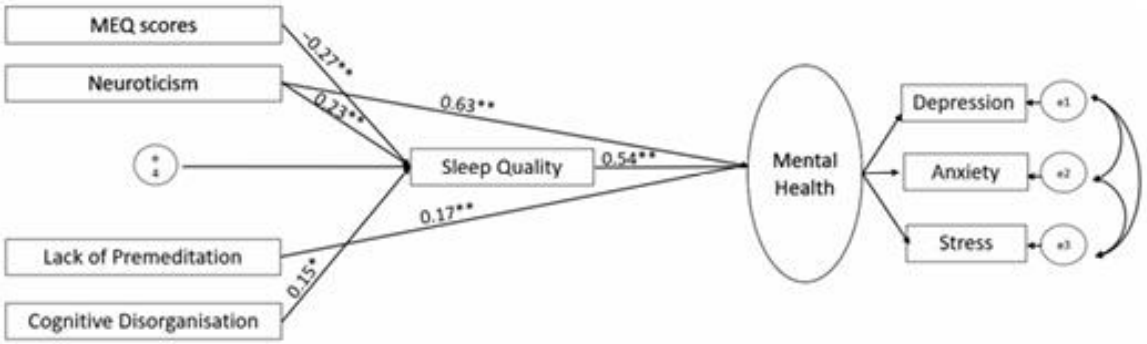

Figure 3. Revised (final) model displaying significant paths (** $p < 0.001$, * $p < 0.005$) in the UK-based sample.

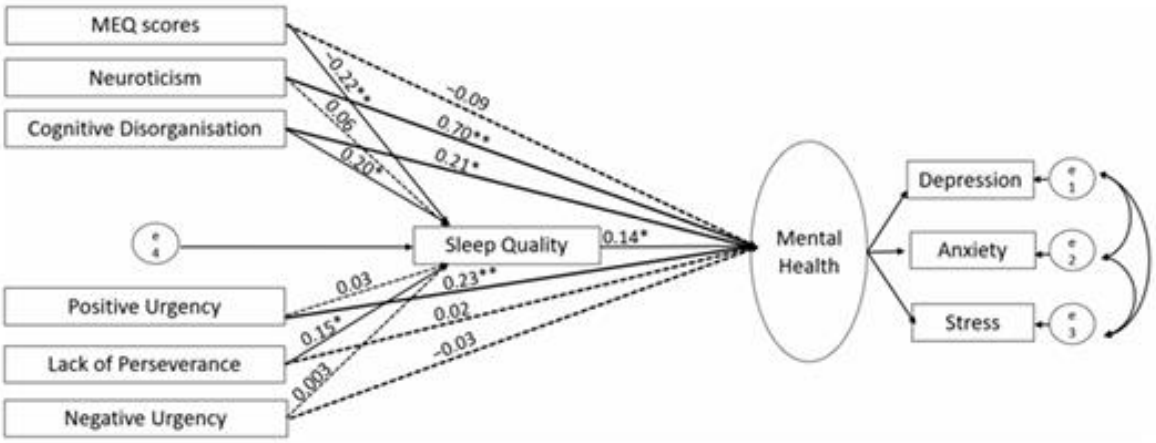

Figure 4. Results of the initial SEM analyses in the Germany-based sample. Solid lines denote significant paths (** $p < 0.001$, * $p < 0.005$) and dotted lines denote non-significant paths.

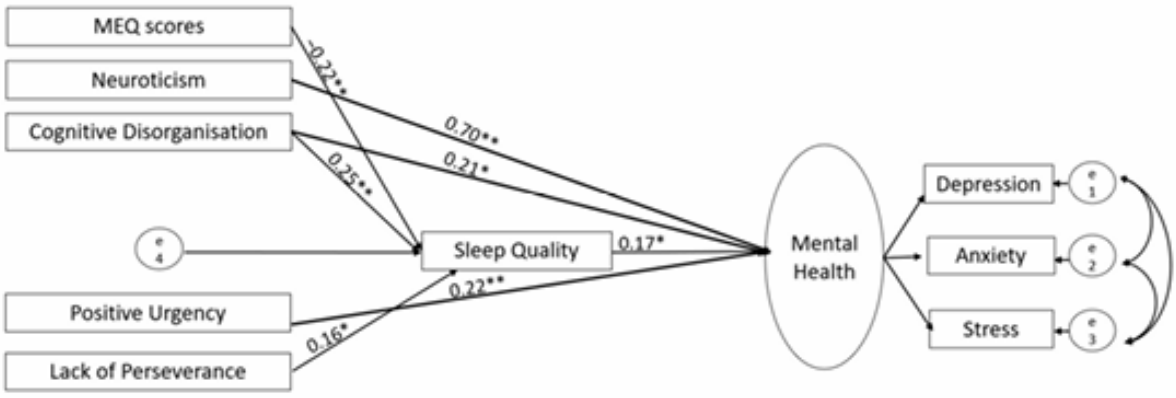

Figure 5. Revised (final) model displaying significant paths (** $p < 0.001$, * $p < 0.005$) in the Germany-based sample.

3. Results

3.1. Sample Characterisation

The demographic characteristics of the UK and German-based samples are presented in Table 1. Overall, the UK-based sample scored higher than the Germany-based sample on Depression ($t_{391} = 4.00$, $p < 0.001$), Anxiety ($t_{391} = 5.18$, $p < 0.001$), Stress ($t_{391} = 2.69$, $p = 0.004$), Neuroticism ($t_{391} = 5.23$, $p < 0.001$), Unusual Experiences ($t_{391} = 8.32$, $p < 0.001$), Cognitive Disorganisation ($t_{391} = 4.05$, $p < 0.001$), Introvertive Anhedonia ($t_{391} = 7.19$, $p < 0.001$), Emotional Abuse ($t_{391} = 4.15$, $p < 0.001$), Physical Abuse ($t_{386} = 6.43$, $p < 0.001$), Sexual Abuse ($t_{390} = 5.85$, $p < 0.001$), Emotional Neglect ($t_{389} = 4.12$, $p < 0.001$), Physical Neglect ($t_{391} = 5.22$, $p < 0.001$), Negative Urgency ($t_{391} = 2.99$, $p = 0.001$), Sensation Seeking ($t_{391} = 5.57$, $p < 0.001$), and Positive Urgency ($t_{391} = 6.04$, $p < 0.001$), and also rated themselves as having poor sleep quality ($t_{391} = 3.30$, $p < 0.001$). The Germany-based sample scored higher on Lack of Perseverance ($t_{391} = 30.02$, $p < 0.001$) and Lack of Premeditation ($t_{391} = 25.77$, $p < 0.001$).

In the UK-based sample, on average, females were younger than males ($t_{183} = 2.03$, $p = 0.022$) and scored higher on Anxiety ($t_{183} = 2.45$, $p = 0.007$), Stress ($t_{183} = 3.28$, $p < 0.001$), Neuroticism ($t_{183} = 5.13$, $p < 0.001$), Sleep Quality ($t_{183} = 2.56$, $p = 0.006$), Unusual Experiences ($t_{183} = 2.26$, $p = 0.012$), Cognitive Disorganisation ($t_{183} = 3.80$, $p < 0.001$), Negative Urgency ($t_{183} = 2.12$, $p = 0.017$), and Emotional Abuse ($t_{183} = 2.28$, $p = 0.012$), while males scores higher in Sensation Seeking ($t_{183} = 2.38$, $p = 0.009$) (Table 2).

In the Germany-based sample, females, on average, had higher scores than males for Stress ($t_{207} = 2.36$, $p = 0.009$), Neuroticism ($t_{207} = 3.66$, $p < 0.001$), Sleep Quality ($t_{207} = 2.78$, $p = 0.003$), Unusual Experiences ($t_{207} = 1.74$, $p = 0.041$), Cognitive Disorganisation ($t_{207} = 2.77$, $p = 0.003$), and Emotional Abuse ($t_{207} = 2.09$, $p = 0.019$), while males scored higher for Sensation Seeking ($t_{207} = 3.06$, $p < 0.001$) and Negative Urgency ($t_{207} = 1.98$, $p = 0.024$) (Table 2).

Table 1. Demographic characteristics of the UK and Germany-based participants.

		UK	Germany
		Frequency (%) of N = 185	**Frequency (%) of N = 209**
Ethnicity	White European	30.3%	79.4%
	Any Other White	0%	1%
	South Asian	46.5%	6.7%
	East Asian	3.8%	1.9%
	West Asian	0.5%	1.4%
	Mixed	7.6%	4.3%
	Black	7%	0.5%
	Other Ethnicities	4.3%	3.8%
	Prefer Not to Say	0%	1%
Stimulant/Sedative Consumption [a]	Caffeine	39.5%	-
	Nicotine	49.2%	-
	Alcohol	7%	-
	Others	2.7%	-
	Prefer Not to Say	1.6%	-
BMI [b]	Underweight	39.5%	42.1%
	Normal	45.4%	52.6%
	Overweight	8.6%	4.8%
	Obese	3.2%	0.5%
Education/Employment	Student	73.5%	95.2%
	Full-time	26.5	4.8%
Sleep Quality [c]	Good (≤5)	57.8%	65.6%
	Poor (6–14)	42.2%	34.4%

Abbreviation: BMI, Body Mass Index. Underweight (<18.5), Normal Weight (18.5–24.9), Overweight (25–24.9), Obese (>30). [a] Data not collected in the Germany-based sample. [b] BMI data missing for six participants in the UK. [c] Score 0–5: good sleepers; score 6 and above: poor sleepers.

Table 2. Descriptive statistics for chronotype, mental health, sleep quality, personality traits, and childhood trauma measures.

Study Variables			UK						Germany					
			Males (n = 86)		Females (n = 99)		All (N = 185)		Males (n = 67)		Females (n = 142)		All (N = 209)	
			Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range	Mean ± SD	Sample Range
Age			25.13 ± 5.27	18–39	23.77 ± 3.77	18–38	24.41 ± 4.57	18–39	23.81 ± 4.12	18–36	23.05 ± 3.39	18–38	23.29 ± 3.65	18–38
Chronotype	MEQ		47.59 ± 8.89	21–68	49.68 ± 11.05	27–78	48.71 ± 10.13	21–78	49.19 ± 10.71	22–74	50.04 ± 9.73	22–71	49.77 ± 10.04	22–74
Mental Health	DASS-21	D	10.23 ± 9.62	0–42	12.57 ± 10.77	0–42	11.48 ± 10.29	0–42	8.03 ± 8.66	0–38	7.76 ± 7.07	0–36	7.85 ± 7.60	0–38
		A	8.74 ± 8.26	0–40	12.02 ± 9.67	0–40	10.50 ± 9.16	0–40	5.46 ± 6.21	0–34	6.59 ± 7.33	0–34	6.23 ± 7.00	0–34
		S	10.72 ± 8.14	0–32	15.05 ± 9.58	0–38	13.04 ± 9.18	0–38	8.78 ± 8.31	0–38	11.58 ± 7.83	0–34	10.68 ± 8.08	0–38
Quality of Sleep	PSQI	SQ	1.02 ± 0.61	0–2	1.17 ± 0.59	0–3	1.10 ± 0.60	0–3	0.96 ± 0.58	0–2	1.02 ± 0.53	0–3	1.00 ± 0.55	0–3
		SL	1.30 ± 0.97	0–3	1.41 ± 0.93	0–3	1.36 ± 0.95	0–3	1.01 ± 0.80	0–3	1.15 ± 0.88	0–3	1.11 ± 0.86	0–3
		SD	0.73 ± 0.78	0–3	0.78 ± 0.73	0–3	0.75 ± 0.75	0–3	0.08 ± 0.26	0–1	0.20 ± 0.48	0–2	0.16 ± 0.43	0–2
		SE	0.56 ± 0.91	0–3	0.77 ± 1.05	0–3	0.67 ± 0.99	0–3	0.32 ± 0.53	0–2	0.47 ± 0.74	0–3	0.42 ± 0.68	0–3
		SDis	1.05 ± 0.44	0–3	1.30 ± 0.50	0–2	1.18 ± 0.49	0–3	0.92 ± 0.40	0–2	1.04 ± 0.38	0–3	1.00 ± 0.39	0–3
		SMed	0.03 ± 0.18	0–1	0.16 ± 0.48	0–3	0.10 ± 0.38	0–3	0.01 ± 0.12	0–1	0.06 ± 0.34	0–3	0.05 ± 0.29	0–3
		DDys	1.05 ± 0.83	0–3	1.26 ± 0.82	0–3	1.16 ± 0.83	0–3	1.07 ± 0.70	0–2	1.25 ± 0.67	0–3	1.20 ± 0.69	0–3
		Global Score	5.21 ± 2.31	0–11	6.12 ± 2.50	1–14	5.70 ± 2.45	0–14	4.35 ± 1.76	0–8	5.21 ± 2.20	0–13	4.94 ± 2.11	0–13
Personality Traits	EPQ	Extrav	6.71 ± 3.40	0–12	7.40 ± 3.41	0–12	7.08 ± 3.41	0–12	7.93 ± 3.70	0–12	7.31 ± 3.49	0–12	7.51 ± 3.56	0–12
		Neuro	5.57 ± 3.44	0–12	7.99 ± 2.96	2–12	6.86 ± 3.40	0–12	4.01 ± 3.21	0–12	5.66 ± 2.93	0–12	5.13 ± 3.11	0–12
	s-OLIFE	UnEx	4.62 ± 3.10	0–12	5.68 ± 3.22	0–11	5.19 ± 3.20	0–12	2.44 ± 2.31	0–10	3.04 ± 2.28	0–9	2.83 ± 2.31	0–10
		CogDis	5.20 ± 3.25	0–11	6.96 ± 3.03	0–11	6.15 ± 3.25	0–11	4.01 ± 2.91	0–11	5.24 ± 3.03	0–11	4.82 ± 3.05	0–11
		IntroAn	3.19 ± 1.95	0–8	3.35 ± 1.94	0–8	3.28 ± 1.94	0–8	1.97 ± 1.76	0–8	1.96 ± 1.70	0–9	1.95 ± 1.72	0–9
		ImpNn	2.75 ± 1.92	0–8	3.07 ± 2.05	0–8	2.92 ± 1.98	0–8	2.79 ± 1.73	0–7	2.64 ± 1.73	0–7	2.67 ± 1.74	0–7
	S-UPPS-P	NegU	8.94 ± 3.04	4–16	9.90 ± 3.11	4–16	9.45 ± 3.11	4–16	8.19 ± 2.50	4–16	8.85 ± 2.10	4–13	8.64 ± 2.25	4–16
		LackP	6.55 ± 1.77	4–11	6.89 ± 2.01	4–14	6.74 ± 1.91	4–14	12.05 ± 1.64	9–16	12.29 ± 1.72	7–16	12.22 ± 1.69	7–16
		LackPre	6.67 ± 2.27	4–15	7.14 ± 2.06	4–13	6.92 ± 2.17	4–15	12.09 ± 1.63	8–16	11.82 ± 1.66	8–16	11.91 ± 1.65	8–16
		SenS	11.89 ± 2.79	5–16	10.90 ± 2.82	5–16	11.36 ± 2.84	5–16	10.61 ± 2.71	5–16	9.45 ± 2.47	4–16	9.82 ± 2.60	4–16
		PosU	8.30 ± 3.19	4–16	8.66 ± 3.04	5–16	8.49 ± 3.11	4–16	7.18 ± 2.52	4–15	6.67 ± 2.19	4–12	6.83 ± 2.31	4–15
Childhood Trauma	CTQ-SF	EAb	9.14 ± 3.91	5–22	10.67 ± 5.02	5–25	9.96 ± 4.59	5–25	7.38 ± 3.49	5–23	8.55 ± 3.88	5–25	8.18 ± 3.79	5–25
		PAb	7.73 ± 3.62	5–19	7.62 ± 4.17	5–24	7.67 ± 3.91	5–24	5.42 ± 1.15	5–11	5.74 ± 2.39	5–24	5.64 ± 2.08	5–24
		SAb	7.02 ± 4.32	5–21	8.02 ± 5.51	5–25	7.56 ± 5.00	5–25	5.14 ± 1.00	5–13	5.50 ± 1.93	5–22	5.38 ± 1.69	5–22
		ENeg	10.87 ± 4.46	5–25	11.41 ± 4.6	5–23	11.16 ± 4.53	5–25	8.90 ± 4.02	5–19	9.49 ± 4.34	5–25	9.30 ± 4.24	5–25
		PNeg	8.35 ± 3.20	5–17	8.00 ± 3.19	5–18	8.16 ± 3.19	5–18	6.67 ± 2.21	5–16	6.69 ± 2.42	5–17	6.68 ± 2.35	5–17

Abbreviations: MEQ: Morningness–Eveningness Questionnaire; DASS-21: Depression Anxiety and Stress Scale-21 (subscales: D, Depression; A, Anxiety; S, Stress); PSQI, Pittsburgh Sleep Quality Index (sleep facets: DDys, Daytime Dysfunction; SD, Sleep Duration; SDis, Sleep Disturbance; SE, Sleep Efficiency; SL, Sleep Latency; SMed, Sleep Medication; SQ, Sleep Quality); EPQ-SF, Eysenck Personality Questionnaire-Revised (subscales: Extrav, Extraversion; Neuro, Neuroticism); s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions (subscales: UnEx, Unusual Experience; CogDis, Cognitive Disorganisation; IntroAn, Introvertive Anhedonia; ImpNn, Impulsive Nonconformity); S-UPPS-P, Impulsive Behaviour Scale-Short Version (subscales: NegU, Negative Urgency; LackP, Lack of Perseverance; LackPre, Lack of Premeditation; SenS, Sensation Seeking; PosU, Positive Urgency); CTQ-SF, short form of Childhood Trauma Questionnaire (subscales: EAb, Emotional Abuse; PAb, Physical Abuse; SAb, Sexual Abuse; ENeg, Emotional Neglect; PNeg, Physical Neglect). Note: Physical abuse data missing for four participants and sexual and emotional abuse data missing for one participant (all German females).

3.2. Associations between Chronotype, Sleep Quality, Mental Health, Personality Traits, and Childhood Trauma

3.2.1. UK

Evening chronotype, indicated by lower MEQ scores, was associated with higher levels of Depression ($r = -0.242$, $p < 0.001$) and higher Extraversion scores ($r = 0.226$, $p = 0.002$). Evening chronotype was also correlated significantly with higher BMI ($r = -0.227$, $p = 0.002$). While some correlations appeared numerically stronger in females than males, none of the correlation differences were statistically significant ($p > 0.05$) (see Table 3).

Table 3. Chronotype (MEQ) associations (Pearson's *r*) with mental health, quality of sleep, personality traits, and childhood trauma.

	Scales	Variables	Chronotype (MEQ Scores)					
			UK			Germany		
			Males	Females	All	Males	Females	All
Mental Health	DASS-21	D	−0.183 (0.091)	−0.304 (0.002)	−0.242 (<0.001)	−0.270 (0.027)	−0.317 (<0.001)	−0.299 (<0.001)
		A	−0.059 (0.590)	−0.207 (0.040)	−0.130 (0.077)	−0.139 (0.262)	−0.131 (0.119)	−0.129 (0.062)
		S	−0.046 (0.675)	−0.179 (0.077)	−0.101 (0.172)	−0.324 (0.008)	−0.200 (0.017)	−0.234 (<0.001)
Quality of Sleep	PSQI	SQ	−0.349 (0.001)	−0.307 (0.002)	−0.296 (<0.001)	−0.227 (0.067)	−0.320 (<0.001)	−0.276 (<0.001)
Personality Traits	EPQ-SF	Extrav	0.102 (0.349)	0.301 (0.002)	0.226 (0.002)	0.154 (0.214)	−0.004 (0.966)	0.049 (0.485)
		Neuro	0.013 (0.908)	−0.239 (0.017)	−0.079 (0.287)	−0.220 (0.073)	−0.225 (0.007)	−0.206 (0.003)
	s-OLIFE	UnEx	0.205 (0.058)	−0.066 (0.514)	0.059 (0.426)	−0.099 (0.424)	−0.130 (0.124)	−0.113 (0.102)
		CogDis	−0.028 (0.799)	−0.238 (0.018)	−0.112 (0.128)	−0.342 (0.005)	−0.303 (<0.001)	−0.302 (<0.001)
		IntroAn	0.084 (0.443)	0.028 (0.782)	0.055 (0.461)	−0.193 (0.119)	−0.012 (0.888)	−0.075 (0.282)
		ImpNn	0.028 (0.797)	−0.103 (0.310)	−0.043 (0.562)	−0.141 (0.255)	−0.125 (0.137)	−0.132 (0.057)
	S-UPPS-P	NegU	0.063 (0.565)	−0.117 (0.247)	−0.027 (0.713)	−0.162 (0.191)	−0.150 (0.076)	−0.147 (0.033)
		LackP	0.030 (0.783)	−0.253 (0.011)	−0.135 (0.067)	0.213 (0.084)	0.130 (0.124)	0.159 (0.022)
		LackPre	0.019 (0.863)	−0.203 (0.044)	−0.093 (0.210)	−0.043 (0.727)	0.101 (0.233)	0.049 (0.481)
		SenS	−0.043 (0.694)	0.051 (0.616)	−0.005 (0.941)	0.048 (0.700)	−0.003 (0.967)	0.007 (0.925)
		PosU	0.063 (0.566)	−0.204 (0.043)	−0.084 (0.255)	−0.292 (0.016)	0.026 (0.756)	−0.096 (0.167)

Table 3. *Cont.*

	Scales	Variables	Chronotype (MEQ Scores)					
			UK			Germany		
			Males	Females	All	Males	Females	All
Childhood Trauma	CTQ-SF	EAb	−0.066 (0.549)	−0.170 (0.093)	−0.113 (0.125)	−0.079 (0.526)	−0.073 (0.389)	−0.068 (0.328)
		PAb	0.109 (0.316)	−0.120 (0.236)	−0.035 (0.637)	−0.150 (0.228)	0.026 (0.761)	−0.007 (0.923)
		Sab	0.031 (0.780)	0.039 (0.701)	0.046 (0.535)	−0.039 (0.752)	0.135 (0.109)	0.097 (0.163)
		ENeg	−0.051 (0.639)	−0.096 (0.343)	−0.071 (0.336)	0.025 (0.842)	−0.002 (0.982)	0.008 (0.906)
		PNeg	0.190 (0.079)	0.010 (0.919)	0.078 (0.292)	0.231 (0.060)	0.041 (0.631)	0.101 (0.145)

Abbreviations: DASS-21: Depression Anxiety and Stress Scale-21 (subscales: D, Depression; A, Anxiety; S, Stress); PSQI, Pittsburgh Sleep Quality Index (SQ, Sleep Quality); EPQ-SF, Eysenck Personality Questionnaire-Revised (subscales: Extrav, Extraversion; Neuro, Neuroticism); s-OLIFE, short Oxford-Liverpool Inventory of Feelings and Emotions (subscales: UnEx, Unusual Experience; CogDis, Cognitive Disorganisation; IntroAn, Introvertive Anhedonia; ImpNn, Impulsive Nonconformity); S-UPPS-P, Impulsive Behaviour Scale-Short Version (subscales: NegU, Negative Urgency; LackP, Lack of Perseverance; LackPre, Lack of Premeditation; SenS, Sensation Seeking; PosU, Positive Urgency); CTQ-SF, short form of Childhood Trauma Questionnaire (subscales: EAb, Emotional Abuse; PAb, Physical Abuse; SAb, Sexual Abuse; ENeg, Emotional Neglect; PNeg, Physical Neglect).

As expected, poor sleep quality, indicated by higher PSQI scores, was correlated with higher levels of Depression ($r = 0.565$, $p < 0.001$), Anxiety ($r = 0.535$, $p < 0.001$), Stress ($r = 0.510$, $p < 0.001$); higher scores on psychopathology-related personality traits, including Neuroticism ($r = 0.379$, $p < 0.001$), Unusual Experiences ($r = 0.236$, $p < 0.001$), Cognitive Disorganisation ($r = 0.363$, $p < 0.001$), Introvertive Anhedonia ($r = 0.175$, $p = 0.017$), Impulsive Nonconformity ($r = 0.203$, $p = 0.006$), Negative Urgency ($r = 0.315$, $p < 0.001$), and Positive Urgency ($r = 0.175$, $p = 0.017$); and also with Emotional Abuse ($r = 0.422$, $p < 0.001$) and Sexual Abuse ($r = 0.230$, $p = 0.002$) (see Supplementary Table S1). Poor sleep quality also correlated with evening chronotype (i.e., lower MEQ scores) ($r = -0.296$, $p < 0.001$), and although this correlation seemed numerically stronger in males than in females, the correlation difference was not statistically significant ($p > 0.05$). Overall, chronotype had small-sized correlations with mental health outcomes, whereas sleep quality had large sized correlations with mental health outcomes.

3.2.2. Germany

In line with the UK findings, evening chronotype was significantly associated with Depression ($r = -0.299$, $p < 0.001$) and Stress ($r = -0.234$, $p < 0.001$), as well as with higher levels of Neuroticism ($r = -0.206$, $p = 0.003$), Cognitive Disorganisation ($r = -0.302$, $p < 0.001$), Negative Urgency ($r = -0.147$, $p = 0.033$), and Lack of Premeditation ($r = 0.159$, $p = 0.022$). Again, some correlations appeared to be numerically stronger in females than in males, but none of these differences were formally significant ($p > 0.05$) (see Table 3).

As expected, poor sleep quality correlated with Depression ($r = 0.275$, $p < 0.001$), Anxiety ($r = 0.305$, $p < 0.001$), and Stress ($r = 0.271$, $p < 0.001$), the personality traits of Neuroticism ($r = 0.244$, $p < 0.001$), Unusual Experiences ($r = 0.308$, $p < 0.001$), Cognitive Disorganisation ($r = 0.289$, $p < 0.001$), Introvertive Anhedonia ($r = 0.196$, $p = 0.005$), Impulsive Nonconformity ($r = 0.186$, $p = 0.007$), and Negative Urgency ($r = 0.157$, $p = 0.024$), and also with Emotional Abuse ($r = 0.261$, $p < 0.001$), Physical Abuse ($r = 0.181$, $p = 0.010$), and Sexual Abuse ($r = 0.188$, $p = 0.007$) (see Supplementary Table S2). Poor sleep quality also correlated with evening chronotype ($r = -0.276$, $p < 0.001$); and, again, although this correlation seemed numerically stronger in females relative to males, the correlation difference was not statistically significant ($p > 0.05$). Overall, both chronotype and sleep quality had small-to-medium-sized correlations with mental health outcomes.

3.3. The Mediating Role of Sleep Quality: SEM Analysis

3.3.1. UK

Our proposed model (Figure 2) had a good fit to the data (χ^2/df = 1.13, $p < 0.001$; RMSEA = 0.01; GFI = 0.96; AGFI = 0.90; CFI = 0.99) but had a poor local fit. We therefore revised it by removing non-significant paths to reach our final model (χ^2/df = 0.99; GFI = 0.97; TLI = 1; CFI = 1; RMSEA = 0.000) (see Figure 3). As evident in Figure 3, there was no significant direct influence of chronotype on mental health; instead, the chronotype–mental health relationship was fully mediated by poor sleep quality. The mental health relationship with Neuroticism and Cognitive Disorganisation was also partially mediated by poor sleep quality. Lastly, we found no sex-related influence in the final model, as indicated by non-significant differences [$\Delta\chi^2(8) = 4.68$, $p = 0.791$; ΔCFI = 0; ΔRMSEA = 0.008] when comparing the model fit of the unconstrained model with that of the structural-weight-constrained model.

3.3.2. Germany

In line with the UK findings, our proposed model (Figure 4) had an acceptable fit (χ^2/df = 4.38, $p < 0.001$; RMSEA = 0.12; GFI = 0.94; AGFI = 0.78; CFI = 0.92) to the data, but it was revised, due to poor local fit, to remove the non-significant paths (model fit indices: χ^2/df = 3.72; GFI = 0.93; TLI = 0.82; CFI = 0.91; RMSEA = 0.11) (see Figure 5). As depicted in Figure 5, we found no direct effect of chronotype on mental health and observed that its relationship with mental health was fully mediated by poor sleep quality. We also found that sleep quality partially mediated the association of mental health with Cognitive Disorganisation and Lack of Perseverance. While exploring sex differences, we found that the comparison of the unconstrained model with the structural-weight-constrained model showed a non-significant chi-square difference $\Delta\chi^2(9) = 16.44$, $p = 0.058$ and RMSEA (ΔRMSEA = 0.003) but a significant difference in CFI (ΔCFI = 0.013). The pairwise difference in the path coefficients of the unconstrained model in males and females showed a significant difference in the path linking sleep quality with mental health [Critical ratio = 2.04; stronger in females (β = 0.252) than males (β = 0.028)], and the path linking Cognitive Disorganisation with sleep quality [Critical ratio = 2.10; stronger in males (β = 0.485) than females (β = 0.128)], suggesting a partial variance in the model.

3.3.3. Chronotype, Sleep Quality, and Mental Health Associations: UK versus Germany

When exploring the possible invariance of the path model across the UK and Germany-based samples, we found the measurement model of mental health to be variant [$\Delta\chi^2(2) = 11.22$, $p = 0.004$; ΔCFI = 0.008; ΔRMSEA = 0.013]. The factor loading of anxiety in the UK (β = 0.675) and Germany (β = 0.531) was found to be significantly different (Critical ratio = 3.36). Additionally, compared to the measurement-weight-constrained model, the structural-weight-constrained model also differed [$\Delta\chi^2(6) = 18.73$, $p = 0.005$; ΔCFI = 0.011] although with a non-significant RMSEA (ΔRMSEA = 0.005). The pairwise difference in the path coefficients of the measurement-weight-constrained model showed a difference in the path linking sleep quality to mental health (CR = 3.84), this being stronger in the UK (β = 0.55) than Germany (β = 0.16).

4. Discussion

The present study aimed to further examine our recent finding of sleep quality as a mediating factor in the chronotype–mental health relationship in young non-clinical (healthy) adults residing in North India [25] in a sample of young non-clinical adults residing in the UK or Germany while also quantifying the role of psychopathology-related personality traits and childhood trauma in this relationship. Unexpectedly, our UK (London)-based participants, on average, were found to have, higher levels of depression, anxiety, and stress, as well as poor sleep quality, compared to those who were residing in Germany (Bonn). This may be related to a difference in the recruitment strategy used in the UK and Germany. In the UK, each recruited participant received GBP 5 for their participation, while

those recruited in Germany were enrolled in a lottery system to win EUR 50. A small but guaranteed financial incentive that was offered to each participant in the UK might have attracted more participants belonging to a lower socioeconomic background which is known to be associated with poor mental health and reduced psychological well-being [54–56].

In relation to our study hypothesis, the key findings of the present study were: (i) Evening chronotype (lower MEQ scores) had small-to-medium-sized associations with metal health outcomes (UK and Germany, *r* values: 0.20–0.30), (ii) Poor sleep quality had large associations with mental health outcomes in the UK-based sample (*r* values: 0.51–0.56), while small-to-medium-sized associations were observed in Germany-based sample (*r* values: 0.27–0.30). (iii) Sleep quality fully mediated the chronotype–mental health relationship, with no significant direct effect of evening chronotype on mental health outcomes in either the UK- or Germany-based samples. Evening chronotype had significant but mostly small-to-medium-sized (*r* values, 0.14–0.34) associations with psychopathology-relevant personality traits in both samples. The association between evening chronotype and severity of childhood emotional maltreatment, although in line with our earlier findings in the North Indian sample [25], was not formally significant in the UK- or Germany-based samples.

In the present study, we employed same methods and replicated our previous findings in a North Indian sample [25] in showing that sleep quality fully mediated the chronotype-mental health association in non-clinical young UK and Germany-based samples, though this effect was weaker in Germany-based sample, possibly due to a limited range of scores on measures of both mental health and sleep (Table 2) as well as a possible difference between the UK and Germany-based samples in resilience that was recently reported to impact both chronotype–mental health and sleep–mental health associations [28]. Nonetheless, our findings across India, the UK, and Germany are generally in line with previous correlational studies that have consistently found an association between evening chronotype and depressive symptoms [4,5] as well as general mental health [57]. Some longitudinal studies show that the prevalence of higher levels of depression predicts evening chronotype, especially in adolescents [58,59], but there are also some longitudinal studies, using actigraphy, that failed to detect an association between depression and evening chronotype in adolescents [60,61]. These studies, however, did not consider sleep-related disturbances, including poor sleep latency, quality, and duration, all of which are known to be more common in evening chronotypes [13,14,25,28], as also shown in the current study. The mediating role of sleep quality in the chronotype–mental health relationship is also visible in clinically depressed individuals [62]. Further support for the mediating role of sleep quality in the chronotype–poor mental health link comes from recent findings suggesting that this link is either attenuated or absent in the presence of sufficient and good quality sleep (for example, in individuals who can work remotely) in evening chronotypes [63].

In the modern world, humans realistically rely less on their internal clock and more on the social clock to sleep, which disrupts and shifts their circadian rhythms [64,65] of melatonin and cortisol secretions [66,67], both linked with psychiatric illnesses such as schizophrenia and depression [68,69]. One of the most noticeable forms of circadian disruption is sleep disturbance and social jetlag, commonly found in evening chronotypes [14,65,70] due to their natural tendency to be awake at later hours, which causes difficulties in sleep restoration and falling asleep [3,71]. Not surprisingly, studies have reported insomnia severity ($\beta = -0.14$) as a significant moderator of the chronotype–mental health relationship [57]. Taken together, non-restoration of sleep and/or poor sleep habits as a result of disrupted circadian rhythms may explain previously observed positive associations between evening chronotype and adverse mental health outcomes. The prevalence of poor sleep quality may render evening chronotypes more susceptible to developing mental health issues. This may be especially true for people who have lower resilience [28,72], though such a possibility was not directly addressed in the current study.

While investigating the influence of psychopathology-related traits, we found a small-sized positive association between evening chronotype and neuroticism in female participants of both the UK and Germany-based samples. This is consistent with previous

findings on this topic [1–3,14]. Interestingly, this relationship was somewhat weaker and non-significant for males, who also scored, on average, lower than females, which is not surprising given known sex differences in neuroticism (females > males) across countries and cultures [73]. Extraversion had a small association with morning chronotype in the UK, which is also consistent with the previous literature [3,14,25]. This relationship, however, was not found in Germany-based sample for reasons that we do not fully understand. There are some other studies that have found no significant associations between extraversion and morning chronotype [1]. We found a small correlation between evening chronotype and impulsivity both in the UK and German-based samples. This has also been seen in previous studies [25,74]. Impulsivity as a personality trait has been linked with impulsive behaviour in healthy and clinical populations [75] and might explain why evening chronotypes may be more likely to engage in substance abuse and addiction [1]. Interestingly, we also replicated our previous findings of a small but significant association between cognitive disorganisation aspect of schizotypy and evening chronotype in both UK (females) and German (all) participants. Individuals scoring high on schizotypy share some characteristics with schizophrenia patients [76], including higher stress-reactivity and anxiety [77–79], which disrupts sleep cycles [80], and sleep deprivation in turn can induce psychosis-like symptoms in healthy adults [19,81,82].

4.1. Limitations and Future Directions

The study had some limitations. First, we used self-report questionnaires and did not control for light exposure, and menstrual cycle phase in females, both of which may influence sleep and mental health [1,83]. Second, we restricted our sample to young adults (≤40 years), and thus the findings cannot be generalised to adolescents (≤17 years) or older adults (>40 years). Third, our study used chronotype as continuous variable and employed a cross-sectional design; therefore, it cannot speak of causation. Further studies employing objective measures of circadian rhythm alongside relevant self-report measures in a longitudinal design and different age groups are needed to substantiate and refine the present findings.

4.2. Conclusions

To conclude, we did not observe any direct impact of chronotype on mental health; instead, this association was found to be fully mediated by poor sleep quality in young adults living in the UK or Germany. These and our previous findings [25] argue against the independent role of chronotype as a transdiagnostic risk factor for mental health problems in non-clinical young adults and highlight sleep disruption and circadian misalignment as important therapeutic targets for improving mental health outcomes. Intervening early on to ensure good sleep quality may be a preventive strategy in combination with attempts to shift circadian preference towards morning.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/brainsci14101020/s1, Table S1: Correlations (Pearson's *r*) between measures of mental health, sleep quality, personality traits and childhood trauma in the UK sample; Table S2: Correlations (Pearson's *r*) between measures of mental health, sleep quality, personality traits and childhood trauma in German sample.

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Appendix 9.4

brain sciences

MDPI

Systematic Review

Pineal Abnormalities in Psychosis and Mood Disorders: A Systematic Review

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Abstract: The pineal gland (PG) is a small interhemispheric brain structure that influences human physiology in many ways, most importantly via secretion of the hormone melatonin which is known to regulate sleep and wakefulness. Here, we systematically reviewed existing neuroimaging studies of PG structure, and/or melatonin release (MLT) in psychosis and mood disorders. Medline, PubMed, and Web of Science databases were searched (on 3 February 2023), yielding 36 studies (8 PG volume, 24 MLT). The findings showed smaller-than-normal PG volume in people with schizophrenia, regardless of symptom severity and illness stage; and smaller-than-normal PG volume in major depression, with some indication of this being present only in certain subgroups, or in those with high scores on the 'loss of interest' symptom. There was considerable evidence of lower-than-normal MLT as well as aberrant MLT secretion pattern in schizophrenia. A similar picture, though less consistent than that seen in schizophrenia, emerged in major depression and bipolar disorder, with some evidence of a transient lowering of MLT following the initiation of certain antidepressants in drug-withdrawn patients. Overall, PG and MLT aberrations appear to represent transdiagnostic biomarkers for psychosis and mood disorders, but further work is needed to establish their clinical correlates and treatment implications.

Keywords: pineal gland; melatonin; MRI; schizophrenia; depression; bipolar disorder; biomarker

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1. Introduction

For centuries, the pineal gland (PG) has been referred to as the 'third eye' or 'ajna chakra', 'pineal eye', and 'seat of the soul', and it was only in the late 19th century that we gained a clear understanding of its structure and various influences on the mammalian physiology, especially its role in the regulation of sleep cycle and wakefulness [1–5]. In humans, the PG is a small interhemispheric brain structure, resting proximally on the posterior aspect of the diencephalon. It is located within 1–2 mm of the midline and becomes visible between habenular and posterior commissures around 7 weeks of gestation [6]. Average PG dimensions in human adults are 5–9 mm in length, 1–5 mm in width, and 3–5 mm in height, and it weighs roughly between 100 and 180 mg depending on the age and sex [7,8]. The main function of the PG is to receive and transmit the light-dark signals from our surroundings and, accordingly, to produce and secrete the hormone melatonin [9]. Pineal melatonin (MLT) is known to modulate circadian rhythms and is involved in sleep regulation [10], reproductive physiology [8,11,12], and immunological regulation [13].

In recent decades, there has been much interest in examining PG and MLT production in people with psychosis and mood disorders, given that poor regulation and/or quality of sleep feature prominently in both of these disorders [14,15]. There are reports of smaller PG volumes, compared to healthy people, both in people with psychosis [16,17] and mood disorders [18] though not all studies have found this (e.g., [19]). It is possible that PG and MLT aberrations represent transdiagnostic biomarkers across these disorders or,

alternatively, they might be associated with certain cross-diagnostic symptom dimensions. Of particular relevance in this context are depressive symptoms that not only characterise mood disorders but are also experienced by a significant proportion (25–70%) of people with schizophrenia [20,21] and may even precede clinical manifestation of psychosis [22,23]. Similarly, psychotic symptoms are experienced by subgroups of people with mood disorders [24]. To our knowledge, there is no published systematic review of PG and MLT aberrations across psychotic and mood disorders.

Our aim, therefore, was to systematically review, synthesise and appraise the findings of previous studies evaluating PG structure and/or MLT production in people with psychosis and/or mood disorders compared to healthy controls, and possible associations of PG structure/function with specific patient characteristics (symptom profiles, illness stage, treatment history, medication dose) within the psychosis and mood disorder groups to establish the extent to which specific PG abnormalities might represent disorder-specific or transdiagnosis effects and, in addition, be explained by illness-related influences (e.g., present in chronic but not first episode psychosis patients). We also consider any implications of our findings in psychosis and mood disorders for future research as well as the treatment and management of these disorders.

2. Methodology

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) structure and guidelines [25].

2.1. Information Sources and Search

A literature search in Medline, PubMed, and Web of Science databases was conducted on 3 February 2023. The search terms included: (Pineal* OR melatonin OR "pineal gland") AND (psychosis* OR psychot* OR schizophrenia*) AND (mood disorders* OR "affective disorders" OR "bipolar disorder" OR depress*). Search results were restricted to English, with no specific time window of publication. Cited references in the selected studies were also examined to identify further eligible literature.

2.2. Eligibility Criteria

Studies yielded by our literature search were assessed against the following inclusion criteria:

1. Study participants must have a diagnosis of schizophrenia/psychosis, bipolar disorder or major depression.
2. Allow comparison of the patient group/s with a health control group.
3. Report data on PG volume determined via magnetic resonance imaging (MRI) or MLT measured via blood, urine, saliva, or cerebrospinal fluid.
4. Studies must be primary research articles that have been peer-reviewed.

Studies without full text and methodology, meta-analyses, dissertation/PhD theses, unpublished papers, books, scoping, and systematic reviews were excluded. Animal studies, genetic and metabolic studies, post-mortem studies, and those with computerised tomography of PG were also excluded.

2.3. Study Selection

All data resulting from the literature search were exported to Zotero. A screen of the results was conducted on a title and abstract basis for relevance and meeting the inclusion criteria by two independent reviewers (SC, AB). If the abstract did not contain sufficient information, the full text was retrieved before making a decision regarding the study meeting our inclusion/exclusion. The two reviewers (SC, AB) independently read the study title, abstracts, and full texts (where needed) and assigned each study a score of 0 (not relevant), 1 (questionable), or 2 (probably suitable). Next, the selection ratings of the two reviewers were compared, and the degree of agreement was assessed. Any discrepancies, as well as any studies with a score of 1, were discussed with a third reviewer (VK) to reach a consensus. The reasons for excluding studies at all stages were documented (for a flowchart of the study selection process, see Figure 1).

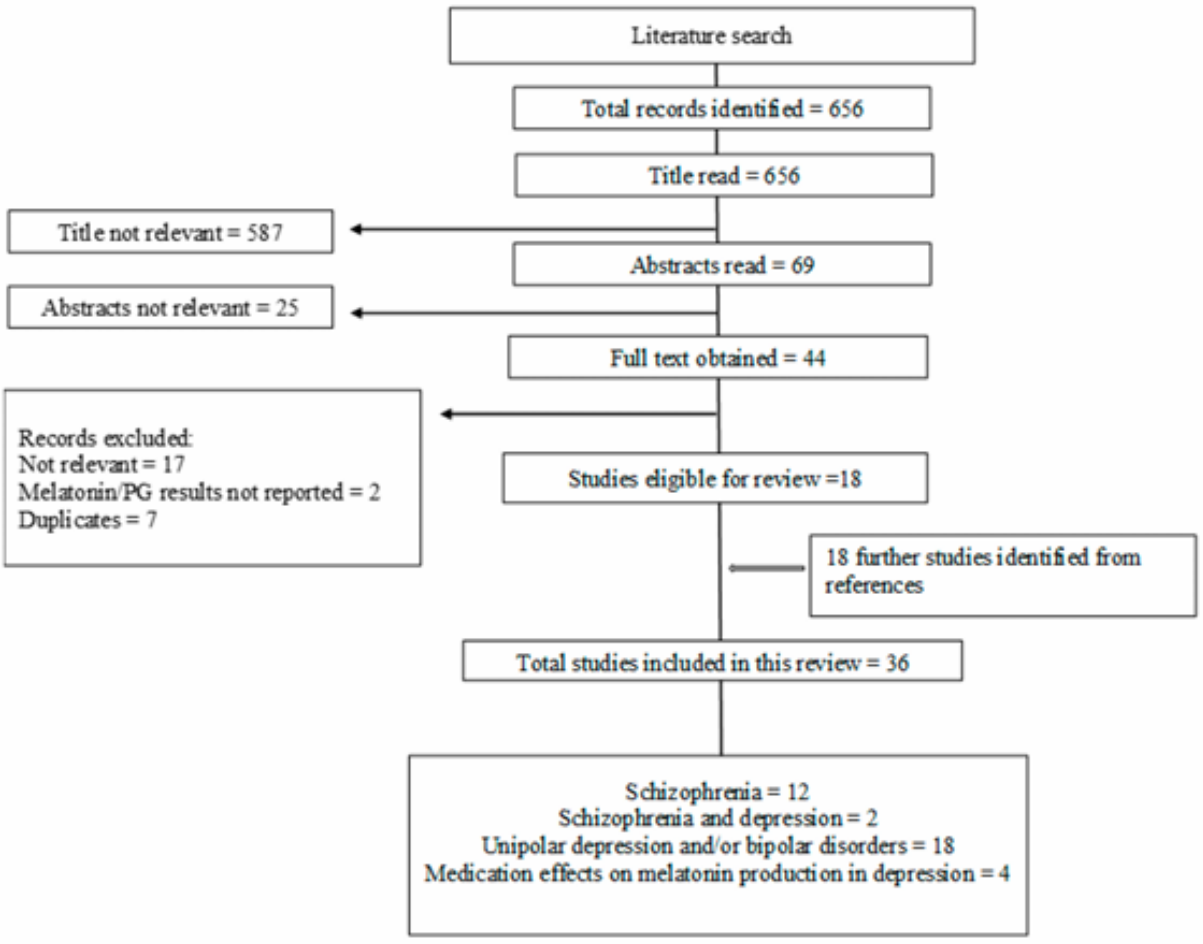

Figure 1. A flowchart of the study selection process following PRISMA guidelines.

2.4. Data Collection Process

Data extraction for all selected studies was conducted by the first author (SC). In addition, data for a random selection of 18 studies were independently extracted by the second author (AB) to verify the extraction process.

2.5. Data Items and Analysis

For each of the selected study, the following data were extracted: author and study year, study population and sample characteristics (sample size, mean age and sex distribution for the patient and healthy comparison groups; and, in addition, for patient groups, diagnosis, age at illness onset, duration of illness, symptoms, current medication, and treatment history), design of the study, imaging modality or methods for assessing PG structure and/or function, intervention characteristics (where relevant), key study outcomes (i.e., diagnosis effects in PG structure and/or function; any association with patient characteristics), and funding sources. For all key outcome variables, group averages (mean, SD) and the size of the correlations (where reported between PG volume/MLT and relevant sample characteristics (e.g., symptoms or medication dose) were also extracted. All extracted data were compiled into a Microsoft Excel spreadsheet and analysed descriptively, considering the statistical significance of the findings as reported by the study authors for group comparisons (patients vs. healthy controls; or involving different patient groups) and/or correlations between the PG structure/function and patient characteristics. We made no specific assumptions where the study authors had assessed relevant sample characteristics (for example, symptoms) but not examined them in relation to the PG structure or function; we simply noted them as 'not reported' in the extracted data.

2.6. Quality Appraisal

The quality of selected studies was assessed using Newcastle-Ottawa Quality Assessment Scale [26] for non-randomised, cross-sectional studies, and Critical Appraisal Skills Programme [27] scores for randomised controlled trials (see Supplementary Tables S1 and S2 for quality rating of the selected studies).

3. Results

Overall, the search yielded 36 studies conducted in 16 different countries (UK, Germany, France, Sweden, Italy, Belgium, Poland, Canada, Brazil, USA, Australia, Turkey, Iran, China, Japan, and Taiwan). There was significant variability in sample sizes ranging between 5 and 87 participants for the healthy group, between 7 and 162 participants for the psychosis group (excluding bipolar disorder as this patient group was included mostly within the context of mood disorders, as bipolar versus unipolar depression), and between 6 and 50 participants for the mood disorders group (major depression or bipolar disorders). Eight of 36 reviewed studies investigated PG structure using MRI (4 studies in psychosis or schizophrenia, 3 studies in mood disorders, and 1 study involved schizophrenia as well as mood disorders), and 24 studies examined MLT in blood, urine and/or cerebrospinal fluid (8 in psychosis, 15 in mood disorders, 1 study involved both schizophrenia and mood disorders). Most of these 32 studies used a cross-sectional study design comparing the patient (psychosis and/or mood disorders) and healthy control groups, and some studies also examined possible associations between PG structure and/or MLT and symptom ratings or medication within the patient samples. Lastly, four studies examined medication effects on MLT in major depression and also included comparison with healthy controls. No study met our eligibility criteria for examining antipsychotic effects on MLT.

3.1. PG Volumes: Effects of Diagnosis and Possible Association with Clinical Characteristics

The details and key findings extracted from the reviewed studies in relation to PG volumes in psychosis and mood disorders are presented in Table 1.

PG volume was found to be significantly smaller in people with schizophrenia or psychosis, compared to healthy controls, in four of the five studies that investigated this [16,17,28,29]. An early study with a modest sample size [19] reported no significant difference between the patient and control groups although the mean PG volume was still numerically lower in the patient group (see Table 1a,b). In the two most recent studies with relatively large sample sizes [17,29], PG volume was found to be smaller-than-normal not only in the first-episode and chronic schizophrenia groups, but also in those at a high risk of developing psychosis. Furthermore, no relationship between the PG volume and age or any clinical characteristics of the patient sample (symptoms, age of illness onset, duration of illness and/or treatment) was detected in any of the four studies that found significantly smaller-than-normal PG volume in psychosis or schizophrenia samples [16,17,28,29].

PG volume was also found to be significantly smaller in people with major depressive disorders, compared to healthy controls, in two of the three studies that examined this [16,18]; however, there was no association between PG volumes and depressive symptom ratings in either of these studies (see Table 1b,c). One study [30] that did not observe a significant difference between the PG volumes of currently depressed or remitted groups of mood disorder patients and healthy controls, however, reported significantly smaller PG volumes in non-melancholic patients, compared to melancholic depressed patients; it also reported a negative association between PG volumes, and the 'loss of interest' symptom ratings but no association with any other symptoms (for example, the Beck Depression Inventory-II scores) when examined across the patient sample. Furthermore, this study [30] showed no significant difference between the PG volumes of bipolar disorder patients and healthy controls, and no significant association between total PG volume and any clinical characteristics, namely, the number of episodes, duration of illness or the medication dose, in this group of patients. A further study of bipolar disorder patients [31] also found them to not differ from healthy controls in PG volumes, although a group of BD patients were found to have smaller PG volumes than the controls in a later study [16].

There was only one study [16] directly comparing PG volumes in schizophrenia and mood disorders, and it showed (i) significantly lower PG volume in the schizophrenia group, compared to patient groups with unipolar depression or bipolar disorder, (ii) no significant difference between unipolar depression and bipolar disorder groups; (iii) and significantly lower PG volumes, compared to controls, in both unipolar depression and bipolar disorder groups (as already noted, both unipolar depression and bipolar disorder groups had larger volumes compared to those in people with schizophrenia).

Table 1. Studies examining pineal gland (PG) volume in patients with psychosis or mood disorders, compared to healthy controls.

Author and Year (in Chronological Order)	Patients (*n*, Diagnosis, Sex and Age)	Healthy Comparison Group (*n*, Sex and age)	Patient Characteristics			Imaging Details	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
a. PG volume in patients with psychosis, compared to healthy controls											
Rajarethinam et al. (1985) [19]	45 SZ or psychosis (31 M, 14 F; mean age: 30.2 ± 9.7)	86 (44 M, 42 F; mean age (27.3 ± 9.6)	Not reported	Not reported	Not reported	MRI with 1.5 GE tesla scanner	Between-groups	No significant difference in PG volume between patients (mean ± SD:0.208 ± 0.099 cm^3) and controls (0.213 ± 0.097 cm^3)	=	Not reported	4
Bersani et al. (2002) [28]	15 SZ (all M; mean age: 26.60 ± 5.28)	16 controls (all M; mean age: 29.26 ± 6.26)	AIO 18.42 ± 4.78 years; DoI 8.28 ± 4.59 years	SAPS: 55.66 ± 22.84; SANS: 62.17 ± 28.58; PANSS: 106.4 ± 22.93	Mean neuroleptic treatment duration (in years): 5.59 ± 5.40	MRI with 1.5 magnetom-siemens	Between-groups	Significantly smaller PG volume in patients (64.05 ± 20.69 mm^3) than controls (74.62 ± 33.53 mm^3).	↓	No correlation between PG volumes and age of clinical characteristics (AOI, DoI, symptoms)	6
Takahashi et al. (2019) [29]	At baseline 64 first-episode psychosis (37 M, 27 F; mean age: 24.0 ± 4.7) 40 chronic SZ (20 M, 20 F; mean age: 29.0 ± 5.5) 22 ARMS (11 M, 11 F; mean age: 19.1 ± 4.1)	At baseline 86 controls (48 M, 38 F; mean age: 23.7 ± 5.4)	At baseline First-episode: AIO 23.1 ± 4.7 years; DoI 11.2 ± 12.2 months; Chronic SZ: AIO 20.9 ± 4.4 years; DoI 96.8 ± 39.8 months	At baseline First-episode: SAPS: 27.3 ± 21.9; SANS: 53.1 ± 25.2 Chronic SZ: SAPS: 30 ± 19.2; SANS: 45.5 ± 18.7; ARMS: SAPS: 20.4 ± 10.9; SANS: 48.5 ± 19.4 Also, BDI: 24.1 ± 10.00; STAI trait: 65.3 ± 10.9; STAI state: 58.4 ± 11.3	At baseline Mean (± SD) medication duration (in months) for ARMS (2.3 ± 4.1); First-episode (8.3 ± 12.6); Chronic SZ (72.4 ± 47.6) Medication type: ARMS (1 typical, 3 atypical); first-episode (18 typical, 43 atypical, 1 mixed); chronic SZ (19 typical, 18 atypical, 3 mixed)	MRI with 1.5 tesla scanner	Between-groups (with a follow-up)	At baseline Significantly smaller PG volumes in ARMS (102.7 ± 43.2 mm^3), first-episode (102.3 ± 46.2 mm^3), and chronic SZ patients (105.7 ± 46.4 mm^3) compared to healthy controls (131.1 ± 60.1 mm^3).	↓	PG volumes not correlated with demographic (age or education level) or clinical variables (AIO, DoI, duration of treatment, symptoms).	7
	At follow-up (after 15.6 ± 17.4 months) 23 first-episode psychosis (15 M, 8 F; mean age: 23.5 ± 4.8) 16 chronic SZ (7 M, 9 F; mean age: 31.6 ± 7.1) 22.7% ARMS developed SZ	At follow-up 21 controls (13 M, 8 F; mean age: 24.5 ± 5.0)		At follow-up First-episode: SAPS: 17.0 ± 17.1; SANS: 38.0 ± 22.5 Chronic SZ: SAPS: 34.9 ± 30.0; SANS: 57.3 ± 18.7	At follow-up Medication type: First-episode (3 typical, 16 atypical, 4 mixed); chronic SZ (4 typical, 8 atypical, 4 mixed)			At follow-up No effect of time, diagnosis or any interaction.	=		
Takahashi et al. (2022) [17]	162 first-episode patients (108 M, 54 F; mean age: 21.5 ± 3.4) 89 chronic SZ (76 M, 13 F; mean age: 34.9 ± 9.6) 135 clinical high risk (78 M, 57 F; mean age: 20.1 ± 3.6)	87 controls (55 M, 32 F; mean age: 26.9 ± 10.1)	First-episode: AIO not reported; DoI 54 ± 87 (days) Chronic SZ: AIO not reported; DoI 4673 ± 3613(days)	Clinical high risk: BPRS total: 44.1 ± 8.3; BPRS psychotic subscale: 8.4 ± 2.6; SANS 18.9 ± 12.7	Mean antipsychotic duration (chlorpromazine equivalent) First-episode: 154.7 ± 118.2 mg/day Chronic SZ: 842.9 ± 715.8 mg/day	MRI with 1.5 tesla scanner	Between-groups	Significantly smaller PG volume in CHR (97.5 ± 50.3 mm^3), FEP (97.7 ± 51.2 mm^3), CSz (99.0 ± 61.5 mm^3) groups than controls (139.4 ± 73.9 mm^3). Pineal parenchymal volume smaller in all clinical groups (CHR: 93.4 ± 42.3 mm^3; FEP:94.2 ± 43.5 mm^3; CSz: 96.8 ± 58.8 mm^3) than controls (132.9 ± 62.7 mm^3, with no significant difference between the clinical groups.	↓	PG and parenchyma volumes not correlated with age, DoI or antipsychotic dose in the first-episode or chronic SZ groups; and not correlated with symptoms in the high-risk group.	6

Table 1. *Cont.*

Author and Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and age)	Patient Characteristics			Imaging Details	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
b. PG volume in patients with schizophrenia, compared to those with major depression or bipolar disorders and healthy controls											
Findikli et al. (2015) [16]	17 SZ (11 M, 6 F; mean age: 36.6 ± 12.7)	30 controls (16 M, 14 F; mean age: 41.1 ± 13.3)	AIO 29.00 ± 12.02 years; DoI 7.8 ± 6.2 years	Not reported	Mean antipsychotic treatment duration 7.1 ± 6.5 years (risperidone, amisulpiride, flupentixol)	MRI with 1.5 Tesla	Between-groups	Significantly smaller PG volumes in SZ patients (83.5 ± 10.1 mm^3) had than controls (99.7 ± 12.03 mm^3). Smaller PG volume in SZ (83.5 ± 10.1 mm^3) compared to BD (93.7 ± 11.4 mm^3) and UD groups (95.1 ± 11.2 mm^3) (see below).	↓	PG volumes not correlated with clinical characteristics (AIO, DoI, treatment duration).	7
	16 UD (8 M, 8 F; mean age: 39.4 ± 13.9) 17 BD (11 M, 6 F; mean age: 30 ± 10.2)	30 controls (16 M, 14 F; mean age: 41.1 ± 13.3)	UD: AIO 35.3 ± 15.5 years; DoI 4.1 ± 4.2 BD: AIO 25.06 ± 10.8 years; DoI 4.3 ± 4.09 years	Not reported	All UD patients on SSRIs Most BD patients on antipsychotics and 2 received lithium treatment.			Smaller PG volume in both UD (95.1 ± 11.2 mm^3) and BD patients (93.7 ± 11.4 mm^3) compared to controls (99.7 ± 12.03 mm^3).	↓		
c. PG volume in patients with unipolar depression or bipolar disorder, compared to healthy controls											
Sarrazin et al. (2012) [31]	16 BD I and II (10 M, 6 F; mean age: 42.8 ± 8.3)	16 controls (8 M, 8 F; mean age: 37.1 ± 11.35)	Not reported	Not reported	15 patients medicated	3-T MRI magnet	Between-groups	No difference in PG volume between patients (115.3 ± 54.3 mm^3) and controls (110.4 ± 40.5 mm^3).	=	Not reported	5
Zhao et al. (2019) [18]	50 MDD (19 M, 31 F; mean age: 42.10 ± 10.52)	35 controls (18 M, 17 F; mean age: 42.74 ± 10.04	Not reported	Patients: HDRS: 29.42 ± 11.59; PSQI: 11.96 ± 5.43; HAMA: 19.06 ± 7.41 Controls: HDRS: 2.49 ± 2.37; HAMA: 2.86 ± 3.72	29 patients on SSRIs (paroxetine, escitalopram, fluvoxamine), 1 on NaSSA (mirtazapine), and 20 on SNRIs (venlafaxine. Duloxetine, sertraline)	MRI 3.0 Tesla MR system	Between-groups	Significantly smaller pineal parenchymal volume in MDD (70.47 ± 28.30 mm^3) relative to controls (89.87 ± 38.81 mm^3).	↓	No correlation between pineal parenchymal volume and symptoms (HAMD, HAMA, and PSQI).	7
Takahashi et al. (2020) [30]	29 cMDD (7 M, 22 F; mean age: 32.5 ± 8.3) 27 rMDD (9 M, 18 F; mean age: 35.1 ± 10.0)	33 controls (12 M, 21 F; mean age: 34.0 ± 9.9)	cMDD: AIO 21.1 ± 8 years; DoI not reported rMDD: AIO 26.0 ± 9.4 years; DoI not reported	cMDD: BDI: 36.8 ± 8.9; PANAS positive affect: 21.6 ± 6.5, PANAS negative affect: 21.2 ± 8.5; MASQ general depression: 47.3 ± 9.2 rMDD: BDI: 13.0 ± 11.7; PANAS positive affect: 28.7 ± 8.0; PANAS negative affect: 14.2 ± 4.7; MASQ general depression: 35.0 ± 11.7 Healthy controls: BDI: 3.6 ± 4.1; PANAS positive affect: 32.9 ± 7.3; PANAS negative affect 11.2 ± 1.6; MASQ general depression: 19.5 ± 7.2	MDD- 21 current and 12 remitted MDD patients took medication in the past 6 months.	MDD- MRI using 1.5 Tesla siemens scanner	Between-groups	No significant difference MDD and control groups: current MDD, PG: 119.2 ± 51.5 mm^3; parenchymal: 115.0 ± 45.1 mm^3; remitted MDD, PG: 119.7 ± 53.7 mm^3; parenchymal: 116.5 ± 48.2 mm^3; controls, (PG: 145 ± 84.9 mm^3; parenchymal: 138.8 ± 71.7 mm^3 Significantly smaller PG volume, however, in the non-melancholic subgroup of MDD (n:19, parenchymal: 101.9 ± 42.4 mm^3) than the melancholic MDD subgroup (n:10; parenchymal: 142.0 ± 40.7 mm^3).	↓=	Total pineal and parenchymal volume in cMDD patients correlated negatively (r = −0.571) with MASQ loss of interest score (but no correlation with number of episodes, and other MASQ, PANAS, and BDI scores).	8

Table 1. *Cont.*

Author and Year (in Chronological Order)	Patients (*n*, Diagnosis, Sex and Age)	Healthy Comparison Group (*n*, Sex and age)	Patient Characteristics			Imaging Details	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Takahashi et al. (2020) [30]	26 BD (8 M, 18 F; mean age: 38.4 ± 10.9) Note: 16 of 28 BD had psychotic symptoms.	24 controls (7 M, 17 F; mean age: 38.7 ± 11.1) (a subsample of the controls noted above)	BD: AIO 13.5 ± 10.1 years; DoI not reported	Not administered	12 BD patients on lithium (dosage, (975 ± 213) and 12 on valproate (1437 ± 594).	BD- MRI using 1.5 Tesla GE sigma scanner		No significant difference between BD (PG: 121 ± 79.0 mm^3; parenchymal: 119.6 ± 76.8 mm^3) and controls (PG: 129.8 ± 62.0 mm^3; parenchymal: 126.4 ± 57.6 mm^3).	=	No correlation between pineal/parenchymal volumes and number of episodes, medication dose, or DoI in patients.	

↓ denotes significantly lower volume in patient group/s compared to the comparison group; = denotes no difference between the patient and the comparison group. Abbreviations: AIO, Age at Illness Onset; ARMS, At Risk Mental State; BDI, Beck Depression Inventory [32]; BPRS, Brief Psychiatric Rating Scale [33]; CAARMS, Comprehensive Assessment of at-Risk Mental State [34]; CHR, Clinical High Risk; cMDD, Current Major Depressive Disorder; DoI, Duration of Illness; F, Females; FEP, First Episode Psychosis; HAMA, Hamilton Rating Scale for Anxiety [35]; HDRS, Hamilton Depression Rating Scale [36]; M, Males; MASQ, Mood and Anxiety Symptom Questionnaire [37]; MDD, Major Depressive Disorder; MRI, Magnetic Resonance Imaging; MRI, Magnetic Resonance Imaging; NaSSA, Noradrenergic and Specific Serotonergic Antidepressants; NOS: Newcastle-Ottawa Quality Assessment Scale [26]; PANAS, Positive and Negative Affect Scale [38]; PANSS, Positive and Negative Syndrome Scale [39]; PG, Pineal Gland; PSQI, Pittsburgh Sleep Quality Index [40]; rMDD, Remitted Major Depressive Disorder; SANS, Scale for the Assessment of Negative Symptoms [41]; SAPS, Scale for the Assessment of Positive Symptoms [42]; SNRIs, Serotonin-Norepinephrine Reuptake Inhibitors; SSRIs, Selective Serotonin Reuptake Inhibitors; STAI, State-Trait Anxiety Inventory [43]; SZ, Schizophrenia, UD, Unipolar Disorder; BD, Bipolar Disorder.

3.2. PG Function (MLT): Effects of Diagnosis and Association with Clinical Characteristics

There were eight studies examining MLT level or MLT secretion patterns in people with schizophrenia (see Table 2). All these studies, except one [44], observed (overall) lower-than-normal MLT level [45–48] or an aberrant pattern of MLT secretion in this group of patients [48–50]. Specifically, there was a different pattern in patients and controls, with MLT increasing at 8 p.m. and peaking at 2 a.m. in controls but no significant peaks in patients [49]; earlier peaks in drug-free patients, relative to controls [49]; and delayed rhythm and atypical sleep-wake cycles in 50% of the patients, relative to controls [50]. In one study [48] that compared acutely unwell and chronic patient groups, acutely unwell patients had higher MLT, relative to chronic patients, but both groups still had lower MLT relative to healthy controls.

There was no relationship between MLT aberrations and symptoms in most of the studies that examined this in people with schizophrenia [45,47,49], and in one study [50] that did observe lower MLT in patients with positive symptoms, relative to those without positive symptoms, this effect was explained by age (Table 2). Antipsychotic medication seemed to be associated with a change towards normalisation of the MLT secretion pattern in that medicated patients did not differ significantly from controls [51]. In the only study [44] that did not find lower-than-normal MLT levels in schizophrenia patients, MLT levels were found to be positively associated with antipsychotic medication dose as well greater symptom severity, possibly reflecting higher antipsychotic doses prescribed to those with greater symptom severity.

There were 15 studies examining MLT level or MLT secretion in people with major depression and/or bipolar disorders (Table 3). Most of these studies showed significantly lower MLT, especially nocturnal MLT, in depressed patients, compared to healthy controls [52–58], or atypical MLT secretion patterns such as delayed peak [59] or delayed onset [60]. Relatively fewer studies showed a non-significantly lower MLT in patients [61], no significant difference between the patient and control groups [62,63], or lower MLT level in patients with psychotic depression, but higher in those with non-psychotic depression, both compared to controls [64]. One of these studies [56] had also examined and observed lower MLT in panic disorder patients, compared to healthy controls. Interestingly, in one study [65] that had assessed MLT in both blood and cerebrospinal fluid (CSF), blood but not CSF MLT was lower in depressed patients, and CSF but not blood MLT was lower in bipolar disorder patients, both relative to healthy controls. However, an earlier study [66] had shown lower serum MLT in bipolar disorder patients (at 1 a.m. and 5 a.m.; but only at 1 a.m. in euthymic subgroup) relative to the healthy group.

Most studies in mood disorders had only small-to-modest and mixed sex samples (with marked inter-study variation in average depression severity, see symptom ratings for individual studies, Table 3), and did not examine relationship with symptom profiles or medication. A few studies which did examine such associations presented a mixed picture, with no relationships between basal MLT or secretion patterns and medication [52] or symptom severity [55], or a negative relationship with depression severity [53]. Some studies also showed MLT to correlate positively with body mass index (BMI), and to be influenced by sex of the participant while others did not (Table 3). Lastly, there was only one study [67] comparing MLT in people with schizophrenia (n = 12) with that in people with depression (n = 60] and, unexpectedly, its findings revealed higher MLT in schizophrenia, relative to depressed patients (Table 4).

There were four studies (all involving 20 or fewer patients) investigating the influence of antidepressant medications on MLT in depressed patients (Table 5). Two of these studies, with only or predominantly females, showed a transient lowering of MLT following certain antidepressants [desipramine [68]; fluoxetine [69]], while the remaining two mixed-sex studies showed no pre- to post-change in MLT [clomipramine [70]; fluoxetine [71]]. Further complicating the picture regarding MLT patterns in depressed patients, three of these four studies [68,69,71] had reported no significant differences in MLT between the patient and control groups at baseline, while one study [70] reported higher MLT in patients, relative to healthy controls (see Table 5).

Table 2. Studies examining melatonin production (MLT) in people with psychosis, compared to healthy controls.

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Ferrier et al. (1982) [45]	21 chronic SZ (all M; mean age: 59.6 ± 8.4)	12 controls (all M; mean age: 54.2 ± 9.1)	Not reported	MRS (data not reported)	All patients drug free for at least 1 year	MLT (at mid-night and 8 a.m.) measured via blood	Between-groups	Significantly lower MLT level in patients (16.2 ± 12.8 mL) than controls (31.9 ± 17.6 mL) at mid-night; and non-significantly lower (9.7 ± 3.2 mL) at 8:00 a.m. than controls (10.8 ± 5.0 mL)	↓	MLT did not correlate with age, DoI or symptom rating. A significant positive relationship between MLT and BMI in both groups (controls: r = 0.66; patients r = 0.35).	7
Beckman et al. (1984) [44]	28 paranoid SZ (all M; mean age: 40.6 ± 8.0)	16 controls (all M; mean age: not reported)	Not reported	BPRS (mean or range not reported)	15 patients treated with butyrophenones and phenothiazines for at least 3 weeks (mean dose: 585 ± 755 mg/day). Remaining 13 patients not on any drug for at least 4 weeks. Prior treatment history not reported.	MLT (between 9–10 a.m.) analysed in the CSF	Between-groups	No significant differences in MLT between the patients with (15 ± 16 mL) or without neuroleptic medication (15 ± 14 mL) and controls (15 ± 25 mL). No difference between medicated and drug free patients.	=	MLT positively correlated with symptom severity (r = 0.34) and antipsychotic dose (r = 0.47).	6
Fanget et al. (1989) [46]	23 SZ (10 M, 13 F; mean age: 41.5 ± 11.6)	26 controls (16 M, 10 F; mean age: 40.7 ± 4.4)	AIO not reported DoI 18.4 ± 9.5 (years)	BPRS: 60.3 ± 15	15 patients on levopromazine, 8 on haloperidol, 21 on anticholinergic drug, 10 on benzodiazepines, and 4 on antidepressants Mean treatment duration: 16 years	MLT concentration (at mid-night) determined via blood radioimmunoassay	Between-groups	Significantly lower MLT in patients (52.3 ± 41.8 mL) compared to controls (75.5 ± 18.7 mL) but significant differences between drug-free patients and those on antidepressants.	↓	Not reported	5
Monteleone et al. (1992) [48]	7 paranoid SZ (all M; mean age: 29.1 ± 3.5)	7 controls (all M; mean age: 30.8 ± 3.3)	AIO not reported DoI 8.8 ± 3.3 (years)	BPRS: 41.1 ± 4.7; HDRS: 6.8 ± 3.7	5 patients drug free for 3 weeks and the remaining 2 for 1 year. Medication doses/type and mean age of medication duration not reported.	MLT concentration (over a 24 h period) determined via plasma using RIA method	Between-groups	Different MLT secretion pattern in patients and controls; MLT increasing at 8 p.m. and peaking at 2 a.m. in controls but no significant peaks observed in patients.	–	MLT not correlated with HDRS and BPRS ratings.	7
Rao et al. (1994) [51]	89 drug-free SZ or schizoaffective disorder (47 M, 42 F; mean age: M, 34 ± 12; F, 36 ± 11) Medicated patients (11 M, 14 F; mean age: M, 26 ± 8; F, 41 ± 14)	34 controls (17 M, 17 F; mean age: M, 24 ± 4; F, 24 ± 2)	AIO not reported DoI > 6 months in all patients	Not reported	25 patients on a stable dose of neuroleptic medication for 5 years, 21 patients were drug free and the remaining 68 were on a minimum of 3 day wash out period. Medication doses/type and mean age of medication duration not reported.	MLT (over a 24 h period) measured via blood	Between-groups	Different MLT secretion pattern in patients and controls; MLT peaked significantly earlier in drug-free patients and similar but non-significant phase advancement in medicated SZ patients, both relative to controls.	–	Not reported	5
Jiang & Wang (1998) [47]	21 paranoid SZ (all M; mean age: 27.3 ± 7.2)	21 controls (all M; mean age: 28.7 ± 11.0)	AIO not reported DoI 0.6–12 months (3.12 ± 2.43)	Patients: BPRS: 48.3 ± 5.8; HDRS: 7.6 ± 3.6 Controls: BPRS: 6.1 ± 4.2; HDRS: 4.8 ± 3.7	All patients on antipsychotic medications (chlorpromazine equivalent 600–1200 mg/day; mean not reported)	MLT (over 24 h period) measured via blood		Significantly lower MLT in patients (38.1 ± 22.5 ng/mL) than patients (22.2 ± 11.6 ng/mL).	↓	MLT did not correlate with age, BMI, DoI or symptom severity. Relationship with medication not reported.	7

Table 2. *Cont.*

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (Dal)	Symptom Rating Measure/s (mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Vigano et al. (2000) [48]	13 SZ (6 M, 7 F; median age: 26; range: 20–37)	20 controls (sex distribution or age not reported)	Not reported	Not reported	Eight patients drug free and 5 on neuroleptic drugs Medication doses/type and mean age of medication duration not reported.	MLT (over a 24 h period) measured via blood	Between-groups	Both daytime and nocturnal MLT levels significantly lower in patients than controls (mean values not reported).	↓	Not reported	6
Wulff et al. (2012) [50]	20 paranoid SZ (15 M, 5 F; mean age: 38.8 ± 8.6)	21 controls (13 M, 8 F; mean age: 37.5 ± 9.6)	AIO not reported Dal 2–33 years (median = 10)	Patients: PSQI: 8.32 ± 3.77; POMS week 1: 13.3 ± 10.7; POMS week 6: 14.3 ± 10; MEQ: EC = 72.3%, IC = 27.8%, MC = 0% Controls: PSQI: 4.83 ± 2.37; POMS week 1: 12.1 ± 8.4; POMS week 6: 9.5 ± 9; MEQ: EC = 65%, IC = 30%, MC = 5%	12 patients on antipsychotics only, 7 received additional psychotropic medication	MLT sulphate concentrations (over a 24 h period) measured in urine by radioimmunoassay	Between-groups	50% of the patient sample reported significant delayed MLT rhythms and free running sleep-wake cycles relative to controls.	–	Lower MLT in patients with (MLT: 467 ± 228.6 ng) than those without positive symptoms (MLT: 1066.3 ± 501 ng). Patients had poor sleep quality than controls but did not differ for chronotype, mood profile or age. MLT did not correlate with antipsychotic medication.	8

↓ denotes significantly lower MLT in patients compared to the healthy controls; – denotes altered MLT secretion pattern in patients relative to healthy controls; = denotes no difference between the patient and the healthy control group in MLT level or secretion pattern. Abbreviations: AIO: Age at Illness; BPRS, Brief Psychiatric Rating Scale [33]; CSF, Cerebrospinal Fluid; EC, Evening Chronotype; F, Females; HDRS, Hamilton Depression Rating Scale [36]; IC, Intermediate Chronotype; MDD, Major Depressive Disorder; M, Males; MC, Morning Chronotype; MEQ, Morningness-Eveningness Questionnaire [72]; MG, Milligram; MIRS, Modified Inpatient Rating Scale [73]; MLT, Melatonin; POMS, Profile of Mood States [74]; PSQI, Pittsburgh Sleep Quality Index [40].

Table 3. Studies examining MLT production in people with depressive and/or bipolar disorders, compared to controls.

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Score
			Age at Illness Onset (AIO) and Duration of Illness (Dal)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Beck-Friis et al. (1984) [52]	30 acutely ill MDD inpatients (13 M, 17 F; mean age: 44 ± 1.9) 24 chronic outpatients with UD (6 M, 6 F) or bipolar disorder (6 M, 6 F; mean age: 51 ± 2.1)	33 controls (14 males, 19 females; mean age: 40 ± 2.2)	Not reported	MDD: CPRS:2 ± 0.1 Chronic UD and BD: CPRS:0.3 ± 0.1 Controls: CPRS:0.0 ± 0.0	All patients on medication (a range of medications used)	Serum MLT (over a 24 h period) measured via blood.	Between-groups	Significantly lower nocturnal MLT in both patient groups (acute MDD: 0.25 ± 0.03 nmol/L; chronic UD or BD: 0.17 ± 0.02 nmol/L) than controls (0.30 ± 0.03 nmol/L).	↓	MLT negatively correlated with BMI ($r = -0.45$) but no association with medication.	5

Table 3. *Cont.*

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Score
			Age at Illness Onset (AIO) and Duration of Illness (Dol)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Claustrat et al. (1984) [54]	11 affective disorder (1 M, 10 F; mean age: 44.5 ± 11.1)	24 controls, including 8 young M (mean age: 27.3 ± 3.1), 8 older M (62 ± 4.2), and 8 young F (24.5 ± 5.1)	Not reported	HDRS: 41.90 ± 6.64	Drug free for at least 10 days	MLT (over a 24 h period) measured via blood	Between-groups	Significantly lower in patients (22.5 ± 19.2 mL) than controls (41.2 ± 9.5 mL). MLT level peaked at 3 a.m. in controls (young males: 86.5 ± 22 mL; ovulating women: 72.9 ± 26 mL; older males = 84.7 ± 20 mL) but decreased in patients (39.3 ± 38.4 mL).	↓	Not reported	6
Brown et al. (1985) [55]	Sample 1 from Philadelphia: 7 depressed melancholia patients (all M; mean age: 42 ± 4)	Sample 1 from Philadelphia: 5 controls (all M; mean age: 32 ± 4)	Not reported	Patients: HDRS: 31 ± 3.4	All patients drug free for at least 7 days, and did not receive electroconvulsive therapy within 3 months of testing.	MLT measured (over 15 h period) via blood	Between-groups	Patients had lower MLT (53 ± 10 mL) than the controls (89 ± 9 mL).	↓	MLT levels did not correlate with age or symptom severity.	6
	Sample 2 from New York: 19 depressed melancholia (5 M, 14 F; mean age: 62.4 ± 2.5) 9 depressed non-melancholia (all F; mean age: 57.3 ± 4.5)	Sample 2 from New York: 7 controls (all M; mean age: 41.4 ± 4)		Depressed melancholia: HDRS: 35.9 ± 4.3 Depressed non-melancholia: HDRS: 23.1 ± 1.7		MLT measured (at 9 a.m. and 11 p.m.) via blood		Significantly lowered MLT at 11:00 p.m. in melancholic (56.4 ± 4.6 mL) and non-melancholic (58.6 ± 9.6 mL) groups relative to controls (69.3 ± 8.0 mL); at 9 p.m., no significant group differences.		MLT levels did not correlate with age or symptom severity.	
Beck-Friis et al. (1985) [53]	32 MDD (14 M, 18 F; mean age: 45 ± 1.9)	33 controls (14 M, 19 F; mean age: 40 ± 2.2)	Not reported	CPRS (mean values not reported)	Not reported	MLT (over 24 h period) measured via blood	Between- groups	Lower in MLT level in patients with abnormal DST (0.19 ± 0.03 nmol/L) but not normal DST patients: (0.30 ± 0.02 nmol/L) relative to controls (0.30 ± 0.03 nmol/L). MLT significantly lower in patients depressed for >3 summer periods (0.17 ± 0.04 mL) compared to those depressed for <3 summer periods. (0.28 ± 0.04 mL).	↓	No relationship found between MLT and Dol or diagnostic subcategories. Negative associations of MLT with CPRS global score, depressed mood, and retardation symptoms (r values not reported). MLT relationship with demographics and medication not reported.	6
Thompson et al. (1988) [62]	9 depressive patients (4 M, 5 F; mean age: 48.1; age range: 26–66; SD not reported)	9 controls (4 M, 5 F; mean age: 46.1; age range: 28–58; SD not reported)	Not reported	CRG7.3 (range: 3–10); SD not reported HDRS 25.1 (range: 10–31); SD not reported	Patients antidepressant-free for at least 6 weeks but allowed benzodiazepines (exact numbers and medication dose not reported)	MLT levels (over 24 h period) measured via blood	Between- groups	No significant difference between patients and controls (mean values not reported).	=	Not reported	5

Table 3. *Cont.*

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Score
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
McIntyre et al. (1995) [56]	11 MDD-melancholic subtype (4 M, 7 F; mean age: 58 ± 5.0) 13 panic disorder (1 M, 12 F; mean age: 36 ± 2.1)	18 controls (4 M, 14 F; mean age: 32 ± 2.2)	Not reported	MDD melancholic: HDRS: 21.2 ± 2.1 Panic disorder: HDRS: < 8	Most MDD patients on antidepressants, 4 drug free at least 5 days. 8 panic disorder patients receiving benzodiazepines, 4 received additional tricyclic antidepressants and 1 drug free. Medication dose not reported.	MLT (between 8 p.m. and midnight) measured via blood	Between-groups	Significantly lower MLT in both MDD (27.1 ± 5.1 mL) and panic disorder (28.4 ± 6.4 mL) groups compared to the controls (51.6 ± 4.1 mL).	↓	Not reported	5
Kennedy et al. (1996) [66]	9 BD (2 M, 7 F; mean age: 33.3 ± 15.5)	12 controls (sex distribution not reported; mean age: 25.3 ± 4.9)	Not reported	Not reported	Patients medication free for least 2 weeks	MLT (between 8 p.m. and 6 a.m.) measured via blood and (over 24 h period) via urine samples.	Between-groups	Lower serum MLT in BD patients than controls at 1 a.m. and 5 a.m. (though euthymic patients had significantly lower MLT levels at 1 a.m. only). Interestingly, no significant difference between the patient and control groups in daytime or nocturnal urinary MLT.	↓	Not reported	5
Shafii et al. (1996) [64]	22 children (9 M, 13 F; age range: 8 to 17) of whom 18 had MDD, 1 dysthymia, and 3 with BD.	19 controls (11 M, 8 F; mean age/range not reported.)	Not reported	Children Depression Inventory, Children Depression Rating Scale (mean values not reported)	Two weeks of drug-naive or drug-free prior to the study.	MLT (between 6 p.m. and 7 a.m.) measured via blood	Between-groups	Significantly higher nocturnal MLT levels in patients (0.18 ± 0.14 nmol/L) compared to controls (0.125 ± 0.10 nmol/L). When the MDD group was split into non-psychotic (n = 15) and psychotic (n = 7) sub-groups, lower MLT in the psychotic subgroup (0.11 ± 0.11 nmol/L), but higher MLT in the non-psychotic subgroup (0.19 ± 0.15 nmol/L) relative to controls.	↑	MLT positively correlated with height (r = 0.09) and weight (r = 0.17) but relationship with symptom ratings, and other variables not reported.	5
Vederholzer et al. (1997) [61]	9 MDD (6 M, 3 F; mean age: 29 ± 7)	9 controls (sex not reported; mean age: 28 ± 7)	AIO not reported DoI 3.9 ± 3.7 (months) Range 2 weeks–10 months	HDRS: 32 ± 6	5 patients drug free and 4 patients who took psychotropic medication underwent a washout period of at least 3 weeks.	MLT (over 24 h period) measured via blood.	Between-groups	Slightly but not significantly lower 24 h and nocturnal MLT in patients (24 h: 33 ± 19 mL; nocturnal: 49 ± 26 mL) than controls (24 h: 36 ± 11 mL; nocturnal: 63 ± 24 mL).	↓	Not reported	7
Crasson et al. (2004) [58]	14 MDD (7 M, 7 F; mean age: 52 ± 8)	14 controls (6 M, 8 F; mean age M 59 ± 8, F 46 ± 5)	Not reported	HDRS: 33.5 ± 5.5	All patients underwent at least 2 week of washout period	MLT measured via blood (over 15 h period) and urine (over 24 h period).	Between-groups	A significant delayed MLT peak (77 min later) in patients (0130 h ± 23 min) than controls (0213 h ± 25 min).	–	Not reported	7

Table 3. *Cont.*

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Score
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Carvalho et al. (2006) [63]	Phase 1: 32 MDD (9 M, 23 F; mean age: 33.6 ± 1.6)	Phase 1: 32 controls (9 M, 23 F; mean age: 33.2 ± 1.7)	Not reported	MDD: HDRS: 17.7 ± 0.9 Controls: HDRS: 0.5 ± 0.2	All patients drug-free for at least 2 weeks	MLT levels (over 24 h period) measured via urine sample.	Between- groups	No significant differences in MLT between patients and controls in phase 1 (patients: 53.50 ± 4.60; controls: 55.60 ± 7.40) or phase 2 (patients: 41.60 ± 6.90, controls: 51.80 ± 4.50).	=	MLT did not correlate with age but relationship between MLT and symptom rating and medication not reported.	7
	Phase 2: 15 MDD patients (5 M, 10 F; mean age: 35.9 ± 1.9)	Phase 2: 15 controls (5 M, 10 F; mean age: 35.0 ± 2.2)		MDD: HDRS: 18.0 ± 1.2 Controls: HDRS: 0.5 ± 0.2							
Buckley & Schatzberg (2010) [57]	6 MDD (2 M, 4 F; mean age: 42.17 ± 11.79)	6 controls (2 M, 4 F; mean age: 35.3 ± 12.65)	Not reported	HDRS: 24.5 ± 2.07	Not reported	MLT (over 18 h period) measured via blood.	Between- groups	Significantly lower MLT in patients (22.67 ± 9.08 mL) relative to controls (47.81 ± 14.76 mL).	↓	Not reported	6
Khalegipour et al. (2012) [58]	42 MDD (14 M, 28 F; mean age: 37.83 ± 7.70)	50 controls (24 M, 26 F; mean age: 36.64 ± 6.82)	Not reported	Patients: BDI-II: 27.57 ± 7.15 Controls: BDI-II: 2.46 ± 2.38	One week prior to melatonin assessment, patients asked to not take any medication. (Medication doses/type and mean age of medication duration not reported)	MLT (over 16 h period) measured via blood.	Between-groups	Significantly lower nocturnal MLT level in patients (41.27 ± 10.29 mL) relative to controls (67.42 ± 16.17 mL).	↓	No significant sex differences in either group for morning MLT levels, but females had significantly reduced nocturnal MLT level in both patients and controls. Relationship between MLT and symptom ratings not reported.	6
Bumb et al. (2016) [65]	44 UD (19 M, 25 F; mean age: 33 ± 9.7) 37 BD (24 M, 13 F; mean age: 34.4 ± 11.8)	27 controls (11 M, 16 F; mean age: 29.1 ± 8.2)	Not reported	UD: HDRS: 18.5 ± 7 BD: YMRS: 17.8 ± 11.4	UD: 6 patients receiving antipsychotics, 24 antidepressants, and 21 receiving benzodiazepines. BD: 16 patients receiving antipsychotics, 4 antidepressants, 12 benzodiazepines and 4 receiving lithium.	MLT (between 8 a.m. and 10 a.m.) measured via CSF and blood.	Between-groups	Reduced CSF (8.5 ± 2.9 mL) (but not serum; 11.4 ± 5.2 mL) MLT in BD patients and reduced serum (9.7 ± 5.6 mL) (but not CSF; 9.1 ± 2.9 mL) in depressed patients, relative to controls (CSF:10.6 ± 7.5 mL; serum:10.4 ± 3.5 mL). No correlation was found between CSF and serum MLT levels.	↓	CSF and serum MLT levels did not correlate with age, symptom ratings (HAMD) or medication but correlated positively with BMI.	7

Table 3. *Cont.*

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics		Treatment History and Medication Duration	Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Score
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)				Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Parry et al. (2019) [60]	9 antepartum women with MDD (mean age: 28.1 ± 6.2)	17 F controls (mean age: 24.9 ± 4.1)	Antepartum AOI not reported DoI 26.3 ± 9.1 (weeks)	Baseline Antepartum patients: HDRS: 13.6 ± 4.1 (range 8–22); SIGH-ADS: 25.5 ± 6.3 (range:18–34) Healthy controls: HDRS: 4 ± 1.8 (range:1–7); SIGH-ADS: 8.9 ± 4 (range = 2–12)	All participants drug free	MLT (over 17 h period) measured via blood.	Cross-over The effects of early-night wake therapy (sleep 3 a.m. to 7 a.m.) and late-night wake therapy (sleep 9 p.m. to 1 a.m.) therapies (cross-over) in the antepartum and postpartum groups.	The baseline time from MLT onset to sleep onset approximately 2 h longer in antepartum patients than healthy controls. Early-night wake therapy realigned melatonin rhythm and increased sleep timing in antepartum depressed group. The postpartum group did not show melatonin rhythm abnormalities.	–	Not reported	9
	16 postpartum women with MDD (mean age: 31.0 ± 5.7)	8 F controls (mean age: 29.6 ± 6.1)	Postpartum AOI not reported DoI 18.2 ± 12.8 (weeks)	Baseline Postpartum patients: HDRS: 15.3 ± 6.1 (range 6–29); SIGH-ADS: 27.6 ± 8.5 (range:14–42) Healthy controls: HDRS: 1.5 ± 1.5 (range 0–4); SIGH-ADS: 3.8 ± 3.7 (range = 1–10)								

↓ denotes significantly lower MLT in patients compared to the healthy controls; ↑ denotes higher MLT in patients relative to the healthy controls; −denotes altered MLT secretion pattern in patients relative to healthy controls; = denotes no difference between the patient and the healthy control group in MLT level or secretion pattern. Abbreviations: AIO, Age at Illness Onset; BDI-II, Beck Depression Inventory Second Edition [75]; BMI, Body Mass Index; CPRS, Comprehensive Psychopathological Rating Scale [76]; CRG, Carney Roth Garside Questionnaire [77]; CSF, Cerebrospinal Fluid; DoI, Duration of Illness; HDRS, Hamilton Depression Rating Scale [36]; MLT, Melatonin; SZ, Schizophrenia; YMRS, Young Mania Rating Scale [78].

Table 4. Melatonin production in people with schizophrenia compared to those with depressive disorders and health controls.

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics			Technique Used to Measure MLT	Study Design	Key Outcomes			Study Quality Assessment (NOS Total) Scores
			Age at Illness Onset (AIO) and Duration of Illness (DoI)	Symptom Rating Measure/s (Mean ± SD)	Treatment History and Medication Duration			Group Differences	Direction of Group Effects	Association with Patient Characteristics	
Steiner et al. (1980) [67]	12 SZ (sex not reported; mean age: 35.3 ± 16.1)	Controls from an earlier study [79] utilised for comparison. Controls (not detailed)	Not reported	HDRS: 19.3 ± 14.9	Participants were not given medications 8 days prior and throughout the study. (Medication doses/type and mean age of medication duration not reported).	MLT (over a 21 h period) measured via blood.	Between and within analysis	Nocturnal MLT was significantly higher in SZ patients (57.2 ± 29.1 mL) than in MDD/DST+ (45.5 ± 32.1 mL), MDD/DST- (45.2 ± 27.9 mL) and IDD (29.2 ± 17.2) at 2 a.m. and also at 11 p.m. (SZ 45.6 ± 25.0 mL; MDD/DST+ 30.0 ± 26.7 mL; MDD/DST- 37.9 ± 28.6 mL; IDD 18.5 ± 7.5 mL). Nocturnal MLT in SZ patients was similar to that reported in the healthy group by Arato and colleagues (1984).	SZ < MDD SZ = Healthy Controls MDD = IDD	MLT did not correlate with demographics (sex, height, weight, height -weight ratio) except for age (r: −0.31) MLT did not correlate with depression (HDRS) ratings.	4
	49 MDD (sex not reported; mean age: 45.7 ± 14.5) 11 IDD (sex not reported; mean age: 39.4 ± 13.1)	Controls (not included)		MDD: HDRS: 22.9 ± 10.3 IDD: HDRS: 17.4 ± 7.5				MLT did not significantly differentiate the MDD/DST+, MDD/DST-, IDD groups. Only at 23.00 h MLT was significantly greater in MDD patients with normal dexamethasone suppression than MDD with dexamethasone suppression or IDD (see above for values)			

Abbreviations: AIO, Age at Illness Onset; DoI, Duration of Illness; IDD, Intermittent Depressive Disorder; MLT, Melatonin; HDRS, Hamilton Depression Rating Scale [36]; DST+, Dexamethasone Suppression Test Non-suppressor; DST-, Dexamethasone Suppression Test Suppressor; SZ, Schizophrenia.

Table 5. Studies examining medication output on melatonin production in patients with mood disorders compared to controls.

Author & Year (in Chronological Order)	Patients (n, Diagnosis, Sex and Age)	Healthy Comparison Group (n, Sex and Age)	Patient Characteristics		Study Design	Intervention & Procedure	Technique Used to Measure MLT	Key Outcomes		Critical Appraisal Skills Programme (CASP) Total Scores
			Age of onset (AIO) and Duration of illness (DoI)	Symptom Rating				Group & Medication Effect in MLT	Association with Symptoms	
Kennedy & Brown (1992) [68]	15 MDD patients (all F; 9 on desipramine, mean age: 38.2 ± 9.6 and 6 on adinazolam, mean age: 37.8 ± 13.6)	13 controls (all F, mean age: 25.2 ± 4.6)	Not reported	Patient on desipramine: HDRS: Week 0: 25.4 ± 5.2 Week 1: 19.2 ± 4.2 Week 3: 19.8 ± 8.2 Week 6: 18.8 ± 9.2 Patient on adinazolam: HDRS: Week 0: 23.7 ± 5.2 Week 1: 16.8 ± 4.9 Week 3: 17.3 ± 6.6 Week 6: 14 ± 8.1 Controls: HDRS: 2.3 ± 2.4	Longitudinal (6-week trial)	All patients drug free for at least 2 weeks at study entry, and received desipramine (n = 9) or adinazolam (n = 6) during the study	6-sulphatoxy MLT (over 24 h period at baseline, week 1, 3, 6) active drug therapy via urine.	At baseline, no significant difference was observed in 24 h 6-sulphatoxy MLT between patient (6.3 ± 3.4 nmoles/24 h) and controls (6.6 ± 0.8 nmoles/24 h). Patients taking desipramine showed significant MLT increase after week 1 (10.2 ± 4.9 nmoles/24 h) relative to baseline (6.6 ± 2.9 nmoles/24 h) but it decreased to baseline by week 6 (7.0 ± 2.2 nmoles/24 h).	MLT did not correlate with depression scores in controls and adinazolam-treated group, but a negative correlation ($r = -0.668$) between MLT and depression in desipramine-treated group after week 3.	11 (Funding information not available)
Childs et al. (1995) [69]	10 seasonal affective disorder patients (1 M, 9 F; mean age: 40 ± 2.9)	10 controls (1 M, 9 F; mean age: 38.3 ± 3.0)	Not reported	HDRS: Baseline: 37.3 ± 2.4 Week 1: 25.5 ± 1.4 Week 6: 20.6 ± 3.3	Longitudinal (6-week trial)	All patients were drugs free for at least 2 weeks at study entry; then received fluoxetine (20 mg/day) during the study	MLT (over 24 h period) measured via blood.	MLT did not differ significantly between patients and controls at any stage. In patients, significant MLT reduction at week 1 of treatment, relative to baseline, observed at 2.00 a.m., 2.30 a.m., and 3.00 a.m. This effect disappeared by week 6. (mean values not reported).	Relationship between MLT, symptom severity and demographics not reported.	10 (Funded by Wessex medical trust and Eli Lilly limited)
Szymanska et al. (2001) [70]	20 major depression patients (5 M, 15 F; mean age: 45.9 ± 8.4)	14 controls (8 M, 6 F; mean age: 41.5 ± 4.0)	AIO Not reported; DoI 2–5 months	HDRS, BDI (mean values not reported).	Longitudinal (6-week trial)	14 patients stopped antidepressants and underwent a 7-day washout period and 6 were medication free for 1+ year before receiving the clomipramine.	MLT (over 24 h period) measured via blood.	Mean MLT was significantly higher in patients (1494.4 ± 159.1 mL/24 h) than controls (986.7 ± 71.8 mL/24 h) at midnight, 2 a.m., and 4 a.m. No significant differences were observed in MLT levels from pre- to post-clomipramine treatment.	MLT did not correlate with symptom severity (HARDS and BDI). No significant difference in MLT found between patients with severe and moderate depression levels.	10 (Funding information not available)
Tan et al. (2017) [71]	13 MDD patients (7 M, 6 F; mean age: 26.85 ± 4.71)	13 controls (sex distribution not reported; mean age: 26.92 ± 4.13)	Not reported	Patients: HDRS: Week 0: 20.08 ± 2.91 Week 1: 13.5 ± 2.51 Week 2: 10.75 ± 3.37 Week 4: 8.13 ± 4.16 Week 6: 5.25 ± 3.33 SDS: Week 0: 53 ± 7.21 Week 1: 46.75 ± 5.92 Week 2: 42.12 ± 4.94 Week 4: 37.5 ± 5.58 Week 6: 33.75 ± 5.52	Longitudinal (4-week trial)	All patients given fluoxetine (20 mg) during the study; and 5 patients took estazolam or lorazepam during the first 2 weeks (if required).	MLT (over 24 h period) measured via saliva.	No significant difference in salivary peak MLT levels of patients (pre-treatment: 86.82 ± 35.72; post-treatment: 42.13 ± 24.43) and controls (68.18 ± 28.08). No significant difference between pre- and post-fluoxetine treatment MLT levels	MLT did not correlate with symptom severity.	10 (Funded by Nature science foundation)

Abbreviations: AIO, Age at Illness Onset; BDI, Beck's Depression Inventory [32]; DoI, Duration of Illness; HDRS, Hamilton Depression Rating Scale [36]; MDD, Major Depressive Disorder; POMS, Profile of Mood States [74]; SDS, Zung Self-Rating Depression Scale [80]; MLT, Melatonin.

4. Discussion

This systematic review evaluated currently existing evidence to identify possible aberrations in pineal gland (PG) volume and melatonin production in people with psychosis or mood disorders and their possible associations with patient characteristics, especially symptom severity.

4.1. PG Volume in Psychosis and Mood Disorders

Our review of existing findings in psychosis and mood disorders yielded consistent evidence of smaller PG volumes in first-episode and chronic schizophrenia patients as well as in people at a high risk of developing psychosis, compared to healthy controls, with no significant influence of symptom severity or medication status [16,17,28,29], and also some evidence of smaller PG volumes in schizophrenia patients, relative to mood disorder patients [16]. The same direction of effects (i.e., smaller PG volume in patients than controls) was present in people with bipolar disorders [16] but not significantly so in all studies [30,31]. Smaller-than-normal PG volume was also present in people with major depression, independent of symptom severity [16,18], although there was also evidence of this being applicable to only certain sub-types, or to those experiencing 'loss of interest' as a symptom [30]. Taken together, these findings suggest that smaller-than-normal PG volume may represent a transdiagnostic biomarker for schizophrenia and mood disorders, deserving of further study in relation to sex differences, functional and clinical outcomes, including treatment responsiveness.

4.2. MLT Production and Secretion Patterns in Psychosis and Mood Disorders

The majority of the existing studies conducted in schizophrenia observed lower-than-normal MLT in acutely unwell as well in chronic patient groups [45–48] or an atypical pattern of MLT secretion in this clinical population [49–51]. The studies, however, also showed some differences between acutely ill and chronic patients [48] and there was cross-sectional evidence of possible normalisation of MLT secretion pattern in medicated patients [51], suggesting that MLT production might be influenced by both illness and medication-related factors. As yet, there are no published longitudinal investigations of such possible influences in MLT production of schizophrenia and related populations.

Our review of studies in people with major depression revealed considerable evidence of lower-than-normal MLT, especially nocturnal MLT [49,52–57], or atypical MLT secretion patterns, including delayed peak [59] or delayed MLT onset [60]. However, this was not found in some studies [62,63] and appeared in others to be dependent on presence of psychotic symptoms [64] or methods for assessing MLT [66]. Some data showed an association between lower MLT and greater depression severity [53]. The findings in bipolar disorder patients were also mixed, again suggesting that MLT in major depression and bipolar disorders may be sensitive to multiple influences. Lastly, there was some evidence of a transient lowering of MLT following the initiation of certain antidepressants in drug-free patients [desipramine [68]; fluoxetine [69]] suggesting that medication may have been a confounding factor and contributed to the mixed pattern of MLT findings in mood disorders. Interestingly, all four studies that investigated medication effects on MLT showed either no MLT difference between the patient and control groups (3 studies), or higher MLT in depressed patients relative to controls (one study), at baseline. This is hard to explain and may relate to some non-specific patient selection bias in such studies (e.g., selection of only those patients who were considered safe enough to withdraw medication for some time in order to meet study eligibility criteria).)

4.3. Limitations of the Reviewed Evidence and the Review Processes

The findings of this systematic review should be considered taking a number of limitations into account. First, most of the reviewed studies had small-to-moderate sample sizes (with $n < 50$ per group), providing limited power to compare PG structure and

function between the patient and healthy control groups and to investigate sex differences in diagnosis-related effects; therefore, they are likely to have been underpowered to meaningfully examine any associations between the PG structure/function and patient characteristics of potential relevance, especially symptom profiles. Second, a number of studies either did not provide sufficient information on patient characteristics or did not examine them in relation to the PG structure or function, which would have allowed greater insight into this topic and a clearer interpretation of negative results (for example, 31). Third, the methods for assessing MLT varied greatly between the reviewed studies with MLT assessed via different routes (in blood, urine, CSF) and the samples collected at different times (e.g., one-off, in the morning or evening, over 8–24 h). Fourth, there were only four studies examining antidepressant effects on MLT in mood disorders, and all of these were of fair quality at best (see Supplementary Table S2); and there were no studies assessing antipsychotic effects on the PG structure or function in people with psychosis. Making solid conclusions about diagnosis or symptom related differences without a clear understanding of medication influences in the PG structure or function is difficult. Lastly, we deliberately focused on psychosis and mood disorders but it is possible that the PG structure and function are also affected in other disorders, and did not conduct a meta-analysis to formally assess the effect of the moderator variables (due to the limited number of studies with required power and information available for review), restricting confidence in some of our findings until they are examined and supported by future research.

5. Conclusions and Future Directions

Our review provided consistent evidence that smaller-than-normal PG volume represents a transdiagnostic biomarker across psychosis and mood disorders, and possibly other disorders linked with sleep dysfunction. We also found lower-than-normal MLT as well as aberrant MLT secretion pattern (flattened or shifted rhythm) in psychosis and mood disorder patients, relative to healthy controls, but the findings on these measures appeared fragile, possibly due to various influencing factors, such as severity of certain symptoms, specific symptom profiles and medications. With these findings, we make a number of recommendations for the future scientific enquiry in this area.

First, we suggest that future clinical studies should employ a transdiagnostic approach involving multiple patient groups and assessment on multiple symptom dimensions, including the quality of sleep and sleep disturbances. A similar approach can be taken to clarify the association between specific symptom dimensions and PG volume and function in non-clinical samples, especially to rule out medication-related confounders and potentially identify underlying latent factors.

Second, we emphasise that future studies should have large enough sample sizes to detect diagnosis related effects of small-to-medium size. The studies should also aim to include sufficient number of males and females to allow meaningful investigation of sex differences, given their influence in many brain structures and function [81] as well as in prevalence rate, prognosis, symptom profile and presentation, and treatment response in many disorders, including schizophrenia [82,83] and affective disorders [84].

Third, we recommend future studies to consider the chronotype of study participants as well as take any regional and seasonal variations into account for both the control and patient groups, given their relevance for mental disorders as well as MLT production [85].

Fourth, we highlight the need for multimodal investigations involving assessment of both PG structure and function in the same samples to clearly understand how PG volume aberrations, with or without covarying for whole-brain volume, may influence MLT production in the short and long-term in interaction with age, BMI, sex, and possible illness- or symptom-related influences in clinical and non-clinical samples.

Finally, we encourage future studies to examine how currently used antipsychotics for treating psychosis might influence the PG volume and MLT in parallel to changes in sleep parameters, and also consider the use of melatonin as potential treatment avenues for reducing side effects of antipsychotics [86–88], ameliorating various cognitive and

information processing disturbances typically present in people with schizophrenia [89,90], and treating sleep disturbances in a range of psychiatric disorders, including but not limited to psychosis and mood disorder [91,92].

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/brainsci13050827/s1, Table S1: Newcastle-Ottawa Quality Assessment Scale (NOS) scores for the selected studies., Table S2: Critical Appraisal Skills Programme (CASP) scores.

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