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Circadian Rhythm: Enhancing Brain Synchronization and Cognition

Uthirakumar Devaraj, Elumalai Balamurugan

Department of Biochemistry and Biotechnology, Faculty of Science, Annamalai University, Tamil Nadu, India

ABSTRACT

Cognition is impaired in many neuropsychiatric disorders and the quality of life is severely affected. A key mechanism for sculpting communication patterns between large-scale brain networks that underpin cognition and its breakdown in neuropsychiatric disorders is synchronous electrophysiological rhythms. According to a study, light has a wide range of effects on the synchronization of circadian rhythms with the external environment and it is found that light influences the urinary excretion of melatonin and controls sleep. Autonomic and neuroendocrine responses such as feedback regulation and the involvement of the immune system have also been shown to influence the circadian rhythm. There have been major advances in our understanding of the retinal photoreceptors mediating these non-image-forming light responses over the last two decades, as well as the neural pathways and molecular mechanisms that generate and energize circadian rhythms in the phase of the light/dark (LD) cycle. Our understanding of the mechanisms by which lighting impacts cognitive processes, on the other hand, is more misleading. Light's effect on different cognitive processes is complex. Indirect effects may also arise due to disrupted circadian rhythm, in addition to the direct effects of light on consciousness. In studies that rely on various cognitive and sensory processes, different assays have been used, which can also contribute to variable outcomes. The physiological basis of these responses and the influence of various lighting environments on cognitive processes are summarized here, taking into account their effects on circadian rhythms, sleep and arousal.

KEYWORDS: *cognition, circadian disruption, sleep disturbance, neuropsychiatric disorders*

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INTRODUCTION

Numerous neuropsychiatric disorders are characterized by cognitive dysfunction. The symptomatic presentations of different psychiatric disorders are deficiencies in cognitive domains such as selective attention, working memory and executive function (Bedrosion et al 2017) In Attention-Deficit/Hyperactivity Disorder (ADHD), schizophrenia, Autism Spectrum Disorders (ASD), anxiety and Obsessive-Compulsive Spectrum Disorders (OCD), attention impairments are found. Inadequate planning and working memory are the major manifestations in ADHD, ASD causes inflexibility, impaired decision-making (Ding et al 1994). Slow initiation of action is the main symptom of major depressive disorder (MDD) and action avoidance issues in OCD and bipolar disorder. Combinations of these with other deficits, such as schizophrenia, are also common. Cognitive impairments lead to real-world disability and are a primary indicator of functional disability. The prime interest in neuropsychiatric medicine is to elucidate the mechanisms that give rise to such impairments and to establish successful therapies (Foster et al 2014) Light does have major effects on the organism and has the power to change circadian rhythms, as well as have effects on the nervous system and the body's ability to control its temperature. It may influence sleep cycles and produce cognitive effects (Foster et al 2005). In the current scenario, the effects of light on circadian rhythm are of special concern, as inadequate light exposure has recently become an extremely common issue for most of the world's adult population (Guler *et al* 2008). This entails not only shift work and jet lag, but also visibility of night light and the impact of cell phones, computers, tablets and smartphones (Freedman et al 1999). Extended periods of abnormal light exposure can lead to circadian disruption, resulting in changes in metabolism, sleep and cognition and increased risk of metabolic and cardiovascular disease (Hastings et al 2014). In several studies of circadian disruption in animal models, sensitivity to irregular light/dark (LD) cycles have been involved (Hannibal et al 2000). While these studies have been significant for understanding how circadian disturbances impact various processes, the immediate effects of light are not easily related to the long-term implications of irregular light exposure. Specifically, both the direct effects of light as well as the irregular LD cycles produces effects on the circadian system which thereby produces physiological changes. These changes, in turn, affect the circadian function thereby influencing sleep, which creates a negative feedback effect on metabolic and physiological processes. On top of this, we will now summarize the effects of light on sleep (Reppert et al 2002), arousal (Preitner et al 2002), cognitive processes (Ralph et al 1990) and we will also discuss the effects of circadian disturbance on cognition.

Rhythm and homeostasis

Homeostasis, which is consistent with life within narrow limits, is a central principle in biology (West et al 2015). However, the invention of methods that measure physiological and biochemical variables over a 24-hour cycle repeatedly and often non-invasively, indicated that normal rhythms can be superimposed on this stability (Turek et al 1985). During the day, human beings appear to have a core temperature of about 1-2 degrees higher than the temperature the day prior, lest they become too hot, and as they age, they have more water and waste excreted through urination and feces which causes the core temperature to drop over the night. From a scientific-data point of view, human beings are diurnal animals. Rhythmic advances are ubiquitous in physiology and biochemistry (Welk et al 1995). These observed rhythms derive partly from our daily life and the rhythmic world in which we live; they also arise from the internal body clock (Marazziti D et al 2010). One of the best ways to explain the presence of this body clock is to execute a 'constant routine' as follows

1. The observed endogenous rhythm should originate from the inside of the body, in the constant routine (Ruby et al 2002). The production of this rhythm is due to the 'body clock.' (circadian pacemaker).
2. Influences on environment and lifestyle are present as the two (full and dashed) different rhythms and are not the same (Mei jer et al 2015); the distinction between these two rhythms is known as exogenous rhythm.
3. These two components are in phase with subjects living in a traditional lifestyle (Lucas et al 2014). The body's clock, which is synchronized with the environment and the body, raises its temperature during daytime, thereby decreasing the core temperature during the night due to body's inactivity (.Karalt soreos et al 2011)

Both physiological and biochemical variables refer to these basic principles, while detailed variations depend on the variable being considered (Le gates et al 2014). The three main differences include normal rhythm pacing, the presence of the exogenous component and the relative strength of both rhythm components (Moria et al 2013). A variety of assessments, including cognitive function measures, are carried out under conditions that are tested as carefully as possible - the subject is set and made comfortable, the ambient temperature (Ouyang et al 1998), humidity and light (Stephan et al 1972) are continuously maintained and previous behavior and food/fluid intake are standardized. Although body clock effects are still present in these situations, the effects of exogenous variable changes would have been reduced.

Body clock: Properties and functions

The body clock consists of the paired suprachiasmatic nuclei (SCN) located in the brain's hypothalamus (Caviochen et al 1998). The body clock is responsible for temperature regulation, hormonal secretion, sleep-wake cycles and feeding. Although the rhythms indicate a period of exactly 24 hours when measured in subjects living in the universe at 24 h (same as the solar day), this interval, measured in time isolation, is closer to 25 hours (De coursey et al 1997). This period of around 25 hours was originally assumed to be the inherent time of the body clock and is usually believed to overestimate the true value due to the impact of luminous exposure during the wake-hours. The circadian rhythm must precisely match the solar day to make the body clock functional (24 h). This transition takes place 24 hours a day and is directly or indirectly triggered by the climate. The dark-light cycle is the most important timekeeper of mankind (Foster et al 1991). Other clocks, such as exercise, social pressure and food consumption seem to play a minor role when compared to the light-dark cycles which on the other hand occurs every day. However, the circadian clock will operate harmoniously under normal circumstances to change the body's mechanism. This correlation between time of light exposure and the body clock phase shift is called a phase response curve (PRC) (Colwell et al 2011). The size of the phase changes created also depends on the intensity of lights; domestic lighting is sufficient to transform the circadian clock into 24 hours in many individuals with very limited natural daylight exposure. Melatonin consumption may alter the phase of the body clock causing half-sleep in the afternoon and early evening or the early mornings. Upon the introduction of light, light inhibits the secretion of melatonin which previously was the maximum secretion, to begin with, has been suppressed to the lowest output and now can be the peak output inside the darkness (Zelinshi et al 2014). Thus, light effects can progress before the light has reached the lowest output and melatonin can be the maximum secretion (and establish a circadian rhythm) (by suppressing melatonin secretion and so preventing the phase-delaying effect that melatonin would have exerted at this time). The clock markers are rhythmic variables whose times are closely correlated with the body's clock. Core temperature and melatonin secretion are the two most-used parameters in circadian rhythm assessment. Core temperature, which relies on rectal temperature recording, is comparatively cheap to monitor. This marker minimizes exogenous variable intervention. In practice, this suggests that core temperature measurement has been established to adjust the temperature rhythm to exogenous effects of the sleep-wake cycle when the subject is in constant routine (Ritcher et al 1971). Melatonin is costly to evaluate but can be measured in plasma (requiring routine sampling of the blood) or urine (requiring frequent emptying of the bladder). Since the melatonin rhythm is not disturbed by sleep and exercise, a constant routine is not required, but as light suppresses the secretion of melatonin, the subject must be kept in dim light. The period of onset of secretion (DLMO, dim light melatonin onset) is often used as a phase marker instead of the entire length since melatonin is typically not secreted during the day. There are two major physiological influences on the body clock.

1. Firstly, it encourages daytime behaviors (physical activity, cognition) and distinguishes them from night-sleep (when mental, physical and biochemical recovery and restitution occur).
2. Secondly, it prepares people to sleep and wake up in the morning, involving an organized series of biochemical and physiological activities.

In short, we are rhythmic creatures adapted to our rhythmic environment: at night, low core temperature and sympathetic nervous system (SNS) activity help us to bias sleep and metabolism towards fat metabolism and glucose conservation (for the brain); at late night and early morning, the body clock prepares us for awakening and at the daytime, high SNS activity and the core temperature is experienced (Moore et al 1995). This integration between us and our environment has tremendous inertia and protects against intermittent changes in our lifestyle (e.g., daytime night or night waking) or our environment (e.g., night lightning flashes or daylight dark thunder clouds) that do not alter the body clock function (Nelson et al 1981) This hefty body clock property has a high ecological benefit but causes problems changing the person's sleep-wake cycle, e.g., after a time zone shift or during night work.

Cognitive rhythms and factors influencing them

The normal relationship between cognitive output, the body clock, and sleep-wake cycle must be understood to understand shifts in time-zone problems and night work. Sleep comfort, sleeping ability and the probability of waking up are all linked to core temperature rhythms and melatonin secretion. Sleep is best when the core temperature decreases or falls (melatonin rises or rises) and when the core temperature rises (melatonin is falling or low). Spontaneous awakening occurs as core temperatures rise (melatonin is falling). This parallelism between sleep propensity and core temperature was interpreted as proof of causality that often occurs in melatonin and adrenaline secretion profiles. The current view is that all these rhythms function concerning the SCN performance and the exact causes of sleep tendency rhythms need to be known.

When exogenous stimuli are standardized or held stable, the cognitive output is calculated primarily by integrating effects due to the circadian variable (from body clock to core temperature rhythm) and time-wake. This combination underpins many models of alertness. One way to distinguish these two elements contribution is to use the "forced desynchronization" protocol. Subjects have an intermittent duration of 21, 27 or 28 solar hours (defined as the time taken to complete an imposed sleep-wake cycle). With a 28-hour 'day,' the subjects' retirement, rising and feeding, as well as all their everyday activities and the imposed light-dark cycle, each 'day' becomes 4 hours later. The body clock cannot be adapted to these time limits and thus displays a 'free-run' period exceeding 24 hours (Fig 1).This time interval is called a beat cycle. Daily data (e.g., cognitive output) were collected over at least one beat duration. Any data point can then be interpreted with the sleep-wake cycle and body clock (circadian time).

When taken into account of the diurnal output patterns, 'simple' ones (with a relatively small cognitive component) typically follow the core and late afternoon temperature, whereas those with more "complex" tasks (with a larger cognitive component) are usually more pronounced earlier. The potential explanation of these different profiles is the combination of rhythmic components parallel to core temperature and an ingredient that decreases with an increasing time. The relative significance of these two variables also depends on the essence of the output task. The simple tasks are less affected by time than complex tasks. The degree to which the time wake effect was based on the cognitive level of a task could be evaluated using different circadian and time wake components with forced desynchronization protocol (see Fig. 2).

The collapse of various performance tests during a constant procedure will be an alternative measure of the above interpretation (Hashtings et al 1997). Studies have explored many tasks involving various levels of awareness using this protocol. The findings were, however 'de-trended' before the study because the purpose of the research was to compare the circadian profiles of certain tasks and a time-wake decline was confusing (Jung et al 2010). Deterrent effects have eliminated both realistic and timely consequences such that the volume of disturbance cannot be perceived unequivocally.

The cognitive output often affects total or partial, acute or chronic sleep loss. Sleep losses of 2 h will result in measurable reductions, which become true options for people who try to sleep during the day when sleep is reduced by external sleep disturbing and attempting to sleep without extending minimum temperature (Moore et al 1972).

People vary in terms of their lifestyles and circadian rhythms, which define their chronotype (Hattar et al 2002). The chronotype of an individual is calculated by the Horne and Ostberg questionnaire which addresses the individual's preferred sleep patterns at periods when they feel more or less capable of doing mental or physical activities and times of relaxation. The difference in the core temperature process remains in a constant routine, which means that the difference is due to the body clock output regardless of the changes in the sleek cycle. Recent work suggests that polymorphism occurs in one of the human clock genes, PER3 and modifications due to the “extreme sleep cycle changes” (Hughes et al 2016).

Irregular sleep and sleeping 'anchor'

Although the sleep-wake cycle varies both during the time zone transition and during night work, the adjustment does not occur each day (except for very quick changing rotation) and is usually predictable. In a military setting in which the active sleep-wake cycle is sometimes and unpredictably changed (Hughes et al 2015). Furthermore, organizational pressures could make it impossible to sleep for eight hours a day causing impaired cognition.

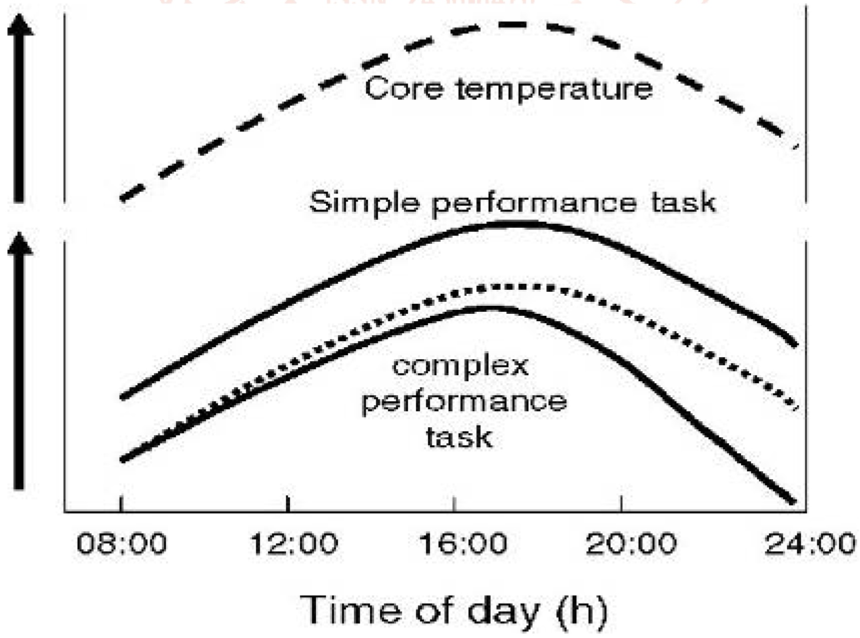

Fig 1: Diagrammatic illustration of the diurnal rhythms of core temperature (top, dashed line) and ‘simple’ and ‘complex’ performance tasks (bottom, full lines). The upward arrows indicate higher temperature and better performance. For the simple performance task, the negative effect of time awake is small, and so the rhythm parallels that of core temperature. For the complex performance task, the effect of time awake is more marked; this makes the peak slightly earlier and the fall in performance after the peak steeper. The dotted line shows the time course the complex performance test would take in the absence of effects of time awake. For more details, see text. Based on Valdez et al. (2008).

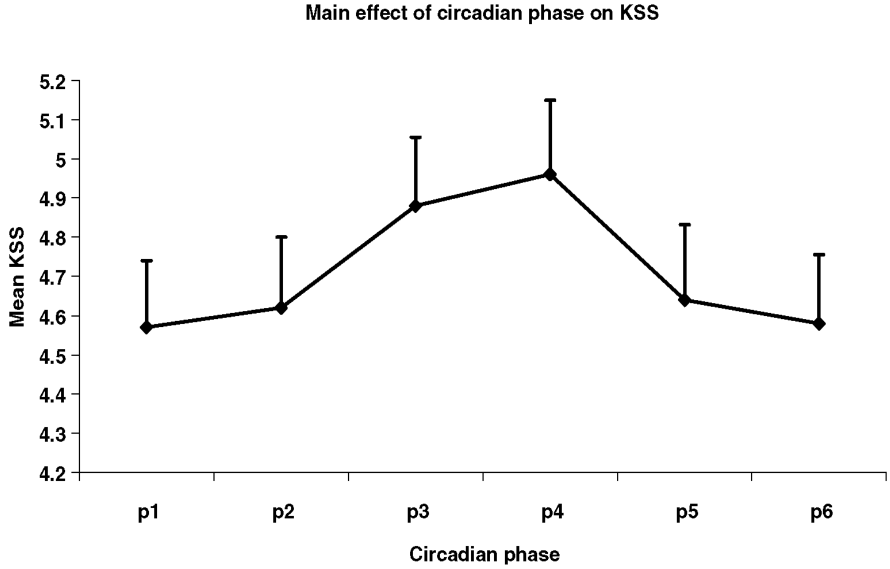

Fig 2: Mean (+SE) scores for the Karolinska Sleepiness Scale (KSS) taken from subjects undergoing a forced desynchronization protocol (imposed 'days' of 28 h). Assessments of KSS were made 1, 4, 7, 10, 13 and 16 h after waking (total waking time was 18.67 h per 'day'). Results shown relative to the circadian phase (p1–p6) of core temperature where p1 indicates a 60º'bin' (where 360º equals the free-running period, tau) centered on the time of temperature maximum (30ºbefore the maximum to 30º after the maximum), p2 indicates a bin 30–90º after this maximum, p3 indicates a bin 90–150º after this maximum, p4 indicates a bin 150– 210º after this maximum (centered on the time of the temperature minimum), p5 indicates a bin 90 150º before the temperature maximum and p6 indicates a bin 30–90º before the temperature maximum. Taken from Harrison et al. (2007).

Implications of 'sleep anchor'

The application of these results to cognitive performance is unclear since the studies just mentioned did not test them. However, it is fair speculation that the findings have some applicability as a cognitive performance variable parallels the core temperature. Even if 4-hour sleep does not control your body clock every day at the same time, this routine has two advantages. First, the measured rhythm (including the exogenous component), which can also be applied to cognitive performance rhythms, is stabilized. The second benefit of two 4-hour sleep block is that the waking time between sleep decreases, minimizing the effect of wake time and cognitive performance fatigue. Possible applications for both will now be considered briefly. The phase consists of the measured circadian rhythms can be extended to night workers. Standard 4-hour sleep on days of late morning rest (the rest of their sleep is taken if it's convenient) would allow night workers to embrace the transition to night work on those rest days. Sleep can also be helpful because of time-zone changes for those who regularly adjust sleep hours. This problem can be understood by duty tours involving long-distance flights with night work and time zone shifts. Reviews of sleep log and actimetry show that sleep remains fractionated and some sleep is taken home during night time, irrespective of whether that time correlates with local time.

Unknown issues in these periods of sleep help to regulate the desirable circadian patterns of cognitive function at home. Such sleeping habits can nevertheless be an indication of self-selection in persons who can manage their lifestyle issues more easily. The other advantage of 'anchor sleep' is that it takes more than a day's sleep. This operation not only decreases the time wake (since last sleep) but may also be more appropriate for complicated schedules of work. When evaluating the output decrease associated with sleep deprivation in a variety of cognitive tasks, the definition of "broken sleep" has been detailed. These authors systemically modified the length of a night 'anchor sleep' and the length of a nap. They found that the decline in cognitive performance was due to total sleep loss every day, irrespective of whether one or two sleep sessions were taken (Hattar et al 2006). This study supplemented previous research showing that the quality of sleep is not adversely affected by more than one sleep a day and that a lack of sleep can as effectively reduce cognitive function.

A sleep routine usually divides sleep into equal amounts. 'Split sleep schedules are feasible and can be used for space operations that involve inadequate night sleep due to mission-critical in scheduling, to improve flexibility for sleep/work schedules (Lucas et al 1999). This typically applies to all existing industrial practices, including restriction of sleep, night activities and changing activities.

Concluding remarks

The cognitive disorder is a debilitating characteristic of many neuropsychiatric conditions that impair skills such as selective care, work memory, executive control and decision making. These interventions are rooted in decades of fundamental research, indicating that the functional framework of cognition relies on organized communication on various spatial time levels in the brain. Synchronized rhythmic behaviour in healthy people during the cognition and rhythmic disturbance in psychiatric disorders demonstrate the importance of organized communication. We suggest that non-invasive, secure and centred cognition-enhancing treatments be accelerated through capitalizing neuromodulation therapy that selectively focuses on the physiological patterns of cognitive dysfunctional coordination that are affected. Since different disorders are defined by patterns of hyper connection and hypo connectivity, circadian rhythm allows bidirectional communication handling and suggests its ability in various clinical disorders. Also, neuronal modulation sub threshold decreases the risk of serious pain and side effects such as seizures. Different studies have tried to combine cognitive performance with concomitant neuroimaging such as EEGs, MEGs and functional brain imaging, including a broad variety of discussions about how these concomitant measurements may be enhanced. Neuromodulation parameters are modified online to reflect the physiological characteristics of the cognitive activity networks in such designs to increase the efficacy of neuromodulation. A better understanding of the distribution of the electric fields spatially at different relative stages, particularly during multisite neuromodulation can lead to improved neuromodulation design, with longer-lasting outcomes. The results of neuromodulation can also be characterized by an analysis of neural networks using graphic theoretical approaches in networking science to describe the broad communication dynamics in the brain holistically. Though rhythmic synchronization still begins at an advanced stage that permits sophisticated multimodal neuromodulation designs for the performance and analysis of circadian effects will allow the clinic's best applications. In conclusion, the development of intervention based on rigorous observations of high-scale electrophysiology during cognition provides exciting potential for the use of rhythmic neuromodulation with synchronization of functionally important brain rhythms in different neuropsychiatric disorders which will provide good and lasting relief from the cognitive deficiencies.

Conflict of interest

The authors declare no conflict of interests

Author contributions

U.D collected the literature and drafted the manuscript. Dr. E. B analyzed and corrected the manuscript.

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