The International Journal of Indian Psychology
ISSN 2348-5396 (Online) | ISSN: 2349-3429 (Print)
Volume 8, Issue 2, April- June, 2020
DIP: 18.01.046/20200802, DOI: 10.25215/0802.046
http://www.ijip.in

Research Paper

The clock is ticking: a critical review of understanding the neural basis for biological clocks

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ABSTRACT

Time and biology share a unique relationship. The biological clock plays a pivotal role in maintaining our daily well-being. There is a presence of cycles which vary from ultradian (short) to circadian (long). The rhythms produced by biological clocks, are responsible for the interaction with cells from various parts of the body. Biological clocks drive basic behaviours such as eating and sleeping as well as complex behaviours such as seasonal migration. The clocks that regulate processes of life do so over an extensive range of time: from seconds of neuronal activity to changes in the season that makes a shift in the daylight over the course of one year. Our biological clocks not only influence our sleep-wake cycles but also hold an important role in regulating other day-to-day activities such as alertness, metabolism, appetite, mood, so on. A dysfunction in biological clock is linked to various disorders such as diabetes, insomnia and depression, among others. The following review is an investigation of timing as it has formed a rich literature. It lays emphasis on the relationship between neural basis and sleep-wake cycle. It addresses the role of serotonin because it synthesizes melatonin, a hormone that is released at night which helps in regulating the body's biological clock. It also addresses the relationship between biological clocks and its neural basis, the role of pineal gland, genes and environment. Lastly, the review emphasises on the need for more research in drug efficacy since there are studies that show a link between the timing of drugs based on our biological clocks.

Keywords: *Circadian Rhythm, Biological Clocks, Superchiasmatic Nuclei, Drugs*

Biological clocks can be defined as the innate timing machine of an organism. Biological clocks are made up of specific molecules which are responsible for the interaction with other cells in the body. Circadian rhythms, on the other hand are the mental and behavioural pattern that follow a day-to-day cycle. They are primarily responsible in responding to light and darkness in the environment. They are found in most living things, including plants. These clocks allow living beings to organise their activities along with a cycle that is predictable, day and night; as a result, giving them a sense of time.

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Received: April 18, 2020; Revision Received: June 3, 2020; Accepted: June 25, 2020

Anatomy of sleep
Even though the term biological clock is used interchangeably with the term circadian rhythm, they are only related, but not the same. Biological clocks are responsible for the production of circadian rhythm. There are diverse lengths when it comes to biological activities: short rhythms to rhythms that last for a day, a week, a month or sometimes even longer and biological clocks are responsible for these rhythms. Scientists have proved that the biological clock present in mammals is located in small structures called the *superchiasmatic nuclei (SCNs)*. It is located in both the left and right hypothalamus and borders the third ventricle. The suprachiasmatic nucleus (SCN) acts like a pacemaker in mammals. The pineal gland, which on the other hand acts as a pacemaker in other phyla. Biological clocks generate circadian rhythms in peripheral tissues. The biological clock in the SCN anterior hypothalamus is responsible for the regulation of human behaviour and changes 24-hours. Studies have shown that the part inside the brain is capable of maintaining a basic, independent rhythm even if the external cues of the cycle (Day/Night) is removed. Glutamate Amino Butic Acid is released by the brain stem reduces arousal, by reducing the activity of action potential. In order to maintain the accuracy, the central biological clock resynchronizes itself almost every day with external stimuli such as brightness, through the optic nerves which in turn bring the information from special ganglion cells in the retina ("THE BRAIN FROM TOP TO BOTTOM", 2019). From each SCN the output pathways consist of axons that inner-tube mainly the hypothalamus. A couple of axons are also found in other parts of the diencephalon, while some others to the mesencephalon. Both SCNs send signals through pineal gland.

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Serotonin
Studies have showed that serotonin plays a vital role in the regulation of sleep. High levels of serotonin would mean lower levels of sleep. Along with this, serotonin is believed to help regulate mood, appetite and digestion. Thus, consuming foods high on amino acid tryptophan helps in keeping the level of serotonin in check. Unfortunately, the lifestyle chosen by human beings is unhealthy leading to a disruption in the production of serotonin which may cause sleep disorders such as insomnia. It also regulates numerous biological processes including cardiovascular function, bowel motility, ejaculatory latency, and bladder control ("The Expanded Biology of Serotonin", 2019).

An experiment was conducted on sleep-wake stages in freely moving rats through polygraphic recordings to study brain 5-HT (Serotonin neuron) functions in sleep. Using a slip ring, EEGs from the frontal cortex, EMGs from the cervical muscle and EOGs from chronically implanted electrodes were derived. Rats that belonged to the experimental group were mostly trained to the light-dark cycle in a period of 10 days after the surgery. The rats were food deprived before injecting TSOI (tryptophan-degrading enzyme called tryptophan side chain oxidase) as well as during experiments. As soon as the TSOI was administered, rats became inactive and less alert and their body movements also reduced. The rats that belonged to the control group started eating food when food was given whereas TSOI treated rats did not seem to show appetite, despite being under fasting environment. The EEG showed that the slow-wave sleep, one that is observed during the light phase, was disintegrated into patterns that looked like fragments. The sleep-wake cycles and body movements returned to normal when the 5- HT levels were regained. The results concluded that 5-HT plays a vital role in the circadian sleep-wake cycles.

A study conducted by Ursin (2002), concluded that serotonin, along with performing an important function in the regulation of circadian rhythm, has a dense serotonergic terminal plexes in the brain. The SCN receives information from the dorsal raphe nucleus, and serotonin SCN is said to modulate circadian rhythms because of its sensitivity to light (Ursin, 2002).

Pineal gland

Despite a plethora of studies conducted in the field of biological clocks, the results are still unclear as to how the central biological clock in the SCN is capable of regulating so many human cyclical behaviours. Pineal gland is located on the roof of diencephalon in the human body produces melatonin, which helps maintain circadian rhythm. It does not amount to a clock on its own; rather the melatonin synthesis is controlled by signals that is received from the superchiasmatic nuclei. Each and every day the pineal gland produces melatonin. As it rises, the body temperature falls, resulting in sleepiness. As the sun rises, the gland's activity is inhibited and the level drops.

Prefrontal cortex

Experiments have concluded that prefrontal cortex mediates normal sleep physiology, dreaming and also in sleep-deprivation phenomenon. During the non-rapid eye movement (NREM) sleep, a high voltage occurs in the frontal cortical activity and brain waves are slower compared to other cortical regions. Several neuroimaging studies have found striking results on the effects of one night's sleep deprivation on the blood flow to the areas of pre-frontal cortex. The majority of neuropsychological performance assessments utilise total sleep deprivation thus depriving subjects of both, the NREM and REM stages of sleep.

The role of genes and environment

Genes also play a significant role in influencing the body's biological clock. The system requires genes as well as light to function. In order to keep the 24-hour cycle going, the brain requires sunlight through eyes in order to reset each day. When human beings are not exposed to light, in other words, kept in continuous darkness, the body's cycle usually lengthens to 25 hours. Similarly, when there is lack of genes that assist in controlling the clock's cycle, the cycle may drift even further. Thus, it is very important for the genes and environment to work hand in hand to keep the system functioning well.

The importance of biological clocks during drug intervention

Due to unhealthy lifestyles choices such as late-night work may lead to stress and irregular sleep schedule. It also has an adverse effect on other physiological processes such as metabolism, movements, differentiation, excretion and so on. Circadian rhythms hold a vital place in medicine practice. It can also affect responses of patients to tests and diagnostics. In order to optimize treatment outcomes**,** rhythmicity in the pathophysiology of medical conditions is the rationale for chronotherapeutics (Smolensky, 2006). Recently, there has been a lot of discussion regarding the usage of body clocks to make drugs more effective. In other words, studying more about the body clocks may prove to be effective to physicians, to time the delivery of medications.

CONCLUSION

Circadian timing is usually similar across many species, along with behaviours, hormones and physiological processes. It is vital to understand how biological clocks assist us to further understand and treat sleep disorders, obesity, mental health, so on and so forth. It can be concluded that research which involves light and dark state alteration is usually conducted on animals to understand biological clocks in a more elaborate way. The SCN clearly represents a very pivotal aspect of the circadian organisation of mammals. No other neural structure is said to play a central role in the circadian pacemaker. Evidence suggests that SCN plays a central role in the generalisation of circadian rhythms: If the SCN is isolated or destroyed, it hampers a number of circadian rhythms, as well as the electrical stimulation of the SCN can alter circadian rhythms. The use of Chronotherapy-progressively accommodating an individual's sleep-wake cycle to time the delivery of medicines so that it is more effective can to be an interesting area of study for future implications.

REFERENCES

Brzezinski, A. (2016). Melatonin and Sleep in Humans. Serotonin and Melatonin, 381–386. doi: 10.1201/9781315369334-27

Circadian Rhythms (2019). Retrieved from https://www.nigms.nih.gov/Education/Pages/Factsheet_CircadianRhythms.aspx (1982). Copyright. Hibernation & Torpor in Mammals & Birds, iv. doi: 10.1016/b978-0-12- 460420-9.50003-9

Gillette, M. U. (2005). *PHYSIOLOGY: Biological Clocks Coordinately Keep Life on Time. Science, 309(5738), 1196–1198.* doi:10.1126/science.1111420

Hunter Stuart. (2013, June 6). Study Shows Living In The City Speeds Up Biological Clock. Retrieved from https://www.huffingtonpost.in/2013/06/06/city-circadian-rhythm-_n_3397194.html

Kudo, T., Horikawa, K., & Shibata, S. (2007). *Circadian Rhythms in the CNS and Peripheral Clock Disorders: The Circadian Clock and Hyperlipidemia. Journal of Pharmacological Sciences, 103(2), 139–143.* doi:10.1254/jphs. fmj06003x3

(n.d.). Lighting up biological clocks; genes from glowing ... Retrieved from https://www.thefreelibrary.com/Lighting up biological clocks; genes from glowing organisms...-a017198839

Matthews, G. V. T. (1973). Biological Clocks and Bird Migration. Biological Aspects of Circadian Rhythms, 281–311. doi: 10.1007/978-1-4613-4565-7_8

Muzur, A., Pace-Schott, E. F., & Hobson, J. A. (2002). *The prefrontal cortex in sleep. Trends in Cognitive Sciences, 6(11), 475–481.* doi:10.1016/s1364-6613(02)01992-7

Nakamaru-Ogiso, E., Miyamoto, H., Hamada, K., Tsukada, K., & Takai, K. (2012). *Novel biochemical manipulation of brain serotonin reveals a role of serotonin in the circadian rhythm of sleep-wake cycles. European Journal of Neuroscience, 35(11), 1762–1770.* doi:10.1111/j.1460-9568.2012. 08077.x

Saper, C. B., Scammell, T. E., & Lu, J. (2005, October 27). Hypothalamic regulation of sleep and circadian rhythms.

Smolensky, M. H. (2001). *Circadian Rhythms in Medicine. CNS Spectrums, 6(06), 467–482.* doi:10.1017/s1092852900008026

Sollars, P. J., & Pickard, G. E. (2015, December). The Neurobiology of Circadian Rhythms.

THE BRAIN FROM TOP TO BOTTOM. (2019). Retrieved 11 December 2019, from https://thebrain.mcgill.ca/flash/i/i_11/i_11_cr/i_11_cr_hor/i_11_cr_hor.html

The Expanded Biology of Serotonin. (2019). Retrieved 12 December 2019, from https://www.annualreviews.org/doi/abs/10.1146/annurev.med.60.042307.110802

Ursin, R. (2002). Serotonin and sleep. Sleep Medicine Reviews, 6(1), 55–67. doi:10.1053/smrv.2001.0174

Walton, A. (2019). Your Body's Internal Clock and How It Affects Your Overall Health. Retrieved 10 December 2019, from

https://www.theatlantic.com/health/archive/2012/03/your-bodys-internal-clock-and-how-it-affects-your-overall-health/254518/
Woller, A., & Gonze, D. (2013). The Bird Circadian Clock: Insights from a Computational Model -. Retrieved from https://journals.sagepub.com/doi/full/10.1177/0748730413512454

Acknowledgements
The author appreciates all those who participated in the study and helped to facilitate the research process.

Conflict of Interest
The author declared no conflict of interest.

How to cite this article: S Shetty (2020). The clock is ticking: a critical review of understanding the neural basis for biological clocks. *International Journal of Indian Psychology*, *8*(2), 391-395. DIP:18.01.046/20200802, DOI:10.25215/0802.046