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CIRCADIAN VARIATION OF BRAIN PROTEINS: IMPORTANCE IN EXPERIMENTS

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CIRCADIAN RHYTHMS AND CHRONOBIOLOGY

Circadian (from the Latin word circa, meaning 'about', and dies, meaning 'day') rhythms are the rhythms occurring within a period of 24 hours and are endogenously driven in biochemical, physiological or behavioral processes [1]. Circadian rhythms are also entrained by the external environmental cues called zeitgebers, the primary one of which is day light [2]. Circadian rhythms have been widely observed in plants, animals, fungi and cyanobacteria [3]. The study of the biological processes that vary during different time of the day, is called chronobiology. A number of studies on mammalian species have confirmed that the circadian pacemaker resides in the supra-chiasmatic nucleus (SCN) that is a part of hypothalamus in the brain [4]. The SCN receives signals from the environment and provides the principal timing cues for synchronizing the daily oscillations of different proteins in brain tissues [5]. So, different physiological activities and behaviors of human and animals vary during 24 hours.

GAP IN THE EXPERIMENTS

As brain proteins vary in different time of the day which are responsible in alteration of respective physiological activities. So, these activities or behavior may be at peak at one time, average at other time and may be down at other point of the 24 hours clock in a circadian fashion. The SCN pacemaker consists of multiple, autonomous single cell circadian oscillators, which are synchronized to generate a coordinated rhythmic output [6]. Studies have shown circadian variation of proteins and different physiological processes. Like, it has also been studied that various bio-chemicals like dopamine neurotransmitter synthesis and release, hormone secretion show circadian variations [7, 8]. Memory performance has also been shown to follow a circadian pattern that is parallel to extracellular signal regulated kinase (ERK) circadian rhythmicity [9]. ERK is considered very important protein in hippocampal long term potentiation that is further responsible for learning and memory. As it is evidenced that the proteins and different physiological processes are different at different time of the day. So, the experiment must be conducted at specific time of day with describing certain rationale of the time of the day in order to make the experiment more standardized and reproducible.

THE WAY FORWARD

Researches should consider the followings accordingly:

1. Laboratory Animals' Experiments: While using the laboratory animals in biomedical research, all the possible zeitgebers (light, temperature, humidity, noise, etc.) should be kept standardized according to experimental requirement. As any change in the zeitgeber/s may alter the circadian profile of the protein and or physiological process that is under your study. Experiment either in vivo or ex vivo should be performed at specific zeitgeber time and this approach will not only help other researchers in reproducing the results but will standardized and synchronize the data.

2. Behavioral experiments: As behaviors are linked with certain bio-chemicals in the brain like dopamine and these bio-chemicals show circadian variations leading to alterations of certain behavior/s at certain zeitgeber time. So, behavioral studies should also follow the concept of chronobiology and experiments should be performed at specific

time of the day for its validity and reproducibility.

3. Pharmacological studies: Time of the day of experiment must be considered for the studies which involve testing of pharmacological drugs in laboratory animals or clinical trials studies. As protein receptors are varying during different time of the day, so pharmacological effect may also vary.

4. Psychological interventions: As psychological interventions are planned to manage cognitive problems especially learning, problem solving etc. Cognitive processes are linked with different neurotrophic factors which have showed circadian variations with peak in the morning. So, if psychological intervention for enhancing cognitive abilities should be planned in the mornings. Hyper- suggestibility is linked with low brain waves which are observed in the evenings and psychotherapy like hypnotherapy is to increase suggestibility. So, if hypnotherapy is planned in the evenings, this will give best outcomes rather planned for other time points of the day.

Briefly, it may be concluded that performing experiment at specific time of the day (Zeitgeber Time), will standardize and synchronize the data. This will not only enhance the quality and reproducibility of the data but will give better outcomes in case of therapeutic intervention either pharmacological or psychological.

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