

What HR Managers need to know about Circadian Clocks?

¹Mohamed S. Mohiya

²Sulphey, M. M.

ABSTRACT--The alteration of day and night, and changes in seasons has been instrumental in bringing out certain peculiar cyclic changes in the habits and behaviours of all living organisms. These cycles of the body known as “circadian cycles” help organisms to (re)act to varying stimuli in their internal and external environments, resulting in certain behavioural rhythms. Subsequent to the Industrial Revolution, humans started adapting the so called 24 x 7 type of life style. With competition raising its amorphous head due to liberalisation and globalisation, the lifestyles of humans have undergone a paradigm shift. This lifestyle often results in acting contrary to the circadian rhythms that have been set since generations, leading to various complications of astronomical proportions that have been unheard of in earlier generations. This work reviews the accumulated literature about circadian system and strives to find its applications in the present wellness programs. It also discusses the implications for HR Managers.

Key words-- Body clock, circadian clock, circadian cycle, circadian rhyme, Circadian Rhyme Disruption

I INTRODUCTION

Since the origin of life on Earth, all fundamental behaviours like feeding, locomotion, sleeping, reproduction, “intra-specific communication”, memory, etc. are found to occur in regular cycles. Further, all living organisms have, by nature, daily cycles in behaviour as well as physiology that facilitate adaptation to their respective environment. These cycles, according to Aschoff and Honma (1959), recur based on certain cyclic environmental changes. It has been the alteration of day and night, and changes in seasons due to rotation and revolution of earth that has been instrumental in bringing out these cyclic changes. The cycles help organisms to act and react to varying stimuli in their environment. The cycles are put in place by “Circadian clocks” in the body. In ordinary parlance circadian clocks are known as body clocks³. There are in existence innumerable number of circadian clocks throughout the body on any organism. It is these circadian clocks that regulate the various metabolic and “behavioural rhythms”.

The recent Nobel Prize in Medicine to three scientists for their work on body clocks has brought in renewed discussions about this wonderful phenomenon. According to the scientists Jeffrey C. Hall, Michael Rosbash and Michael Young, whose work earned them the Nobel Prize for Medicine in 2017, these clocks run every cell of our bodies. These inner clocks are assigned to adapt the physiology to the various phases of each day with a high level of precision. It is these clocks that regulates and synchronises various critical functions including

¹Assistant Professor and Head, Department of HRM, College of Business Administration, Prince Sattam Bin Abdulaziz University, Saudi Arabia (m.mohiya@psau.edu.sa)

²Professor, College of Business Administration, Prince Sattam Bin Abdulaziz University, Saudi Arabia (s.manakkattil@psau.edu.sa)

behaviours, hormonal levels, body temperatures and even metabolic activities. Desynchronizing with these body clocks will result in many maladies ranging from weight gain to a host of metabolic diseases. Now there is accumulated evidence towards the need for have more sensitivity to these clocks. Any chronic misalignment between lifestyles and the body clock would result miseries and diseases of untold nature. Though the utility of circadian clocks were previously limited to prescription of drugs my practitioners in medical science, now it has found application in various fields. Some such fields include dietary science, human resource management, organizational psychology, etc. The objective of the present work is limited to conducting a thorough review of literature to have a fair understanding about the utility of circadian clocks for Human Resource Management (HRM) professionals.

II Review of literature

The role of HR managers has undergone drastic changes in the last few decades. Now the position of an HR manager is of strategic in nature and outlook. For an HR manager to facilitate effectiveness of his organisation, he should have the quality of being ambidextrous in nature, with the knowledge and capability of identifying “explorative” and “exploitative” activities. These qualities are an absolute necessity in the quest towards achievement of organizational sustainability (Sulphey and Alkahthani, 2017; Sulphey, 2019). The HR manager should be capable of keeping the entire flock of employees ready to face the changing scenario by keeping them physically and mentally hale and healthy. Further, the HR personnel, in addition to deep knowledge about various legislative and regulative aspects, should have a sound understanding of human behaviour and their various complex and interconnected causative factors. They should also put in honest and earnest efforts towards the safety at workplace and to reduce employee turnover (Sandhya and Sulphey, 2019). The importance of circadian clock in safety management has been highlighted by an early study of Bieber (1990). There is thus no second opinion that body clocks are now getting renewed attention due to its ability to make or mar the physiology and psychology of human beings. This paper intends to examine the available literature about circadian clocks and rhymes and identify what HR managers should know about it.

Circadian Clocks

All living organisms have daily rhythms of various cycles in their life, which are mostly categorized as innate. These cycles are based on changes that occur in the environment. Research about these cycles were initiated as early as the 18th century when Jean Jacques d’Ortous de Mairan, an astronomer studied the “touch-me-not” (*Mimosapudica*) plants. He observed that the leaves of these plants opened during daytime and closed towards dusk. He experimented by placing the plants in constant darkness. It was found that irrespective of sunlight, the leaves followed a normal pattern of daily oscillations, and hence a biological clock. Later on scientists found that all organisms, including animals and humans have biological clocks and rhythms that adapt the physiology based on the changes in sunlight. This adaptation is termed as the circadian rhythm. The term has been derived from the Latin work *circa* (around) and *dies* (day). It is this rhythm that helps humans to involve in activities in the day time and sleep during night. Based on biological clock the alertness and activities (both physical and mental) vary with different times of the day.

In human being the locus of control of circadian cycles and rhythms are with the “Central Circadian Pacemaker” and the “Suprachiasmatic nucleus” (SCN). It is the SCN, contained in the hypothalamus that coordinates a host of other oscillators or initiators of cycles within the brain and other organs (Reppert and Weaver, 2002). The SCN has a direct connection with the eye (retinohypothalamic tract), which synchronizes the light-dark cycles (Moore and Lenn, 1972). SCN has the important function of being a “time keeper” as well as a “gate keeper”. As a time keeper it transmits a time base that is required for circadian patterning. As a gate keeper, it channels the clock sensitivity that helps in recognizing nocturnal light to bring in the required re-synchronizing adjustments (Gillette and Tischkau, 1999).

The two basic and main components of the circadian clock in mammals are the “*Circadian Locomotor Output Cycles Kaput*” (CLOCK) and “*Brain and Muscle Arnt-Like Protein-1*” (BMAL1) proteins. The CLOCK and BMAL1 are transcription/dictation factors that promote transcription of many genes. Some such circadian genes include the “*Period genes*”, the “*Cryptochrome genes*”, etc. (Reppert and Weaver, 2001; Takahashi, Hong, Ko, and McDearmon, 2008). These proteins and circadian genes are expressed very widely throughout the brain. There are also in existence certain SCN-independent pacemakers. These SCN-independent pacemakers are mostly related with “nonphotic stimuli”, which are not associated with day light – for instance food, drugs, etc. (Iijima, Nikaido, Akiyama, Moriya and Shibata, 2002; Stephan, 1984). A host of metabolic processes also are found to have sizeable influence on the circadian system (Green, Takahashi and Bass, 2008; Rutter, Reick, and McKnight, 2002). In addition to the above, the endocrine system, the ventral/dorsal striatum, cortex, limbic system, etc. also involve in the circadian regime (Beckstead, Domesick and Nauta (1979).

The circadian system is found to be capable of automatically responding to the health conditions and behaviours of individuals, and reacts dynamically to various exogenous and endogenous environmental cues. It could also interact with and influence the progression and severity or otherwise of several diseases (Martino, Tata, Belsham, et al., 2007; Martino, Oudit, Herzenberg, et al, 2008).

Circadian rhythm

The circadian rhythm is essential for biochemical and physiological functions of any organism, and not merely a behavioural phenomenon. While most of the cycles in other mammals are fairly stable throughout the year, the circadian rhythm is highly complex in nature in human beings. The body clock brings about daily rhythms in many aspects of human body. Some of them which exert widespread effects on the human body include temperature, plasma and hormonal concentrations, sleep-wake cycles, etc. As a result of this the body has a rhythmic effect of around 24 hours. This rhythm is made possible mostly due to solar cycles. As such these rhythms and cycles are closely associated with (un)availability of day light. Thus behaviours are mostly based on a few endogenous components (effects from the body clock) and exogenous components (environment and lifestyles).

The clock within the body initiates and drives the routine expression of all vital homeostatic functions varying from feeding/drinking to regulation of body temperature and hormonal secretions. This clock is instrumental in organizing all body functions into 24 hour oscillations or cycles. These cycles are known as “circadian rhymes”. It was in the 1970’s that a scientist Seymour Benzer and his student Ronald Konopka

proposed that the cycles were made possible due to certain genetic build-up and identified the circadian genes of fruit flies.

Humans have multitude of rhymes in their body which include separate rhymes for body temperature, systolic blood pressure (BP), endocrine system, plasma growth hormone and so on. For instance, body temperature and BP tends to be low during nights and peak at day time. Growth hormones often peak after lights off. Examples are Plasma adrenocorticotrophic hormone (ACTH) and Plasma melatonin (PM). While ACTH rises throughout the night and peaks at lights on, PM peaks during midnight (Schwartz, 1993).

According to Gillette (1996), the circadian cycles can be divided into discrete time domains – day, night, dawn and dusk. The reaction of the body during these times vary in a unique pattern. The details of the change in the body during one day is presented in Table 1. At any given point of time the circadian clock becomes receptive only to a single subset of the different domains (Gillette and Tischkau, 1999). Now substantial evidences exist to show that behaviours of beings oscillate in environments that are devoid of timing information. For instance, constant darkness, change in temperature, (un)availability of food, water, etc. could lead to wide swings in behaviours. Further, in the absence of stable environmental cues, a relatively stable rhythm is sought to be expressed in weeks. With the passage of time in such a changed condition, the normal active phase drifts from the relative position of the cycle under which the organism has been entrained and realign (Gillette and Tischkau, 1999).

Table 1: Reaction of the body based on the time of the day

	Time	Reaction of body
Day	6 – 12	Cortisol release → Fastest increase in BP → High alertness
	12 – 18	Best coordination → Fastest reaction time → Highest body temperature
Night	18 – 24	Highest BP → Melatonin secretion
	24 – 6	Deep sleep → Lowest body temperature

Circadian rhythm disruption

Circadian rhythm disruptions (CRD) are events that alter or interrupt circadian rhythms. CRD could result in various physiological and behavioural impacts of unknown repercussions. With increase in age there would be a certain amount of natural and normal alteration of circadian rhythms like changes in sleep patterns, waking up early in the mornings, increased frequency and requirement of daytime napping, etc. According to Brown and Antunano (2009) CRD could result in:

“Difficulty falling and staying asleep, late-night insomnia, increased daytime sleepiness, a general lack of energy in the morning, an increase of energy in the evening or late at night, difficulty concentrating, being alert, or accomplishing mental tasks, oversleeping and trouble getting up, increased negative moods.”

Implication of Circadian clocks for HR Managers

Humans have multitude of cycles and clocks working within their bodies. These clocks help in promoting activity during the daytime and facilitate recovery, recuperation and restitution during night times. The secretion

of melatonin, which happens at the early part of the night, is associated with the propensity of sleep (Waterhouse, Reilly, Atkinson and Edwards (2007). In addition of melatonin, body temperature is also driven by circadian clock. The body temperature normally falls at night, while the level of melatonin increases. This rhythm combined with certain environmental factors like absence of light and sounds provides humans with the possibility of having quality sleep.

Evidences exist that shows a steep fall in the level of alertness due to increase in time awake. This also happens in the event of increased levels of fatigue and the consequent need for sleep. There are also clear evidences about the direct relationship between body clock and health. How and when a person work is now a matter of high importance. A person who works continuously at night could have serious implications for his health (Nic, 2012). According to Webb, Lehman and Coolen (2015) the circadian system is involved in the influence of motivations, emotions, as well as various timely and ultimately behaviours. Tinkering with body cycles and clocks could lead to many problems, complications and diseases.

Some aspects that could create problems for employees due to working against body clock include shift work, jetlag, untimely and erratic sleep patterns/habits, alcoholism and drug abuse, etc. A number of empirical studies have been done to assess the problems associated with offsetting of body clocks (Amaral, *et al*, 2014; Boivin, and Boudreau, 2014; Brown and Antunano, 2009; Cho, *et al.*, 2015; ; Ozburn, Falcon, Mukherjee, Gillman, Arey, Spencer and McClung, 2013; Verwey, Dhir and Amir, 2016; Woodfine, 2012). A few of the problems faced by working executives are presented in the following sections.

Shift work

During daytime, light produces virtually no changes to the SCN. At night, depending on when the light is delivered, artificial lights could produce “strong phase advances or phase delays” in the SCN; and produce shifts to certain behavioural and physiological rhythms (Abe, *et al*, 1999). Artificial lights could also offset the synchrony of SCN with the environment and exacerbate serious disruptions of the circadian cycle, including the sleep pattern (Verwey, *et al*, 2016). Substantial evidence now exists regarding the negative consequences of artificial light at night on mood, sleep, health, and disease (Amaral, *et al*, 2014; Boivin, and Boudreau, 2014; Cho, *et al.*, 2015).

For any shift worker, the body clock will definitely be at odds with the shift timings. They often have trouble adjusting to being awake at night and sleeping at day time. This is because the external environment tends to keep their body on a day shift pattern. This could lead to CRD. The adverse effects of CRD in shift workers like performance issues, accidents and health issues is an aspect that has been well documented (Brown and Antunano, 2009). Employees working in conditions of exposure to light due to successive night shifts get their behavioral rhythms to realign. With the so called 24 X 7 type of life now adopted by modern man the situation has aggravated. In such situations one is compelled to work against the body clock leading to sleep deprivations. These sleep deprivations could result in insomnia. It is estimated that during night times, humans require about 7½ to nine hours of quality undisturbed sleep. However, for any individual, a minimum of six hours of sleep per day is an absolute requirement for optimum performance. Individuals who get less sleep than that is required by the body continually are likely to accumulate “a sleep debt”. This debt would result in increased fatigue levels, and consequent reduced productivity and even accidents. This is an area which HR Managers have to provide

due and adequate attention. Another area where HR Managers have to focus is long distance heavy truck drivers. Though there are a host of reasons for occurrence of accidents, driver fatigue as a result of continuous driving at nights offsetting body clocks have been identified as one of the many prominent reasons for accidents (Woodfine, 2012).

Jetlag

Jetlag (rapid time zone change syndrome) is an aspect that needs to be tackled by executives on the move. It is one of the biggest stressors with adverse effects that executives have to face. Jetlag could result in excessive sleepiness at day time and a lack of alertness, as a result of travel spanning different time zones. Certain other problems related to jetlag include “fatigue, insomnia, disorientation, headaches, digestive problems, lightheadedness” (Brown and Antunano, 2009). HR managers have an important role to play in helping such executives on the move to tide over the problems of fatigue and alertness associated long distance air travel and jetlag. According to Abarca, Albrecht and Spanagel (2002) changes in the light–dark cycle that causes jetlag could stimulate certain cognitive deficits that affect “fear-conditioning”.

Alcoholism and drug abuse

Substantial evidence exists to prove that alcoholism is closely associated with disruptions in their circadian rhythms (Brower, 2001; Kuhlwein, Hauger and Irwin, 2003; Landolt and Gillin, 2001; Ozburn, et al, 2013; Sano, Suzuki, Yazaki, Tamefusa, Ohara, Yokoyama, et al. (1993)). This could lead to a vicious cycle, as experiments in rodents showed that chronic alcoholism could alter the genetic build-up causing disruptions in the SCN and activity rhythms (Chen, Kuhn, Advis, and Sarkar, 2004; Seggio, Logan and Rosenwasser, 2009). There is a definite need to tread cautiously since in humans, variations in the CLOCK genes has been found to be associated with increased levels of alcohol consumption (Spanagel, Rosenwasser, Schumann and Sarkar, 2005; Sjoholm, Kovanen, Saarikoski, Schalling, Lavebratt and Partonen, 2010). Evidences also point towards the fact that drug abuse could alter the circadian regime (Iijima, et al, 2002).

HR Managers thus have to include the need of enlightening employees about the adverse effects of alcohol and drug use in organizational wellness programs (Sulphey, 2014). Studies conducted on rodents’ show that frequent alcohol consumption and drug abuse could cause disruption to the set circadian patterns, resulting in offsetting a wide variety of rhythms (including behavioural and hormonal) (Iijima, et al, 2002). Even abuse of foods like untimely consumption could adversely affect the rhythms (Kosobud, Gillman, Leffel, Pecoraro, Rebec and Timberlake, 2007, Madeira, Andrade, Lieberman, Sousa, Almeida and Paula-Barbosa, 1997; Ozburn, et al, 2013; Rajakrishnan, Subramanian, Viswanathan and Menon, 1999; Rosenwasser, Fecteau, and Logan, 2005; Spanagel et al, 2005).

III DISCUSSION

From the foregone discussions it can be seen that the circadian system exerts immense pressure on all living organisms. Progressive organizations now embark on ambitious wellness programs to make the employees physically and mentally fit (Sulphey, 2014). HR managers are saddled with the responsibility of these wellness

programs. To make the wellness programs successful, it would be advisable for HR managers to have a fair knowledge of circadian clocks and the grave implications if it is disrupted. Disruptions to the circadian systems due to the modern fast track 24 x 7 lifestyles are causing unimaginable consequences and repercussions to human beings. That the circadian system has immense influence on any organism is a fact that is beyond doubt. However, there is the need for further research to understand the complexities associated with the intra/inter connections between various external and internal environments that lead to circadian cycles and rhythms. For instance, there is a definite need to understand the importance of the circadian time for consumption of food (Arble, *et al.*, 2009) as untimely consumption could adversely affect the rhythms (Kosobud, *et al.*, 2007; Ozburn, *et al.*, 2013). It is also assumed that simple changes like altering the time of food consumption could either exacerbate or even mitigate the problem of weight gain. Evidences point towards the fact that weight gain could even be independent of the quantity of calories consumed, thereby pointing towards the impact of metabolic activities (Verwey *et al.*, 2016).

Unravelling the complexities of these interactions between light availability, circadian systems and metabolism would definitely be an area of interest to many. This would, in addition to many other aspects, also help in suggesting appropriate mealtimes or quantities of food that could facilitate the required adaptive adjustments in the biological clock and help in the normalization of CRDs caused by external environmental changes like jetlag, night shifts, or other psychopathological conditions. Further, the circadian system has very high relevance on human behaviour. Due to this there is now renewed interest among scientists to understand the behavioral and neuro-chemical implications on circadian clocks (Webb, Lehman, and Coolen, 2015).

IV CONCLUSION

The increased knowledge about circadian system has enabled a better understanding of the routine biological processes, and various aspects related to health and diseases. However, this is only an emerging area of study, and lots need to be known to unravel the various mysteries of the circadian system. According to Verwey, *et al.* (2016) the “links between site-specific clock gene expression and functional consequences in behavior and physiology continue to be another ongoing and major challenge for future research”. Thus it can be construed that the present accumulated knowledge is only the tip of an iceberg and more needs to be known about this fascinating and challenging area. More scientific knowledge about the circadian clock would go a long way in making the wellness programs of business organizations a grand success.

As the “trustees of the human resource repository” in any organisation, HR managers have a definite need to have high quality human resources that are healthy (both mentally and physically), motivated, engaged, and willing. The current knowledge about circadian cycles has helped in having better awareness about the need for a careful choice of lifestyle that will have human resources that are of high quality. However, there is a definite need to know more about the behavioural, physiological and psychological implications of body clocks and oscillations. Neuroscientists and Endocrinologists are now involved in conducting in-depth studies about circadian clocks and oscillations. The Nobel Prize in medicine for three scientists involved in research about circadian clocks has helped in generating renewed interest about the topic. Researchers are now focusing on the relationship of circadian rhythms with neurological, neuro-chemical, hormonal, and metabolic factors. There is

now a definite need for multi-disciplinary studies involving experts from the fields of Management, Organizational psychology, Endocrinology, Neurology, etc. to unravel the mysteries of circadian cycles and its effects on humans. Such inter/multi-disciplinary studies involving experts from diverse fields of medical, applied and social science will help in its application in the organisational settings so that life at workplace can be made better, healthier and happier. It is expected that more fascinating facts about the circadian cycles and rhythms, their causative factors and their applications in organizational settings will be unravelled in the near future.

V REFERENCES

1. Abe, H., Honma, S., Namihira, M., *et al.* (1999). Phase-dependent induction by light of rat Clock gene expression in the suprachiasmatic nucleus. *Brain Res Mol Brain Res.*, 66(1–2), 104–10.
2. Amaral, F. G., Castrucci, A. M., Cipolla-Neto, J., *et al.* (2014). Environmental control of biological rhythms: effects on development, fertility and metabolism. *Journal of Neuroendocrinology*, 26(9), 603–12.
3. Aschoff, J. and Honma, K. (1959). *Z. Vergl. Physiology*, 35, 481–600.
4. Bieber, R. M. (1990). Safety management is time management, *Professional safety* 35(1), 25–26.
5. Boivin, D. B. and Boudreau, P. (2014). Impacts of shift work on sleep and circadian rhythms. *Pathol Biol (Paris)*, 62(5), 292–301.
6. Brower, K. K. J. (2001). Alcohol's effects on sleep in alcoholics. *Alcohol Research Health*, 25, 110–125.
7. Brown, J. R. and Antunano, M. J. (2009). *Circadian Rhythm Disruption and Aviation*, Publication No. AM-400-09/3, Federal Aviation Administration, Civil Aerospace Medical Institute. Available at www.faa.gov/pilots/safety/pilotsafetybrochures/
8. Chen, C. P., Kuhn, P., Advis, J. P. and Sarkar, D. K. (2004). Chronic ethanol consumption impairs the circadian rhythm of pro-opiomelanocortin and period genes mRNA expression in the hypothalamus of the male rat. *Journal of Neurochemistry*, 88, 1547–1554.
9. Cho, Y., Ryu, S. H., Lee, B. R., *et al.* (2015). Effects of artificial light at night on human health: A literature review of observational and experimental studies applied to exposure assessment. *Chronobiol International*, 32(9), 1294–310.
10. Gillette, M. U. (1996). *Prog. Brain Research*, 111, 121–132.
11. Iijima, M., Nikaido, T., Akiyama, M., Moriya, T. and Shibata, S. (2002). Methamphetamine-induced, suprachiasmatic nucleus-independent circadian rhythms of activity and mPer gene expression in the striatum of the mouse. *European Journal of Neuroscience*, 16, 921–929.
12. Kosobud, A. E. K., Gillman A. G., Leffel, J. K., Pecoraro, N. C., Rebec, G. V., Timberlake, W. (2007). Drugs of abuse can entrain circadian rhythms. *Scientific World Journal*, 7, 203–212.
13. Kuhlwein, E., Hauger, R. L. and Irwin, M. R. (2003). Abnormal nocturnal melatonin secretion and disordered sleep in abstinent alcoholics. *Biological Psychiatry*, 54, 1437–1443.
14. Landolt, H. P. and Gillin, J. C. (2001). Sleep abnormalities during abstinence in alcohol-dependent patients: Aetiology and management. *CNS Drugs*, 15, 413–425.

15. Madeira, M. D., Andrade, J. P., Lieberman, A. R., Sousa, N., Almeida, O. F., Paula-Barbosa, M. M. (1997). Chronic alcohol consumption and withdrawal do not induce cell death in the suprachiasmatic nucleus, but lead to irreversible depression of peptide immunoreactivity and mRNA levels. *Journal of Neuroscience*, 17, 1302–1319.
16. Martino, T. A., Tata, N., Belsham, D. D., *et al.* (2007). Disturbed diurnal rhythm alters gene expression and exacerbates cardiovascular disease with rescue by resynchronization. *Hypertension*, 49(5), 1104–1113.
17. Martino, T. A., Oudit, G. Y., Herzenberg, A. M., *et al.* (2008). Circadian rhythm disorganization produces profound cardiovascular and renal disease in hamsters. *Am Journal of Physiol Regul Integr Comp Physiol*, 294(5), 1675–1683.
18. Moore, R. Y. And Lenn, N. J. (1972). *Journal of Comp. Neurology*, 146, 1-14.
19. Gillette, M. U. and Tischkau, S. A. (1999). Suprachiasmatic Nucleus: The Brain's Circadian Clock, *Recent Progress in Hormone Research*, 54, 33-59.
20. Nic, P. (2012). Human body clock: what makes it tick? *Occupational Health*, 64, September, 9;
21. Ozburn, A. R. Falcon, E., Mukherjee, S., Gillman, A., Arey, R., Spencer, S. and McClung, C. A. (2013). The Role of Clock in Ethanol-Related Behaviors, *Neuropsychopharmacology*, 38, 2393–2400.
22. Rajakrishnan, V., Subramanian, P., Viswanathan, P., Menon, V. P. (1999). Effect of chronic ethanol ingestion on biochemical circadian rhythms in Wistar rats. *Alcohol*, 18, 147–152.
23. Reppert S. M. and Weaver, D. R. (2001). Molecular analysis of mammalian circadian rhythms. *Annual Review of Physiology*, 63, 647–676.
24. Reppert S, M., and Weaver, D. R. (2002). Coordination of circadian timing in mammals. *Nature*, 418, 935–941.
25. Rosenwasser, A. M., Fecteau, M. E., and Logan, R. W. (2005). Effects of ethanol intake and ethanol withdrawal on free-running circadian activity rhythms in rats. *Physiological Behavior*, 84, 537–542.
26. Sano, H., Suzuki, Y., Yazaki, R., Tamefusa, K., Ohara, K., Yokoyama, T. et al. (1993). Circadian variation in plasma 5-hydroxyindoleacetic acid level during and after alcohol withdrawal: phase advances in alcoholic patients compared with normal subjects. *Acta Psychiatr Scand*, 87, 291–296.
27. Sandhya, S. and Sulphay, M. M. (2019). An assessment of contribution of employee engagement, psychological contract and psychological empowerment towards turnover intentions of IT employees. *International Journal of Environment, Workplace and Employment*, 5 (1), 22-31. <http://doi:10.1504/IJEWE.2019.097186>
28. Schwartz, W. J. (1993). *Advances in Internal Medicine*, 38, 81-106.
29. Seggio, J. A., Logan, R. W. and Rosenwasser, A. M. (2009). Chronic ethanol intake modulates photic and non-photoc circadian phase responses in the Syrian hamster. *Pharmacology and Biochemistry of Behavior*, 87, 297–305.
30. Sjöholm, L., Kovanen, L., Saarikoski, S., Schalling, M., Lavebratt, C. and Partonen, T. (2010). CLOCK is suggested to associate with comorbid alcohol use and depressive disorders. *Journal of Circadian Rhythms*, 8: 1.
31. Spanagel, R., Rosenwasser, A. M., Schumann, G, and Sarkar, D. K., (2005). Alcohol consumption and the body's biological clock. *Alcohol Clinical Exp Research*, 29, 1550–1557.

32. Stephan, F. K. (1984). Phase-shifts of circadian rhythms in activity entrained to food access. *Physiology of Behavior*, 32, 663–671.
33. Sulphrey, M. M. &Alkahtani, N. S. (2017). Organizational ambidexterity as a prelude to corporate sustainability, *Journal of Security and Sustainability Issues*, 7 (2), 335-347. [https://doi.org/10.9770/jssi.2017.7.2\(13\)](https://doi.org/10.9770/jssi.2017.7.2(13))
34. Sulphrey, M. M. (2014). Construction & Validation of Employee Wellness Questionnaire, *Indian Journal of Industrial Relations*, 49 (4), 690-700.
35. Sulphrey, M. M. (2019). Could adoption of Organizational Ambidexterity have changed the history of Nokia? *South Asian Journal of Business and Management Cases*, 8 (2), 167-181. <http://doi:10.1177/2277977919833752>
36. Takahashi, J. S., Hong, H. K., Ko, C. H. and McDearmon, E. L. (2008). The genetics of mammalian circadian order and disorder: implications for physiology and disease. *Nat Review of Genetics*, 9, 764–775.
37. Verwey M, Dhir S and Amir S. (2016). Circadian influences on dopamine circuits of the brain: regulation of striatal rhythms of clock gene expression and implications for psychopathology and disease, *F1000Research*, 5, 2062 (doi: 10.12688/f1000research.9180.1)
38. Waterhouse, J., Reilly, T., Atkinson, G. and Edwards, B. (2007). Jet lag: trends and coping strategies, *The Lancet*; 369, 1117-1129.
39. Woodfine, V. (2012). Watching the clock. *The Safety & Health Practitioner*, 30, 59-60.
40. Mikal Rekdal, Aravind Pai, Ravi Choudhari, MuddukrishnaBadamaneSathyanarayana. "Applications of Co-Crystals in Pharmaceutical Drugs." *Systematic Reviews in Pharmacy* 9.1 (2018), 55-57. Print. doi:10.5530/srp.2018.1.11
41. Bitbol, M. Consciousness, situations, and the measurement problem of quantum mechanics (2008) *NeuroQuantology*, 6 (3), pp. 203-213.
42. Wang, Q. Study of emotional changes based on neural management and electroencephalogram experiments on low-carbon consumption behavior (2018) *NeuroQuantology*, 16 (2), pp. 25-31.