International Journal of Biology Research
ISSN: 2455-6548
Impact Factor: RJIF 5.22
www.biologyjournal.in
Volume 3; Issue 1; January 2018; Page No. 268-272

Effect of sleep deprivation on higher cognitive functions in Wistar albino rats

[1] Archana Arjunan, [*2] Dr. Sathya Narayanan Govindarajulu

[1] Research Scholar, Department of Physiology, Dr. ALM Post Graduate Institute of Basic Medical Sciences, University of Madras, Taramani, Chennai, Tamil Nadu, India

[2] Assistant Professor, Department of Physiology, Dr. ALM Post Graduate Institute of Basic Medical Sciences, University of Madras, Taramani, Chennai, Tamil Nadu, India

Abstract

Introduction: Sleep deprivation severely compromises the ability of human beings to respond to stimuli in a timely fashion. The prevalence of sleep disorders is increasing in modern societies, where constant exposure to artificial light and interactive activities, such as television and the internet, combine with social and economic pressures to shorten the time spent asleep Experimental sleep deprivation in animals allows us to gain insight into the complications that are not possible to study in human subjects.

Objectives: The aim of the study is to investigate the effect of 48 hours of sleep deprivation on higher cognitive functions and social preferences in male Wistar albino rats.

Methods: Adult male Wister albino rats are exposed to sleep deprivation for 48 hrs and were tested for weight and various behavioral alterations. Adult albino rats were randomly divided into two groups. Each group contains six animals. Rats were tested in Novel object location, Novel object recognition for testing, learning and memory, memory retention, and novelty preference. For analyzing social behavior, rats were tested on Social preference task.

Results: The rats exposed to sleep deprivation show behavioral alterations such as impairment in learning and memory, memory retention, novelty preference, decreased social preference behavior and increased social avoidance.

Conclusion: The results revealed that Sleep deprivation leads to cognitive impairment and social avoidance in Wistar albino rats.

Keywords: sleep deprivation, behavior, novel object, learning, memory, social preference

Introduction

Sleep occupies approximately one-third of a person's life, but its impact on health and medical conditions remains partially unrecognized. The prevalence of sleep disorders is increasing in modern societies, where constant exposure to artificial light and interactive activities, such as television and the internet, combine with social and economic pressures to shorten the time spent asleep [1]. Disturbances in the sleep-wake rhythm and Sleep Deprivation (SD) are increasingly frequent due to events that are progressively more common in modern life in more developed countries [2]. Many individuals are chronically sleep-deprived as a result of their current lifestyle [3].

Sleep in mammals is composed of two major stages, rapid eye movement sleep (REM) and non-rapid eye movement sleep (nREM). Sleep and wakefulness are controlled by a network of brain nuclei that interact in a complex fashion, integrating homeostatic and circadian regulations [4]. Sleep plays an essential role in cognitive functions such as attention, emotion and memory, independent of any physical manifestations of sleep loss such as sleepiness or drowsiness [5]. Sleep, especially rapid eye movement sleep, has an essential role in learning and memory process in the hippocampus [6].

As SD experiments play a key role in elucidating the functions of sleep, many of the studies documented characteristic behavioral changes after prolonged wakefulness. In this respect, sleep loss or deprivation is usually defined as experimentally induced lack of sleep for a certain period of time. Both animal and human studies have confirmed that sleep plays an important homeostatic role and that chronic SD is a potent stressor that leads to metabolic and cognitive disturbances in brain areas involved in learning, memory and emotion such as the hippocampus, amygdala, and prefrontal cortex [7].

Materials and Methods

The experimental procedures described were performed in accordance with the Ethical Principles in Animal Research adopted by the Committee for the Purpose of Control and Supervision of Experiment on Animals (CPCSEA). The animals used in this experiment were approved by Institutional Animal Ethical Committee (IAEC) of Institute of Basic Medical Sciences (IBMS), University of Madras, Chennai. 12 adult male Wistar albino rats weighing about 200 gms aged 12 weeks were used in this study. The animals were bred and raised in the animal house of Institute of Basic Medical Sciences. The animals were housed as a colony in standard cages with a normal room temperature and a 12-h/12-h light/dark cycle. The animals had free access to food and water. The water in the tank was changed daily throughout the experimental period. Animals were divided into two groups: Control group and 48 hrs sleep deprived animals. Six animals per group were used in this study. Control animals were maintained in the same tank with same setup but without water.

REM sleep deprivation procedure

Adult male Wistar albino rats were subjected to 48hrs of sleep deprivation by means of modified multiple-platform method (MMPM) [8]. MMPM consisted of a tilted water tank with 6 circular platforms of 6.5 cm diameter. The tanks were filled with water to a level of 1 cm below the surface of the platforms. The rats were placed individually on top of each platform, so that the rats could move within the tank by jumping from one platform to another. When the rat enters the REM phase of sleep, muscle atonia set in, causing the imbalance in rats that they fell into the water and remained awake during the REM sleep.

Novel object recognition task (NORT)

The test is based on the basis of the innate behaviors of rats to spend more time in exploring novel object. The test was performed in square arena (100 × 100 × 40cms) whose floor and walls are painted black. The arena was illuminated with dim light during all the phases of experiments. This consists of three phases habituation, familiarization and test. During habituation, animals were placed in the arena for 10 minutes in two sessions, with an interval of 4 hours in between the sessions. Familiarization session was conducted 24 hours after habituation. Two identical objects heavy enough for the rats to displace was used for the study. Each rat was presented either two identical objects placed at the opposite corners of the arena which were 90 cms apart. The time spent by each rat in exploring the objects was recorded for 5 minutes. The test protocol was conducted with an intra-trial interval of 1 hour, after familiarization phase. Each rat was presented with a familiarized object placed at same position as that of familiarization phase and a novel object at place of second familiar object. The time spent in exploring the familiarized object and novel object was recorded for a period of 5 minutes.The objects and box were wiped by 70 % ethanol after each trial to remove the odor of the previous rat. The positions of the objects were similar during training and test [9].

Novel object location task (NOLT)

Novel object location is typically used to assess spatial memory and discrimination in rodents. The novel object placement apparatus consists of an open field arena (40x40x49cm) made of the wooden box with a white floor. The arena is digitally divided into 12 equal quadrants. The corner nearest the center of the northeast, northwest, southeast, and southwest corners serves as placement locations for the objects. On Day 1 (habituation) of the novel object placement task, a single rat is placed in the center of the empty open field and behavior is recorded for 10 min to confirm that there is no difference in anxiety-related behavior. The arena is cleaned with a 70% ethanol solution. On Day 2 of the task, the two identical objects are placed at adjacent northern locations of the arena and a single rat is placed into the center of the arena. Behavior is recorded for 5 min and the time spent investigating each of the objects is measured. After the 5-min exploration period, the arena is cleaned and one object is returned immediately to its former location while the other object is placed in a new location. After a predefined period of time, the same mouse is returned to the arena and time spent exploring each object is recorded and analyzed for the second trial (T_2). The T_2 fraction is calculated by dividing the amount of time spent exploring the object in the novel location divided by the amount of time spent exploring both objects (T2 = ((Time Novel)/ (Time Old + Time Novel)) X 100) [10].

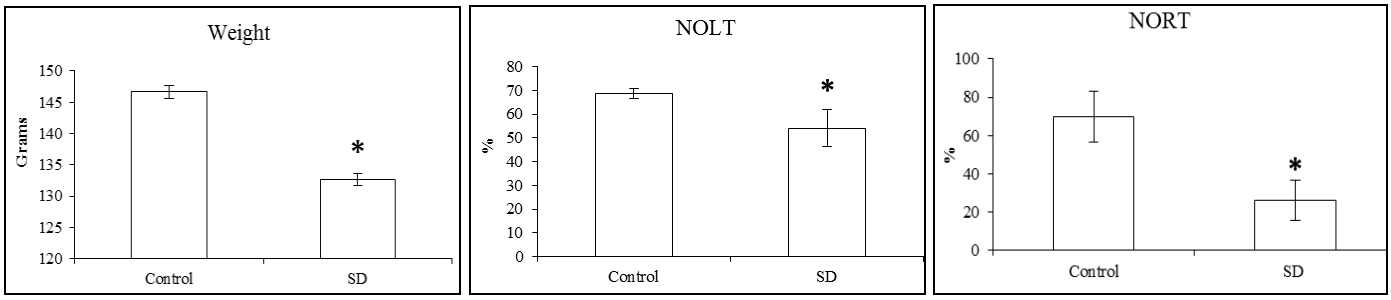
Social preference task

The social preference test was conducted in a rectangular, three chambered box (a center compartment of 20 cm X35 cm X 35 cm with a left and aright compartment of 30 cm X35cm X35 cm) fabricated from opaque gray polycarbonate. The dividing walls had retractable doorways allowing access to each chamber. The test rat was placed in the middle chamber and allowed to explore the entire apparatus for 5 min. Each of the two side chambers contained an empty wire cage. The wire cages were 10 cm in height, with a bottom diameter of 9 cm and bars spaced 1 mm apart. A weighted plastic cone was placed on the top of each cage to prevent climbing by the test rats. Four sets of wire cages were used during the experiment, and all of the cages were washed with water and dried properly between each use. For habituation to the wire cage, each novel pre-pubertal male rat used in the social interaction test had been previously placed in the wire cage in the apparatus without the test rat for 5 min on 3 consecutive days preceding the social test. On the day after the last habituation session, a test rat was placed in the center compartment and allowed to explore the entire apparatus for 10 min. An unfamiliar rat was placed in one of the wire cages located on either side of the social test box during the 10 min session. A Rectangular colored object was placed in the other wire cage on the other side of the box. The location of the stranger and the object in the left and right sides of the chamber was counterbalanced for different animals. Placing the strange rat in a wire cage prevented direct physical contact between the rats and ensured that the social approach was only initiated by the test rat. The time spent sniffing each wire cage was video recorded and manually scored to evaluate the level of preference for the unfamiliar rat as compared to the object. The entire apparatus was cleaned with water and dried thoroughly between each tested rat [11].

Results

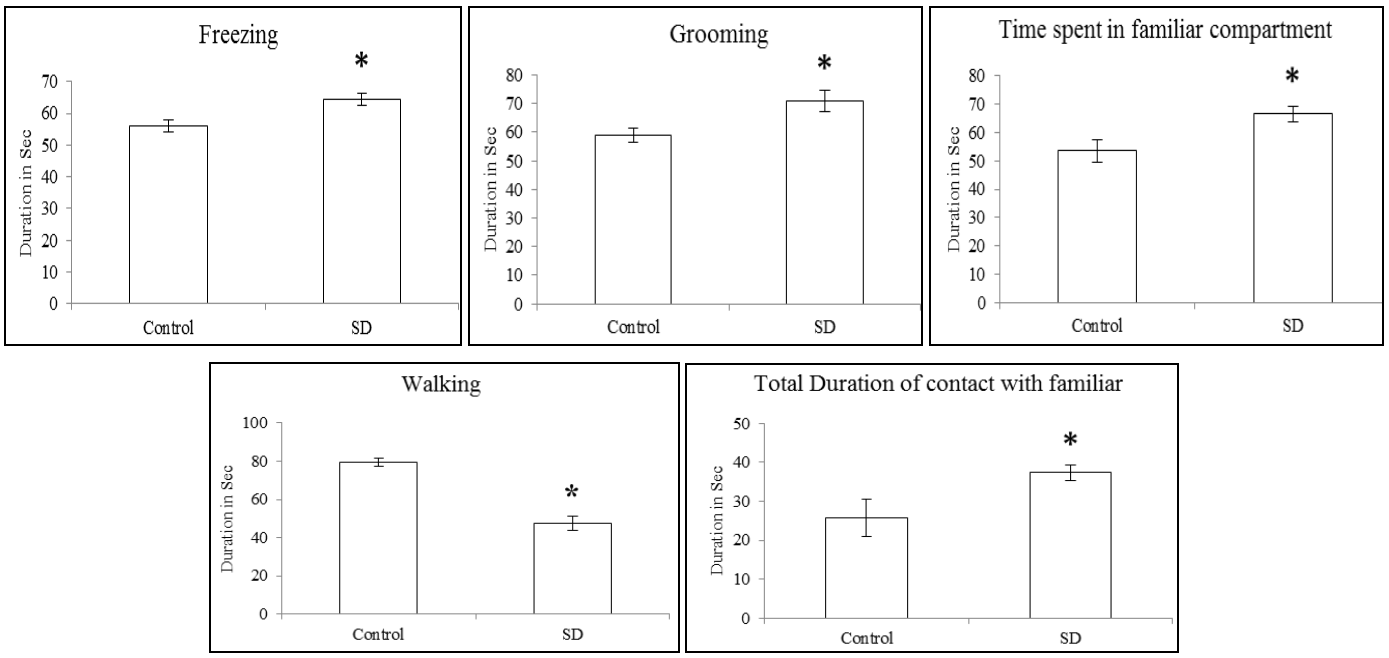
Data were presented, in the form of the bar diagram with mean ± SD. Data are analyzed by paired students t test and $p<0.05$ was considered as significant. The weight of the SD group animals showed a significant ($p<0.05$) decrease compared to control animals (Figure 1). In novel object location task and novel object recognition test sleep deprived animals showed a significant decrease in novelty seeking and novelty preference when compared to control animals (Figure 1). In social preference task with familiar objects, sleep deprived animals showed a significant increase in freezing, grooming, time spent in familiar compartment and total duration of contact with familiar animal when compared to control animals (Figure 2). A significant decrease in walking was observed in social preference task with familiar objects compared with control animals. Assessment of Social Preference with familiar and unfamiliar objects showed a significant increase in freezing, time spent in familiar and

significant decrease in grooming, walking, time spent and contact with unfamiliar when compared to control animal. No significant change in Contact with familiar when compared to control animals (Figure 3).



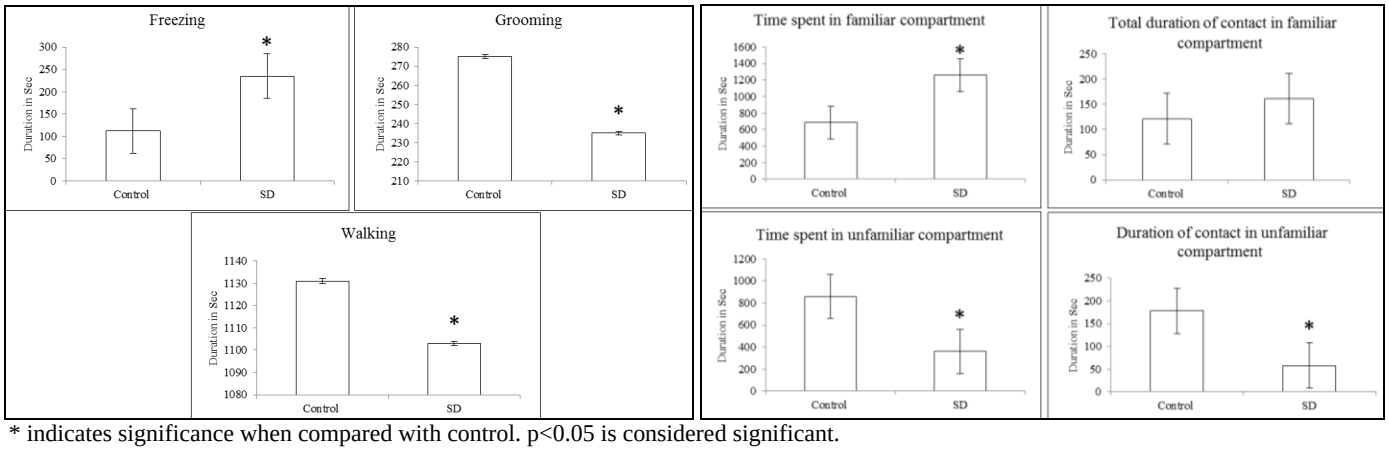
* indicates significance when compared with control. p<0.05 is considered significant.

Fig 1: Weight, NORT and NOLT



* indicates significance when compared with control. p<0.05 is considered significant.

Fig 2: Social preference with familiar



* indicates significance when compared with control. p<0.05 is considered significant.

Fig 3: Social preference with familiar VS unfamiliar

Discussion

Sleep deprivation is a way of life for many people who perform critical societal roles [12] Therefore, it is important to have a thorough understanding of the role of sleep deprivation on reasoning and decision making. The classical view of the effects of sleep deprivation is one of an overall slowing of cognitive abilities. In the current study, the results of 48 hours sleep deprivation shown that the decrease in weight of the SD group animals than control. Reduction in body was also observed after exposure to different from most stressors like paradoxical sleep deprivation paradigm, such as the rotation disk, the flower pot, the cuff pedestal, or the MMPM with concomitant increase or no change in food intake [13].

In the present study decrease in novelty preference and less novelty seeking behavior were observed in NORT and NOLT respectively in sleep derived group animals when compared to the control animals. The negative impact of SD on LTP and synaptic plasticity is thought to be a product of disruptive changes in intracellular signaling molecules and receptors, including NMDA [14, 15] and AMPA receptors [16]. The expression of key signaling proteins and trophic factors, e.g. CREB and BDNF, involved in LTP and memory are impaired in the hippocampus after 8, 24, and 48 hours of SD [17, 18]. Also, SD has shown to have negative impact on intracellular signaling pathways such as the cAMP/PKA pathway, which plays an important modulatory role in LTP and memory. Sleep loss, for as little as 5 hours has shown to increase the levels of phosphodiesterase IV, which in turn impairs LTP expression and decreases the levels of cAMP [19].

Study of Cortese *et al*., 2010 revealed that paradoxical sleep deprivation induced a significant increase in glutamate levels in hippocampus and thalamus. PSD induced impairment in the acquisition, consolidation and retrieval of a discriminative avoidance task [20].

The disruptive effect of REM SD may be related to alterations in the levels of essential signaling molecules involved in memory and synaptic plasticity [21]. Both short- and long-term SD imaging studies in humans have shown reduced alertness and impairment in not only simple tasks such as tests of reaction time or attentions, but complex tasks as well that test working memory, logical reasoning and decision-making [22]. PET studies have shown that 24-72 hours of SD attenuated global brain glucose metabolism, by 6-8% and as much as 15% in the prefrontal cortex, frontal cortex and thalamus, which are key areas involved in mediating attention and higher order cognitive functions [7].

In Social Preference Task SD group exposed to familiar only shown that the increased anxiety behave ours like freezing, grooming, time spent in familiar, contact with familiar and decreased walking when compared to the control animals. Studies are shown that SD detoriate the social stability in SD group animals by the influence of high ACTH and CORT secretion during SD period [13]. Animal's single platform PSD rats had reduced locomotor activity and augmented anxiety-like behavior [23]. The relationship between SD and anxiety remains largely enigmatic, an emerging link is the involvement of oxidative stress in this process and recently reported that SD is associated with specific changes in oxidative stress and antioxidant enzyme levels as well as alterations in anxiety-like behavior of rats [7].

This result paints a more complex picture than the hypothesis that sleep deprivation worsens overall performance in decision making tasks.

Conclusion

From our study 48 hours Sleep deprivation which shown the deleterious effects on new acquired learning and retrieval memory as well as impairs in Social interaction, increases the social avoidance in experimental animals. So we conclude that the sleep is essential for enhance the cognition and social interaction behavior to fulfill their daily needs of the individual.

Acknowledgement

The authors would like to acknowledge Department of Physiology, University Of madras, for providing the opportunity and laboratory facilities to do the research work.

References

1. Tufik S, Andersen ML, Bittencourt LR, Mello MT. Paradoxical sleep deprivation: neurochemical, hormonal and behavioral alterations. Evidence from 30 years of research. Anais da Academia Brasileira de Ciencias. 2009; 81(3):521-38.
2. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. The lancet. 1999; 354(9188):1435-9.
3. Miro E, Cano- Lozano MC, Buela- Casal G. Electrodermal activity during total sleep deprivation and its relationship with other activation and performance measures. Journal of Sleep Research. 2002; 11(2):105-12.
4. Fuller PM, Gooley JJ, Saper CB. Neurobiology of the sleep-wake cycle: sleep architecture, circadian regulation, and regulatory feedback. Journal of biological rhythms. 2006; 21(6):482-93.
5. Orzeł-Gryglewska J. Consequences of sleep deprivation. International journal of occupational medicine and environmental health. 2010; 23(1):95-114.
6. Marshall L, Born J. The contribution of sleep to hippocampus-dependent memory consolidation. Trends in cognitive sciences. 2007; 11(10):442-50.
7. Alkadhi K, Zagaar M, Alhaider I, Salim S, Aleisa A. Neurobiological consequences of sleep deprivation. Current neuropharmacology. 2013; 11(3):231-49.
8. Deborah S, Sergio T. Social stability attenuates the stress in the modified multiple platform method for paradoxical sleep deprivation in the rat. *Physiology Behavior*, 2000; 68:309-316.
9. Bowman RE, MacLusky NJ, Sarmiento Y, Frankfurt M, Gordon M, Luine VN, *et al*. Sexually dimorphic effects of prenatal stress on cognition, hormonal responses, and central neurotransmitters. Endocrinology. 2004; 145(8):3778-87.
10. Ennaceur A, Neave N, Aggleton JP. Spontaneous object recognition and object location memory in rats: the effects of lesions in the cingulate cortices, the medial prefrontal cortex, the cingulum bundle and the fornix. Experimental brain research. 1997; 113(3):509-19.
11. Castro JE, Diessler S, Varea E, Márquez C, Larsen MH, Cordero MI, *et al*. Personality traits in rats predict

vulnerability and resilience to developing stress-induced depression-like behaviors, HPA axis hyper-reactivity and brain changes in pERK1/2 activity. Psych neuroendocrinology. 2012; 37(8):1209-23.
12. Marriott BM. Food components to enhance performance. InAn evaluation of potential performance-enhancing food components for operational rations. National Academy Press London, 1994.
13. Suchecki D, Tufik S. Social stability attenuates the stress in the modified multiple platform method for paradoxical sleep deprivation in the rat. Physiology & behavior. 2000; 68(3):309-16.
14. Chen C, Hardy M, Zhang J, LaHoste GJ, Bazan NG. Biochem Biophys Res Commun. 2006; 340:435-440.
15. Ravassard P, Pachoud B, Comte JC, Mejia-Perez C, Scote-Blachon C, Gay N, *et al*. Sleep. 2009; 32:227–240.
16. Hagewoud R, Whitcomb SN, Heeringa AN, Havekes R, Koolhaas JM, Meerlo P, *et al*. A time for learning and a time for sleep: the effect of sleep deprivation on contextual fear conditioning at different times of the day. Sleep. 2010; 33(10):1315-22.
17. Guzman-Marin R, Ying Z, Suntsova N, Methippara M, Bashir T, Szymusiak R, *et al*. Suppression of hippocampal plasticity-related gene expression by sleep deprivation in rats. J Physiol. 2006; 575:807-19.
18. Alhaider IA, Aleisa AM, Tran TT, Alkadhi KA. Caffeine prevents sleep loss- induced deficits in long- term potentiation and related signaling molecules in the dentate gyrus. European journal of neuroscience. 2010; 31(8):1368-1376.
19. Vecsey CG, Baillie GS, Jaganath D, Havekes R, Daniels A, Wimmer M, *et al*. Sleep deprivation impairs cAMP signalling in the hippocampus. Nature. 2009; 461(7267):1122.
20. Cortese BM, Mitchell TR, Galloway MP, Prevost KE, Fang J, Moore GJ, *et al*. Region-specific alteration in brain glutamate: possible relationship to risk-taking behavior. Physiology & behavior. 2010; 99(4):445-50.
21. Colavito V, Fabene PF, Grassi-Zucconi G, Pifferi F, Lamberty Y, Bentivoglio M, *et al*. Experimental sleep deprivation as a tool to test memory deficits in rodents. Frontiers in systems neuroscience. 2013, 7.
22. Thomas M, Sing H, Belenky G, Holcomb H, Mayberg H, Dannals R, *et al*. Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. Journal of sleep research. 2000; 9(4):335-52.
23. Suchecki D, Tiba PA, Tufik S. Hormonal and Behavioural Responses of Paradoxical Sleep- Deprived Rats to the Elevated Plus Maze. Journal of neuroendocrinology. 2002; 14(7):549-54.