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Effects of Sleep Deprivation on Learning and Memory: A Review Study

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Abstract

Considering the importance of learning and memory and the effects of sleep deprivation on these cognitive functions and knowing that sex hormones have an effect on the sleep and wake cycle in both sexes, this study was designed to investigate the effects of sleep deprivation and sex hormones on learning and memory. Sleep is necessary for the development and survival of the brain and increases the capacity of the brain for cognitive actions. After learning, sleep consolidates newly encoded memories during waking hours. Insufficient sleep is common in modern societies and certain occupations, and this sleep deprivation causes cognitive impairment. The prevalence of sleep problems in adults, especially in women, increases with age and causes severe disorders such as cognitive disorders and problems in quality of life. Also, sex hormones affect brain structure, behavior, learning, and memory in both sexes. Loss of hormonal function is associated with sleep disturbances, and learning and memory decline, especially in women. It can be concluded that ovarian hormones may be an important protective factor against learning and memory disorders in sleep-deprived people.

Keywords: Sleep, Learning, Memory, Hormones

Introduction

Sleep as a natural physiological process has two stages: sleep with rapid eye movements (REM Rapid Eye Movement) and sleep without rapid eye movements (NREM. Non Rapid Eye Movement) (Walker & Stickgold, 2004; van Enkhuizen *et al*., 2014; Abukanna *et al*., 2022). According to the theory of the National Sleep Foundation, 7-8 hours of sleep is necessary for cognitive performance in adults. Restriction or deprivation of sleep is a serious and expanding problem in today's modern societies and special jobs, and the number of people who are regularly deprived of sleep due to the pressures caused by work and psycho-social stress is increasing (van Enkhuizen *et al*., 2014; Makhdoom *et al*., 2021). Studies have shown that disrupting the natural and physiological order of sleep and being deprived of it, depending on the duration and type of deprivation, causes consequences such as stress, pathological anxiety in humans, imbalance between the production of oxidative substances, and cleaning by the antioxidant defense system. Today, it is accepted that sleep plays an essential role in the normal functioning of the body, such as the central nervous system and cognitive functions. Studies have shown that after learning, adequate sleep increases the retention of new information and makes the newly acquired information processed and consolidated without the involvement of the sensory system (Diekelmann & Born, 2010).

Some researchers believe that due to increased brain activity during REM sleep, this part of sleep plays a role in converting short-term to long-term memory. In this connection, it has been shown that after receiving information, REM sleep increases and memory consolidation takes place (Maquet, 2001; Almansour *et al*., 2021).

Sleep disorders affect different aspects of human life and cause changes in the physiological function of humans and animals. Also, the number of people who regularly suffer from sleep deprivation due to work pressure and psycho-social stress is increasing. Interrupted sleep or deprivation of it for a long period can lead to changes in mood and mental disorders, disrupt performance, and have harmful effects on cognitive and motor functions (Scott *et al*., 2006; Phan, 2021; Adewoyin *et al*., 2022). For example, many animal studies have reported that sleep deprivation leads to impaired hippocampal memory and emotional memory and increases anxiety levels (Fernandes-Santos *et al*., 2012). These changes are explained by the fact that the hippocampus is highly sensitive to the effects of sleep deprivation. Accordingly, sleep deprivation hurts hippocampal-dependent learning and memory. Similar studies have shown that sleep deprivation impairs learning and judicial memory and the induction of LTP and decreases the level of brain-derived neurotrophic factor (BDNF) in the hippocampus (Zagaar *et al*., 2013; AlMogbel *et al*., 2021).

It seems that cognitive functions, such as memory, and learning, as well as various aspects of sleep, including sleep quality and pattern, are different in the two sexes (Paul *et al*., 2006; Baker, 2013; Nam *et al*., 2021; Agrawal *et al*., 2022). Changes in sleep pattern are often related to hormonal factors, especially estrogen levels (Paul *et al*., 2006). According to certain research, estrogen

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levels may be a major factor in controlling how well people sleep and think. Furthermore, women report sleep disorders more frequently than males do, with the former group experiencing more sleep issues. Additionally, women report experiencing sleep issues during and after menopause at a higher rate than they do before (Wise *et al*., 2001).

Considering the importance of learning and memory and the effects of sleep deprivation on these cognitive functions and knowing that sex hormones have an effect on the sleep and wake cycle in both sexes, this study was designed to investigate the effects of sleep deprivation and sex hormones on learning and memory.

Sleep

Sleep is a behavior that is observed in most organisms and is opposite to wakefulness and is characterized by a decrease in response to environmental stimuli. Two mechanisms affect the sleep-wake cycle: (1) Biological clock (circadian rhythm): Sleep and wakefulness, like many physiological behaviors and activities, have a 24-hour cycle and follow a regular circadian rhythm. Circadian rhythm is one of the endogenous rhythms that can continue without the influence of environmental factors, but in a natural state, it is affected by the passage of time in the external environment, which is regulated by it. An important internal clock in mammals is the suprachiasmatic nucleus, which is located in the anterior part of the hypothalamus. When these nuclei are destroyed, the circadian period of sleep is lost, like many circadian rhythms; (2) Physiological need for sleep to maintain the stable conditions of the indoor environment: as the duration of waking up increases, the amount of sleep increases. Humans usually fall asleep by entering the stage of light sleep (NREM) and then enter the deeper stage of sleep (NREM) and then the person enters REM sleep, where most dreams are seen in this phase of sleep. In young people, each cycle lasts 90 minutes and repeats about 3-5 times a night (Fuller *et al*., 2006).

REM Sleep Duration

REM sleep begins in the 30th week of pregnancy in the human fetus. A significant portion of sleep is spent in the REM state in mammals whose brains are relatively immature when they are born. In premature babies, REM sleep accounts for 80% of total sleep, whereas in full-term babies, it makes up 50% of total sleep. After that, the proportion of REM sleep decreases rapidly and stabilizes at around 25%, and it decreases even more in old age. There is a theory that suggests early exposure to high levels of REM sleep speeds up brain growth. Additionally, the quantity of REM sleep and the quantity of synaptic formation during this time are strongly correlated. It has also been shown that the high REM sleep time during infancy increases the synaptic density in some areas of the brain such as the hippocampus, which plays an important role in brain development and strengthening the circuits involved in memory. Also, in children, the fourth stage of sleep is with slow waves, and the total sleep time is longer than in adults (Paul *et al*., 2006; Baker, 2013; Salari *et al*., 2015).

The Relationship Between Different Stages of Sleep, Learning and Memory

The results of studies indicate that sleep has beneficial effects on news and non-news memory. During sleep, previously encoded memory strands are reactivated and finally stabilized in the cerebral cortex as a result of changes in neural mediators and cellular processes (such as gene expression). Some researchers have shown that NREM sleep has a facilitating role in consolidating informative memory and hippocampus-dependent memory, and REM sleep has a facilitating role in consolidating non-informative memory. If other research shows the beneficial effects of NREM sleep on news memory. Although these studies show conflicting results, most researchers agree with the sleep sequence theory. This theory states that both REM and NREM sleep stages are useful in memory consolidation. Provided that the appropriate steps or sequence occur (Rauchs *et al*., 2005; Nguyen & Hoang, 2022).

Sleep is a process that consolidates newly acquired information. According to studies, slow wave sleep (SWS) promotes systemic consolidation, and rapid eye movement sleep promotes synaptic consolidation of memory. In this way, during wakefulness, memory streaks are coded in the temporary (hippocampus) and permanent (cerebral cortex) places of memory. During slow wave sleep, an active system consolidation occurs that reactivates the newly encoded memory in the temporary memory (hippocampus) and permanent memory (cerebral cortex), which process reorganizes and integrates new memories into The long-term memory network in the cerebral cortex. During REM sleep, the connection between short-term and long-term memory storage is lost, allowing local and separate synaptic consolidation to occur, and in this type of consolidation, local increase in synaptic plasticity at high levels of Goli mediator. Nerves occur in the cortex. This system also eliminates weakened synapses but strengthens stronger synapses or prevents synaptic saturation during reactivation. Under normal conditions, REM sleep is necessary for learning and memory, and after learning, it is also necessary for memory consolidation. Studies related to psychology, neurophysiology, and neuroanatomy confirm this issue (Manber & Armitage, 1999; Smith, 2001; Sohal *et al*., 2022).

During wakefulness, newly acquired memory strands are encoded, and during sleep, they are reactivated by slow waves of neurons in the hippocampus or the temporary memory storage area. Newly encoded memories are transferred from the hippocampus to the cortex at the same time. This function causes newly acquired memories to be separated and reorganized from the hippocampus during SWS sleep, and local consolidation processes take place in the cortex during REM sleep (Diekelmann & Born, 2010). The involvement of REM sleep in learning and memory can be demonstrated by studies of the deprivation of REM sleep and the increase of REM sleep during learning and after it (Smith, 1985; Smith & Kelly, 1988; Boujguenna *et al*., 2023). Some brain regions are involved in both memory processing and REM sleep control. For example, the locus coeruleus plays an important role in the initiation and maintenance of REM sleep. It is also involved in memory and its stimulation leads to a significant increase in learning (Majumdar & Mallick, 2003; Takahashi *et al*., 2010; Huzaifa *et al*., 2023).

The Relationship Between Sleep Deprivation, Learning, and Memory

Chronic lack of sleep is one of the problems of today's modern societies. Many studies have shown the relationship between sleep deprivation and cognitive functions in humans and animals. Sleep deprivation has shown negative effects on memory and other cognitive functions and synaptic plasticity, and these cognitive disorders following sleep deprivation are probably caused by cellular and molecular changes such as neurotransmitter growth factors and signaling molecules in some involved brain areas. It is in this phenomenon (Saadati *et al*., 2014a, b; Martyshuk *et al*., 2022). As REM sleep is necessary for memory consolidation, much evidence also shows that deprivation of REM sleep causes cognitive disorders (Esmaeilpour *et al*., 2015).

The findings of studies have shown that sleep deprivation before and after learning disrupts memory. It has also been shown that, in addition to causing severe behavioral deficits, sleep deprivation severely reduces membrane and synaptic excitability in CA1 pyramidal neurons of the hippocampus and prevents the production of synaptic LTP (Vecsey *et al*., 2018). Also, the negative effects of sleep deprivation on synaptic plasticity, as a result of changes in signaling molecules and receptors such as N-Methyl-D-aspartate (NADA) and AMPA-amino-3-hydroxy-5-methylisoxazole-4-propionic acid) falls. Also studies Others have reported a significant decrease in the ratio of NMDA to AMPA subunits in CA1 pyramidal cells as the reason for the decrease in LTP induction in REM sleep-deprived rats and have shown that there is no change in sensitivity to glutamate, but MR1 subunits and NR2B NMDA receptors remain in the cytoplasm after REM sleep deprivation and as a result the surface expression of NMDA is altered (Chen *et al*., 2006; Lopez *et al*., 2008; Saaty, 2022).

The deleterious effects of REM sleep deprivation on cognitive functions are investigated using different models (such as a cylindrical platform on water) in animals. In this model, as a result of the loss of mental capacity, there is a significant reduction (95-90 (%)) in REM sleep, which has been proven in studies using EEG recording in sleep-deprived animals (Machado *et al*., 2004).

The Role of Sleep Deprivation and Sex Hormones in Cognitive Actions

The Effect of Sex Hormones on Sleep and Its Deprivation

The biological importance of adequate sleep is revealed when a person experiences physiological and psychological disorders related to sleep deprivation. Women experience more sleep disorders than men, and most of these disorders occur in connection with the sexual cycle. Women experience many hormonal changes during the sexual cycle, especially during puberty, pregnancy, and menopause. It is hypothesized that normal sleep control mechanisms in women may be affected by circulating sex steroids (Moline *et al*., 2004; Dzaja *et al*., 2005). Sex hormones (testosterone in men and estrogens and progestin in women) play a role in modulating sleep-related behaviors. A cohort study in men aged 65 years and older has shown that low testosterone levels are associated with decreased sleep efficiency, increased nocturnal awakenings, and decreased SWS time. If the results of another study indicate that testosterone aggravates sleep apnea. Although the basic structure of sleep does not show a significant difference in women and men (Baker & Driver, 2007), EEG recording during the sexual cycle in women shows an increase in brain activity and a decrease in the delay of entering stage 3 sleep with slow waves during the luteal phase. REM sleep also changes during the sexual cycle. Especially in the luteal phase, the duration of REM sleep decreases. The results of these findings show that estrogen and progesterone levels may play an important role in sleep regulation (Driver *et al*., 2008). In women who have gone through menopause, the function of female sex hormones in controlling sleep is more evident. These individuals have lower amounts of circulating estrogen, and the women exhibit a higher prevalence of sleep disturbances than the men. In the luteal phase as opposed to the follicular phase, middle-aged women with and without sleep problems demonstrated lower SWS and more frequent sleep excitability awakenings. Also, in both groups, sleep spindles in the luteal phase compared to the follicular phase show a clear increase in number, length, duration, and frequency higher than 14-17 Hz (de Zambotti *et al*., 2013). In general, there is disagreement about the effects of sex steroids on sleep in both sexes, as the mechanisms underlying how sex steroids affect the sleep cycle are not fully established.

The Effect of Sex Hormones on Memory and Learning

Electrophysiological and molecular behavioral studies have shown that ovariectomized animals are more sensitive to cognitive disorders caused by sleep deprivation (Hajali *et al*., 2012). Also, treatment with synthetic estrogen in postmenopausal women increases REM sleep and improves sleep quality (Polo-Kantola *et al*., 1998). The mentioned results in animal studies have also shown that mice without ovaries show less REM sleep than themselves. The decrease in testosterone in males affects the quality of sleep and makes the person prone to sleep deprivation. Testosterone level has periodic changes, the peak of which is during sleep. Gender affects the cycle of sleep and wakefulness, REM and NREM sleep, and sex hormones, whose receptors exist in the central nervous system, are probably responsible for the difference in the sleep patterns of both sexes. On the other hand, hormones Sex, especially estrogen, has a powerful effect on memory and cognition, strengthens glutamate synaptic transmission, modulates its receptors, and facilitates memory formation (Scharfman & MacLusky, 2005). Numerous investigations into the anatomy, physiology, and cognitive processes associated with the hippocampal region have also demonstrated the importance of estrogen. For instance, estrogen enhances memory and increases the density of dendritic spines in the hippocampus of female rats. (Luine & Frankfurt, 2013). Many studies implicate BDNF as a potential mediator of estrogen effects in the brain. It has been found that there is an estrogen-responsive element (ERE) in the BDNF gene, through which estrogen regulates the expression of BDNF. According to this hypothesis, ovariectomy in female rats reduced BDNF expression in their hippocampus, while estrogen administration restored it to normal levels (Luine & Frankfurt, 2013). In several studies, different effects of experimental interventions on the responses of both males and females have been reported (Driver *et al*., 2008; Hajali *et al*., 2012; de Zambotti *et al*., 2013; Saadati *et al*., 2015).

Effects of Sleep Disturbance in the Elderly with Age

There is a significant disturbance in the structure and normal pattern of sleep, sleepiness during the day, and consecutive waking up during the night, and the percentage of REM sleep decreases. The prevalence of insomnia in people aged 65 and above is between 12-30% and this sleep disorder disrupts daily functioning and quality of life. Disruption of the sleep pattern in old animals causes a decrease in brain functions, including response to stimulation, sleep quality, memory, and cognitive functions (Hornung *et al*., 2005; Dresler *et al*., 2013; MacLeod *et al*., 2018). Sleep and memory are affected by brain aging processes, such as atrophy of white and black matter, synaptic degeneration, decreased blood flow, and neurochemical changes. Many studies show the relationship between sleep disorders during the night and cognitive performance in elderly people, Alzheimer's patients, and postmenopausal women, as a result of the increase in the number of these people in today's societies, an intervention that can correct the quality of sleep is needed (Hornung *et al*., 2005).

In the end and based on the findings of this research, it is suggested that due to the profound and proven effects of sleep on learning and memory consolidation, as well as gender differences in aspects such as basic sleep patterns, learning and memory abilities, structure, and organization. The excitability of the hippocampus and the effects of sex hormones on cognitive processes and the existence of sleep problems in women, especially the elderly and postmenopausal, it is necessary and necessary to conduct more studies in this field.

Conclusion

Sleep is necessary for the development and survival of the brain and increases the capacity of the brain for cognitive actions. After learning, sleep consolidates newly encoded memories during waking hours. Insufficient sleep is common in modern societies and certain occupations, and this sleep deprivation causes cognitive impairment. The prevalence of sleep problems in adults, especially in women, increases with age and causes severe disorders such as cognitive disorders and problems in quality of life. Also, sex hormones affect brain structure, behavior, learning, and memory in both sexes. Loss of hormonal function is associated with sleep disturbances, and learning and memory decline, especially in women. It can be concluded that ovarian hormones may be an important protective factor against learning and memory disorders in sleep-deprived people.

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