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Original Article

The effect of citalopram treatment on memory performance, mood state, catalase, BDNF, and MDA in REM sleep-deprived rats

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Abstract

Rapid-eye movement (REM) sleep is a critical stage of sleep that plays a pivotal role in memory formation, consolidation, and mood regulation. While REM sleep deprivation (REM SD) has been shown to impair cognitive and affective functions, findings across studies remain inconsistent. REM SD may also influence the expression of brain-derived neurotrophic factor (BDNF), a key protein involved in memory and mood-related processes. In this study, we investigated the effects of REM SD (6 h/day for 7 days) on behavioral and cognitive performance, BDNF levels in the prefrontal cortex, and serum markers of oxidative stress—catalase (CAT, an antioxidant enzyme) and malondialdehyde (MDA, a lipid peroxidation product). Additionally, we evaluated the potential therapeutic effect of citalopram (20 mg/kg, i.p., for 7 days) on REM SD-induced behavioral deficits. Our results demonstrated that REM SD increased locomotor activity and rearing behavior, impaired passive avoidance memory, and reduced pain threshold. REM SD also downregulated prefrontal BDNF expression but did not alter serum CAT or MDA levels. Citalopram treatment reversed REM SD-induced hyperlocomotion, increased rearing, pain hypersensitivity, and BDNF downregulation; however, it did not significantly improve memory impairment. Depressive-like behavior remained unchanged across groups. These findings suggest that BDNF modulation may underlie both the detrimental effects of REM SD and the therapeutic actions of citalopram, whereas peripheral oxidative stress markers (CAT and MDA) do not appear to play a major role in this paradigm.

Keywords: Rapid-eye movement (REM), Sleep deprivation (SD), Brain-derived neurotrophic factor (BDNF), Catalase (CAT), Malondialdehyde (MDA).

1. Introduction

Insufficient sleep or sleep deprivation (SD) has deleterious effects on cognitive and behavioral functions and mood state. Evidence has shown that SD potently increases neuroinflammation and oxidative stress, impairs cognitive functions, and attenuates neurogenesis and synaptic plasticity [1-6]. Also, rapid-eye movement (REM) stage of sleep, as a critical stage of sleep, is significantly involved in the modulation of mood and cognition [7-9]. Previous reports have shown that REM SD leads to mood disturbances and cognitive dysfunctions such as memory impairments, mania, and obsessive-compulsive disorder (OCD) and anxiety [10-14].

REM SD can manipulate the oxidative status of the body. Unfortunately, most studies have evaluated the effects of total SD but not REM SD on the oxidative status. Previous research has shown that REM SD for 72h may increase malondialdehyde (MDA) and decrease catalase (CAT) levels in the thalamus of rats [15]. Furthermore, REM SD increases MDA and nitric oxide levels in the hippocampus of rats [16]. However, another study has shown no significant changes in MDA levels following 72h REM SD in rats [12]. Also, it has been shown that 48h REM SD has no effect on the hippocampal level of MDA [17]. But evidence is very limited.

REM SD also affects the level of brain-derived neurotrophic factor (BDNF). BDNF modulates mood state and cognitive abilities [18]. BDNF dysfunction is related to mood disturbances, cognitive dysfunctions, and neuropsychiatric disorders [19-21]. It has been shown that REM SD potently decreases BDNF expression levels in the hippocampus of female rats [10]. Maternal short-term REM sleep deprivation decreases BDNF levels in the rats' offspring [22]. However, there are many inconsistent reports on the effect of REM SD on BDNF levels [23, 24].

Citalopram is a selective serotonin reuptake inhibitor (SSRI) that is used for the treatment of depression, OCD, and anxiety disorders [25]. Evidence has shown that citalopram may affect the expression level of BDNF. It has been shown that citalopram at the doses of 30 and 50 mg/

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kg decreases BDNF levels in the hippocampus of rats, leading to memory deficits [26]. Furthermore, citalopram decreases BDNF protein levels in the hippocampus of rats [27]. Previous research has reported that citalopram has no effect on the decreased BDNF level induced by 3, 4-methylenedioxymethamphetamine (MDMA) in rats [28]. However, another study has shown that citalopram increases BDNF levels in the serum of mice [29]. Citalopram also increases BDNF levels in the hypothalamus but not the hippocampus and the prefrontal cortex of rats [30]. Also, it has been revealed that citalopram improves synaptic function via increasing BDNF activity in the hippocampus of rats [31]. Citalopram may also affect the level of MDA and CAT. Previous study has shown that citalopram increases CAT and reduces MDA levels in rats exposed to cigarette smoke [32]. However, evidence is so limited.

According to the mentioned findings, the present study aims to investigate the effect of citalopram on cognitive functions and mood state, BDNF, CAT, MDA, and nitric oxide levels in male rats.

2. Material and Method

2.1. Animals

The present study used sixty-three male rats (200-220g, 9-10 weeks old), which were divided into nine groups (n = 7). All seven rats in each group were exposed to behavioral tests, while three rats per group were selected for gene expression analyses. In the lab, there was a standard 12h: 12h light/dark cycle (lights on at 07:00) and stable temperature (22±2°C). All the rats were born and bred in Cognitive Neuroscience Lab, Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran, and had free access to food and water. Our experimental protocol was designed in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals [33].

2.2. Citalopram

Citalopram (Tehran Darou, Tehran, Iran) was intraperitoneally injected at a dose of 20 mg/kg [34, 35] for seven consecutive days during sham-REM SD or REM SD period. Saline was also intraperitoneally injected in a volume of 0.5 mL/rat.

2.3. REM SD apparatus

REM sleep deprivation (RSD) was induced using the standard multiple-platform tank (platform diagonal 7 cm; water level 2 cm below platform), 6 h/day for 7 consecutive days; sham-RSD rats were placed on larger platforms (15 cm) that allow REM. This setup reliably interrupts REM by precipitating awakenings upon atonia-related loss of posture. Procedures followed our previously published protocol with minor adaptations [13].

2.4. Open field test (OFT)

Locomotion and exploratory rearing were quantified in a clear 30 × 30 × 40 cm arena during 300 s; crossings were counted as motor activity and vertical rears as anxiety-sensitive exploration. Testing was performed 30 min after the last RSD/injection session as detailed previously [36-38].

2.5. Hot plate

Thermal nociception was assessed on a 50 °C plate; latency to first paw-lick was recorded with a 100 s cutoff, 30 min after OFT, per our prior methods [39, 40].

2.6. Forced swim test (FST)

In a transparent cylinder (water depth ≈ 2/3 body length), rats swam for 300 s; cumulative immobility time was scored as depressive-like behavior, 30 min post–hot plate, following our established protocol [41].

2.7. Passive avoidance memory

A two-trial step-through paradigm was used (0.5 mA, 2 s foot shock during training); 24 h later, latency to enter the dark chamber (max 300 s) indexed retention, as previously described [26].

2.8. Real time PCR

Total RNA from prefrontal cortex was extracted and reverse-transcribed; relative BDNF expression was quantified by SYBR-green qPCR using GAPDH as the reference and the 2^-ΔΔCt method. Primer validation and melt-curve analyses followed our published procedures [42, 43].

The specific sequences of the primers used are shown in Table 1.

2.9. Experimental groups

The present study included 9 groups (n = 7):

Control rats (Three groups):

Group 1 (No injection): There was no intervention.

Group 2 (Saline): The rats were injected with saline (0.5 mL/rat) for seven consecutive days.

Group 3 (Citalopram): The rats were injected with citalopram (20 mg/kg) for seven consecutive days.

Sham-REM SD rats (Three groups):

Group 4 (No injection): The rats were placed on REM SD apparatus with larger platforms for seven consecutive days (6h/day).

Group 5 (Saline): The rats were placed on REM SD apparatus with larger platforms and were injected with saline (0.5 mL/rat) for seven consecutive days (6h/day).

Group 6 (Citalopram): The rats were placed on REM SD apparatus with larger platforms and were injected with citalopram (20 mg/kg) for seven consecutive days (6h/day).

REM SD rats (Three groups):

Group 7 (No injection): The rats were deprived of REM phase for seven consecutive days (6h/day).

Group 8 (Saline): The rats were deprived of REM phase and were injected with saline (0.5 mL/rat) for seven

Table 1. Primer sequences used for real-time PCR analysis of BDNF gene expression.

Gene	Primer Sequence (5' → 3')	Product Size (bp)
BDNF	Forward: ACGGTCACAGTCCTGGAGAAAG Reverse: ACGATTGGGTAGTTCGGCATT	189

GAPDH was used as the endogenous reference gene for normalization. All primers were designed and validated for specificity and efficiency prior to use.

consecutive days (6h/day).

Group 9 (Citalopram): The rats were deprived of REM phase and were injected with citalopram (20 mg/kg) for seven consecutive days (6h/day).

2.10. Humane endpoints and euthanasia

At the end of all behavioral assessments, animals were humanely euthanized in accordance with our institutional guidelines and the NIH Guide for the Care and Use of Laboratory Animals (2011) and the approved protocol IR.IAU.PS.REC.1403.185. Rats were deeply anesthetized with an intraperitoneal injection of ketamine/xylazine (80/10 mg/kg, i.p.). Loss of pedal withdrawal and corneal reflexes was verified before proceeding. For animals designated for molecular analyses, blood was collected by cardiac puncture under deep anesthesia (to obtain serum for CAT and MDA), immediately followed by cervical dislocation (secondary physical method) to ensure death; the brain was rapidly removed, and the prefrontal cortex was dissected on an ice-cold plate and snap-frozen (−80 °C) to preserve RNA integrity. For animals not used for molecular sampling, euthanasia was completed by cervical dislocation after confirmation of a deep surgical plane of anesthesia. This sequence minimizes pain and distress, prevents agonal changes in RNA/proteins, and avoids confounding due to perfusion or fixatives for the targets measured in this study.

Rationale. We selected ketamine/xylazine to achieve a rapid, stable surgical plane of anesthesia prior to a physical secondary method, consistent with widely accepted humane endpoints for rodents. Avoidance of transcardial perfusion (fixatives) was intentional to prevent dilution or alteration of BDNF mRNA/protein and serum redox markers.

2.11. Statistical analyses

After the completion of all behavioral and molecular tests, data analyses were done using the SPSS software (V.26). Any significant difference was assessed using one-way ANOVA and post hoc Tukey test. Data were provided as mean S.D. and $P<0.05$ was assigned as the level of statistical significance.

3. Results

3.1. Locomotor activity

Significant differences between control groups were measured using one-way ANOVA and showed no differences ($F_{2, 18} = 0.56$, $P > 0.05$). Significant differences between sham-REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18} = 0.01$, $P > 0.05$). Significant differences between REM SD groups were measured using one-way ANOVA and showed differences ($F_{2, 18} = 31.20$, $P < 0.001$). Locomotor activity was increased in REM SD rats, while citalopram restored this effect, as shown by the Post hoc Tukey test ($P < 0.001$) (Figure 1).

The results of two-way ANOVA to compare control and sham-REM SD groups showed that the effect of REM SD ($F_{1, 36} = 0.02$, $P > 0.05$), injections ($F_{2, 36} = 0.05$, $P > 0.05$), and REM SD*injections ($F_{2, 36} = 0.20$, $P > 0.05$) was not significant. The results of two-way ANOVA to compare sham-REM SD and REM SD groups showed that the effect of REM SD ($F_{1, 36} = 25.29$, $P < 0.001$), injections ($F_{2, 36} = 19.80$, $P < 0.001$), and REM SD*injections ($F_{2, 36} = 19.48$, $P < 0.001$) was significant. Post hoc Tukey test showed that locomotor activity was increased in REM SD rats and REM SD rats received saline ($P < 0.001$), however, citalopram reversed this effect ($P < 0.001$) (Figure 1).

3.2. Rearing

Significant differences between control groups were measured using one-way ANOVA and showed no differences ($F_{2, 18} = 0.52$, $P > 0.05$). Significant differences between sham-REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18} = 1.52$, $P > 0.05$). Significant differences between REM SD groups were measured using one-way ANOVA and showed differences ($F_{2, 18} = 74.64$, $P < 0.001$). Rearing was increased in REM SD rats, while citalopram restored this effect, as shown by the Post hoc Tukey test ($P < 0.001$) (Figure 2).

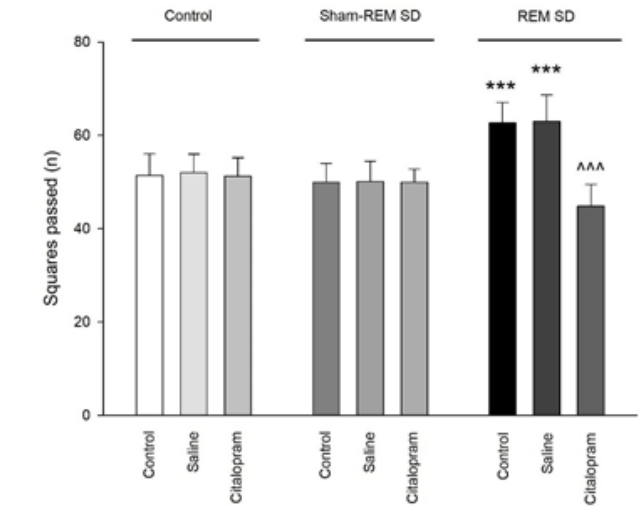


Fig. 1. Locomotor activity (number of squares passed) in all experimental groups (control or sham-REM SD or REM SD rats received no injection, or saline 0.5 mL/rat, or citalopram 20 mg/kg) [***P < 0.001 compared to respective group in sham-REM SD rats, ^^^P < 0.001 compared to control REM SD rats; n = 7].

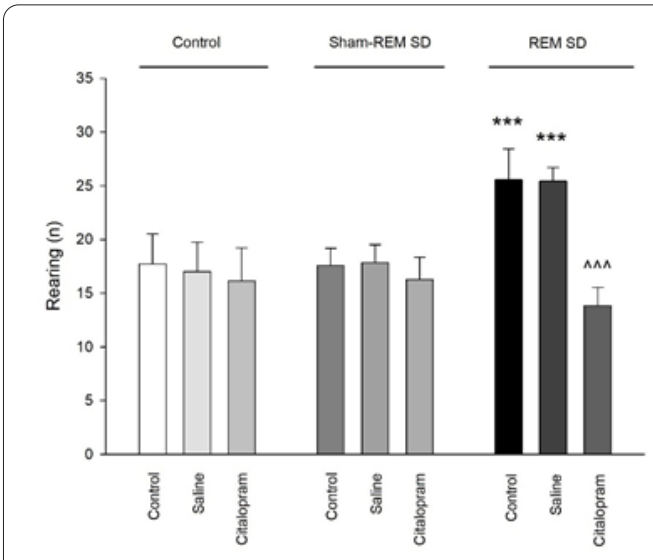


Fig. 2. Anxiety-like behavior (number of rearing) in all experimental groups (control or sham-REM SD or REM SD rats received no injection, or saline 0.5 mL/rat, or citalopram 20 mg/kg) [***P < 0.001 compared to respective group in sham-REM SD rats, ^^^P < 0.001 compared to control REM SD rats; n = 7].

The results of two-way ANOVA to compare control and sham-REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 0.15, P > 0.05), injections ($F_{2, 36}$ = 1.44, P > 0.05), and REM SD*injections ($F_{2, 36}$ = 0.16, P > 0.05) was not significant. The results of two-way ANOVA to compare sham-REM SD and REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 54.03, P < 0.001), injections ($F_{2, 36}$ = 53.44, P < 0.001), and REM SD*injections ($F_{2, 36}$ = 32.68, P < 0.001) was significant. Post hoc Tukey test showed that rearing was increased in REM SD rats and REM SD rats received saline (P < 0.001); however, citalopram reversed this effect (P < 0.001) (Figure 2).

3.3. Pain threshold

Significant differences between control groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 0.25, P > 0.05). Significant differences between sham-REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 0.24, P > 0.05). Significant differences between REM SD groups were measured using one-way ANOVA and showed differences ($F_{2, 18}$ = 25.61, P < 0.001). Pain threshold was decreased in REM SD rats, while citalopram restored this effect, as shown by the Post hoc Tukey test (P < 0.001) (Figure 3).

The results of two-way ANOVA to compare control and sham-REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 0.00, P > 0.05), injections ($F_{2, 36}$ = 0.48, P > 0.05), and REM SD*injections ($F_{2, 36}$ = 0.00, P > 0.05) was not significant. The results of two-way ANOVA to compare sham-REM SD and REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 30.53, P < 0.001), injections ($F_{2,36}$ = 11.32, P < 0.001), and REM SD*injections ($F_{2,36}$ = 8.67, P < 0.001) was significant. Post hoc Tukey test showed that pain threshold was decreased in REM SD rats and REM SD rats received saline (P < 0.001); however, citalopram reversed this effect (P < 0.001) (Figure 3).

3.4. Immobility

Significant differences between control groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 0.20, P > 0.05). Significant differences between sham-REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 1.16, P > 0.05). Significant differences between REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 2.38, P > 0.05) (Figure 4).

The results of two-way ANOVA to compare control and sham-REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 0.08, P > 0.05), injections ($F_{2, 36}$ = 1.02, P > 0.05), and REM SD*injections ($F_{2, 36}$ = 0.23, P > 0.05) was not significant. The results of two-way ANOVA to compare sham-REM SD and REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 2.99, P < 0.001), injections ($F_{2, 36}$ = 0.35, P < 0.001), and REM SD*injections ($F_{2,36}$ = 3.01, P < 0.001) was not significant (Figure 4).

3.5. Passive avoidance memory

Significant differences between control groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 0.00, P > 0.05). Significant differences between sham-REM SD groups were measured using one-way ANOVA and showed no differences ($F_{2, 18}$ = 0.00, P > 0.05). One-way ANOVA revealed a significant impairment of passive avoidance memory in REM SD rats compared with sham-REM SD controls (P < 0.001). However, citalopram treatment did not significantly improve latency to enter the dark chamber in REM SD rats (P > 0.05).Passive avoidance memory was impaired in REM SD rats, while citalopram had no effect, as shown by the Post hoc Tukey test (P < 0.001) (Figure 5).

The results of two-way ANOVA to compare control and sham-REM SD groups showed that the effect of all variables was not significant (all the rats stayed 300 seconds in the light chamber). The results of two-way ANOVA to compare sham-REM SD and REM SD groups showed that the effect of REM SD ($F_{1, 36}$ = 137.18, P < 0.001) but not injections (F2, 36 = 0.35, P > 0.05) and REM SD*injections ($F_{2, 36}$ = 0.35, P < 0.001) was significant. Post hoc Tukey test showed that passive avoidance memory was impai-

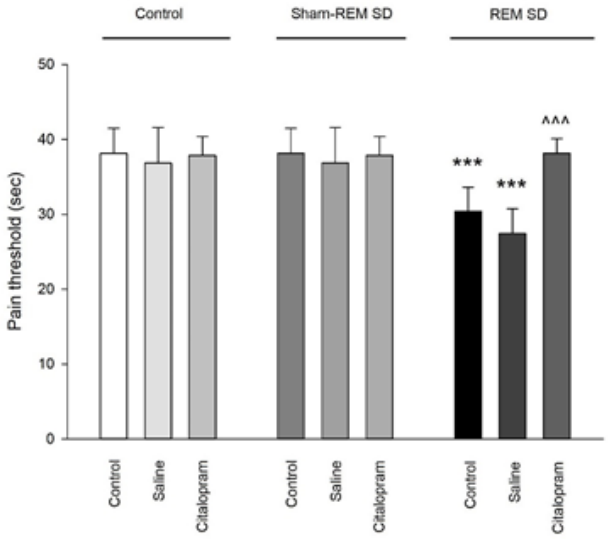


Fig. 3. Pain threshold (sec) in all experimental groups (control or sham-REM SD or REM SD rats received no injection, or saline 0.5 mL/rat, or citalopram 20 mg/kg) [***P < 0.001 compared to respective group in sham-REM SD rats, ^^^P < 0.001 compared to control REM SD rats; n = 7].

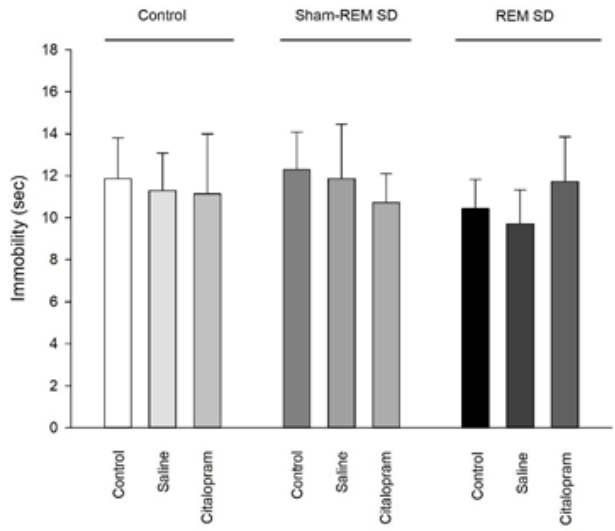


Fig. 4. Depressive-like behavior (sec, the duration of immobility) in all experimental groups (control or sham-REM SD or REM SD rats received no injection, or saline 0.5 mL/rat, or citalopram 20 mg/kg) [n = 7].

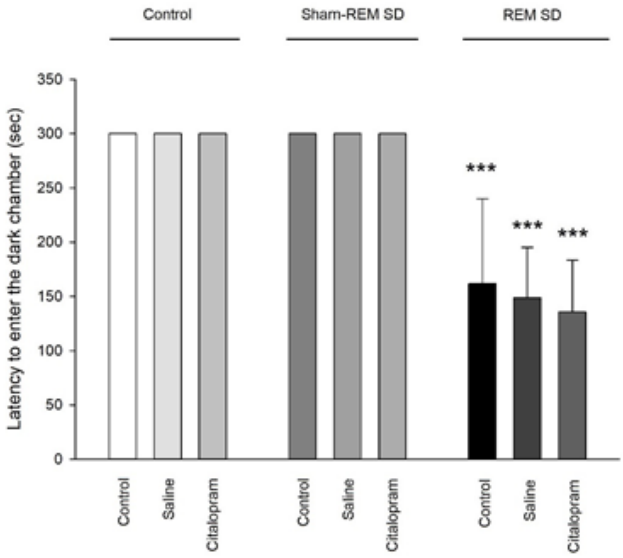


Fig. 5. Latency to enter the dark chamber (passive avoidance memory performance) in all experimental groups (control or sham-REM SD or REM SD rats received no injection, or saline 0.5 mL/rat, or citalopram 20 mg/kg) [***P < 0.001 compared to respective group in sham-REM SD rats; n = 7].

red in all groups (P < 0.001) and citalopram had no effect (Figure 5).

3.6. Molecular results

BDNF- Significant differences between groups were measured using one-way ANOVA and showed differences ($F_{2, 6}$ = 17.15, P < 0.01). BDNF expression levels were decreased in REM SD rats, as shown by the Post hoc Tukey test (P < 0.01). Citalopram reversed REM SD-induced BDNF downregulation (P < 0.01) (Figure 6).

Catalase- Significant differences between groups were measured using one-way ANOVA and showed no differences ($F_{2, 6}$ = 0.80, P > 0.05) (Figure 7).

MDA- Significant differences between groups were measured using one-way ANOVA and showed no differences ($F_{2, 6}$ = 0.28, P > 0.05) (Figure 8).

4. Discussion

As the results showed, REM SD potently increased locomotor activity and rearing behavior, impaired memory performance, and decreased pain threshold. REM SD attenuated BDNF expression levels, while it had no effect on CAT and MDA. On the other hand, citalopram reversed all the effects of REM SD on behavioral parameters and BDNF levels, while having no effect on CAT and MDA. Depressive-like behavior was also unaffected. Therefore, it seems that BDNF regulation is involved in the deleterious effects of REM SD and therapeutic effects of citalopram, while CAT and MDA were unaffected.

REM SD has deleterious effects on cognition and behavior [10, 44, 45], while there are many inconsistent reports [24, 46]. REM stage of sleep is characterized by brain activity like wakefulness, atonia of postural muscles, and myoclonic events [47]. REM stage of sleep has a main role in the modulation of synaptic function, learning and memory processes [48, 49]. REM stage of sleep also critically modulates memory consolidation [50]. Early evidence has shown that REM stage of sleep is significantly increased after learning sessions in rodents [51-53]. It has

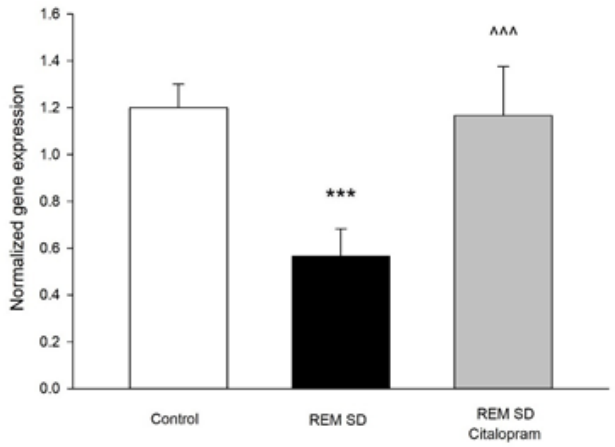


Fig. 6. BDNF expression level in experimental groups with significant changes in behavior (control rats, REM SD rats, REM SD rats received citalopram) [***P < 0.001 compared to no injection, ^^^P < 0.001 compared to REM SD; n = 3].

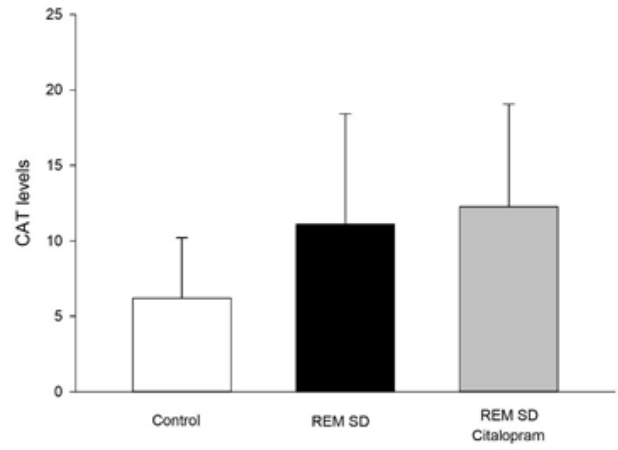


Fig. 7. Catalase level in experimental groups with significant changes in behavior (no injection rats, REM SD rats, REM SD rats received citalopram) [n = 3].

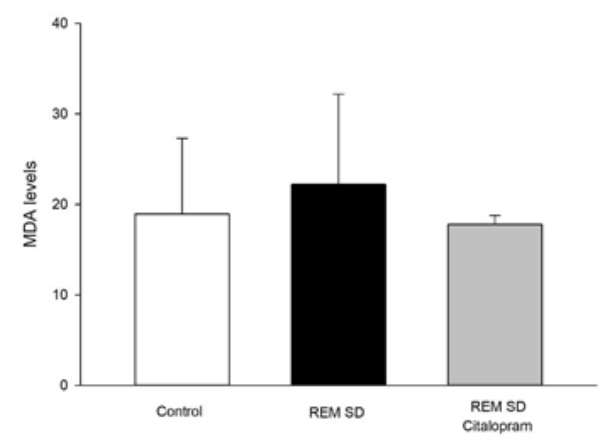


Fig. 8. MDA level in experimental groups with significant changes in behavior (no injection rats, REM SD rats, REM SD rats received citalopram) [n = 3].

been reported that rats living in enriched compared with impoverished environments show increased REM sleep, although increases in non-REM sleep have also been observed[54, 55]. REM SD often impairs memory formation

on complex tasks, shown in many preclinical studies [10, 56-58]. It has been shown that REM SD potently disrupts passive avoidance memory [59, 60].

REM stage of sleep also has a main role in the modulation of emotional reactivity and mood [61, 62]. The role of REM alteration in mood disturbances has been revealed in many studies. Evidence has shown that REM stage disruption may lead to mood disorders, or vice versa. For example, it has been shown that decreased REM sleep latency (faster entry into REM), a prolonged first REM period, and an increase in REM density are the important hallmarks of depression [63, 64]. Early evidence has revealed that short (< 65 min) REM sleep latency predicts both response to antidepressant treatment and risk of relapse in major depression [65, 66]. However, it has been shown that REM SD may decrease immobility in the forced swim test [67]. A recent study has shown that chronic REM SD in female rats significantly decreases immobility in the forced swim test [10]. Another study has suggested that REM SD has an anti-immobility effect in the forced swim test [68]. In addition, many studies have considered an anti-depressant effect for REM SD [69-71]. Therefore, the interplay between REM stage of sleep and REM SD, and depression seems to be so complicated. The results of the present research showed impaired passive avoidance memory in REM SD rats, while immobility was unaffected.

In the open field test, REM SD rats showed hyperactivity and increased rearing behavior. REM SD may lead to hyperlocomotion; however, evidence is so limited. For example, a recent report has shown that chronic REM SD induces hyperlocomotion in female rats [13]. Another study has shown the same effect [10]. It has been shown that REM SD in rats increases rearing and crossing square in the open field test [12]. Another study has also shown that 72h REM SD significantly increases rearing behavior in the open field test [72]. On the other hand, large evidence has shown changes in pain threshold following REM SD. Sleep disturbances drastically increase pain sensitivity in clinical and preclinical studies [73]. A previous study has shown hyperalgesia induced by REM SD in female rats [10]. It has been revealed that REM SD is closely correlated with increased pain behaviour score in the thalamus [15]. Furthermore, significant increases in the behavioral responses to noxious mechanical, thermal, and electrical stimuli have been shown in rats exposed to REM SD [74]. The results of the present research showed hyperlocomotion and increased rearing, but a decrease in pain threshold, in rats exposed to REM SD.

Our data also showed no changes in CAT and MDA levels in the serum of REM SD rats. Catalase (CAT) is an enzyme ubiquitous in living organisms that has a main role in mitigating oxidative stress via catalyzing the decomposition of hydrogen peroxide (H2O2) into water and oxygen [75]. On the contrary, malondialdehyde (MDA) is an important biomarker to measure oxidative stress in various biological samples [76]. Total and REM SD may affect the level of CAT and MDA, although evidence on the effect of REM SD is limited. Previous study has shown that total SD for 24h (but not 4h) significantly decreases CAT and increases MDA levels in the serum of rats [4]. Another study has shown that 24h total SD decreases CAT and increases MDA levels in the serum of rats exposed to streptozotocin-induced Alzheimer's disease-like sporadic dementia [77]. Moreover, there are other studies with the same result [78, 79]. However, REM SD effects on CAT and MDA have not been well investigated. A previous study has shown that 72h REM SD in rats increases MDA and decreases CAT in the thalamus [15]. But more studies are needed. The present research has shown no changes in CAT and MDA serum levels following seven days of REM SD. However, since CAT and MDA were assessed only in serum, the possibility of region-specific oxidative alterations in brain tissues cannot be excluded. Therefore, the absence of changes in peripheral oxidative markers should not be interpreted as definitive evidence against the involvement of oxidative stress in REM SD–induced neural dysfunction.

This effect may be due to a compensatory mechanism after days of deprivation.

We also showed BDNF downregulation in the prefrontal cortex of rats, which was restored by citalopram. SD has deleterious effects on the function of BDNF. It should be noted that the molecular analyses in the present study were conducted with a relatively small sample size (n = 3 per group), which may limit statistical power and the generalizability of the findings. Therefore, although the observed changes in BDNF expression are consistent with behavioral alterations, mechanistic interpretations should be made with caution. Future studies employing larger sample sizes and complementary protein-level analyses are required to confirm these findings. Many studies shown BDNF downregulation following total SD [80, 81] or REM SD [10, 82]. However, BDNF changes induced by REM SD are controversial and some studies have shown BDNF upregulation [23, 24, 70]. With respect to the normal level of CAT and MDA, it seems that BDNF downregulation in the prefrontal cortex is involved in the deleterious effects of REM SD on memory and behavioral functions. On the contrary, citalopram restored BDNF levels. Therefore, we suggested that BDNF upregulation may be an important mechanism induced by citalopram for its pro-cognitive effect. Previous studies have also shown this effect [30, 31], although inconsistent reports have also been reported [26, 27].

Due to a wide-range of inconsistent reports, the present study was conducted and showed that 7 days (6h/day) REM SD increased locomotor activity and rearing, decreased pain threshold and BDNF levels in the prefrontal cortex, and did not affect depressive-like behavior, and CAT and MDA serum levels. On the other hand, Citalopram partially ameliorated REM SD–induced behavioral alterations, particularly locomotor hyperactivity, rearing behavior, pain sensitivity, and BDNF downregulation, while it failed to improve passive avoidance memory via upregulating BDNF levels in the prefrontal cortex.

Declaration

Ethics approval

The ethical approval for the current research was granted by the Ethics Committee of the Islamic Azad University, Science and Research Branch, under the protocol number IR.IAU.PS.REC.1403.185. All experimental methods adhered to the ethical principles outlined in the 2011 guidelines by the U.S. National Institutes of Health for the Care and Use of Laboratory Animals, ensuring humane treatment throughout the study.

Consent for participation
Not applicable.

Consent for publication
Not applicable.

Availability of data and materials
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Elham Mahdavi designed and conducted the experiments, performed the behavioral and molecular assessments, analyzed the data, and drafted the initial version of the manuscript.
Fereshteh Atabi contributed to the experimental design, data analysis, literature review, and critical revision of the manuscript.
Batool Ghorbani Yekta supervised the project, reviewed the manuscript for intellectual content, and approved the final version for submission. She is also the corresponding author for this article.
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References

1. Li ZR, Zhang Y, Li HL, Wang Y, Wang F, Yang JM, Hu YY, Zhang ZJ, Wang ZQ (2022) Sleep deprivation leads to further impairment of hippocampal synaptic plasticity by suppressing melatonin secretion in the pineal gland of chronically unpredictable stress rats. Eur J Pharmacol 930: 175149. doi: 10.1016/j.ejphar.2022.175149
2. Yao ZY, Ma YT, Chen YJ, Liu Y, Zhang L, Wang Y, Zhang XD, Li XH, Chen J, Li Y (2022) Maternal sleep deprivation induces gut microbial dysbiosis and neuroinflammation in offspring rats. Zool Res 43(3): 380–390. doi: 10.24272/j.issn.2095-8137.2021.404
3. Wang X, Wang ZH, Wu YY, Tang H, Tan L, Gao XY, Xiong YS, Liu D, Wang JZ, Zhu LQ (2021) Melatonin ameliorates anxiety-like behaviors induced by sleep deprivation in mice: Role of oxidative stress, neuroinflammation, autophagy and apoptosis. Brain Res Bull 174: 161–172. doi: 10.1016/j.brainresbull.2021.06.010
4. Kholghi G, Vaseghi S, Karimi S, Nasehi M, Zarrindast MR (2023) The Interaction Effect of Sleep Deprivation and Treadmill Exercise in Various Durations on Spatial Memory with Respect to the Oxidative Status of Rats. Neurochem Res 48(5): 1357–1368. doi: 10.1007/s11064-022-03825-4
5. Arjmandi-Rad S, Vaseghi S, Nasehi M, Zarrindast MR (2022) Do Sleep Disturbances have a Dual Effect on Alzheimer's Disease? Cell Mol Neurobiol 42(5): 1399–1413. doi: 10.1007/s10571-020-01031-w
6. Vaseghi S, Arjmandi-Rad S, Nasehi M, Zarrindast MR (2021) Inconsistent effects of sleep deprivation on memory function. EXCLI J 20: 1011–1027. doi: 10.17179/excli2021-3730
7. Greenberg R, Pearlman CA, Gampel D (1983) Memory, emotion, and REM sleep. J Abnorm Psychol 92(3): 378–381. doi: 10.1037//0021-843x.92.3.378
8. McNamara P, Auerbach S, Johnson P, Harris E, Doros G (2010) Impact of REM sleep on distortions of self-concept, mood and memory in depressed/anxious participants. J Affect Disord 122(3): 198–207. doi: 10.1016/j.jad.2009.06.030
9. Groch S, Wilhelm I, Diekelmann S, Born J (2013) The role of REM sleep in the processing of emotional memories: evidence from behavior and event-related potentials. Neurobiol Learn Mem 99: 1–9. doi: 10.1016/j.nlm.2012.10.006
10. Abbasi N, Eydipour Z, Nasehi M, Vaseghi S (2024) Chronic REM sleep deprivation leads to manic- and OCD-related behaviors, and decreases hippocampal BDNF expression in female rats. Psychopharmacology 241(2): 245–257. doi: 10.1007/s00213-023-06476-7
11. Kim SM, Park S, Kim Y, Lee SH, Lee JH, Kim YS, Ryu JH, Kim HY (2021) REM Sleep Deprivation Impairs Learning and Memory by Decreasing Brain O-GlcNAc Cycling in Mouse. Neurotherapeutics 18(4): 2509–2522. doi: 10.1007/s13311-021-01124-4
12. Turan I, Ozacmak HS, Ozacmak VH, Barut F, Arasli M (2021) The effects of glucagon-like peptide 1 receptor agonist (exenatide) on memory impairment, and anxiety- and depression-like behavior induced by REM sleep deprivation. Brain Res Bull 174: 194–202. doi: 10.1016/j.brainresbull.2021.06.006
13. Houshyar M, Eydipour Z, Nasehi M, Vaseghi S (2024) Crocin (bioactive compound of Crocus sativus L.) potently restores REM sleep deprivation-induced manic- and obsessive-compulsive-like behaviors in female rats. Behav Pharmacol 35(1): 32–42. doi: 10.1097/FBP.0000000000000752
14. Kumar T, Jha SK (2012) Sleep deprivation impairs consolidation of cued fear memory in rats. PLoS One 7(10): e47042. doi: 10.1371/journal.pone.0047042
15. Anis Syahirah MS, Fadzilah MN, Kamaruddin MY, Mohd Yusof NA, Mohd Moklas MA, Sulaiman MR (2022) Impact of Rapid Eye Movement Sleep Deprivation on Pain Behaviour and Oxidative Stress in the Thalamus: Role of Tualang Honey Supplementation. Malays J Med Sci 29(2): 69–79. doi: 10.21315/mjms2022.29.2.8
16. Olonode ET, Aderibigbe AO, Adeoluwa OA, Eduviere AT, Ben-Azu B, Ajayi AM (2019) Morin hydrate mitigates rapid eye movement sleep deprivation-induced neurobehavioural impairments and loss of viable neurons in the hippocampus of mice. Behav Brain Res 356: 518–525. doi: 10.1016/j.bbr.2018.08.021
17. Sahin L, Ozkan A, Ozturk A, Akakin D, Yegen BC (2021) Mild regular treadmill exercise ameliorated the detrimental effects of acute sleep deprivation on spatial memory. Brain Res 1759: 147367. doi: 10.1016/j.brainres.2021.147367
18. Vaseghi S, Arjmandi-Rad S, Nasehi M, Zarrindast MR (2023) Intricate role of sleep deprivation in modulating depression: focusing on BDNF, VEGF, serotonin, cortisol, and TNF-alpha. Metab Brain Dis 38(1): 195–219. doi: 10.1007/s11011-022-01045-x
19. Tsai SJ (2018) Critical Issues in BDNF Val66Met Genetic Studies of Neuropsychiatric Disorders. Front Mol Neurosci 11: 156. doi: 10.3389/fnmol.2018.00156
20. Binder DK, Scharfman HE (2004) Brain-derived neurotrophic factor. Growth Factors 22(3): 123–131. doi: 10.1080/08977190410001723308
21. Autry AE, Monteggia LM (2012) Brain-derived neurotrophic factor and neuropsychiatric disorders. Pharmacol Rev 64(2): 238–258. doi: 10.1124/pr.111.005108
22. Khodaverdiloo A, Rashidy-Pour A, Vafaei AA, Bandegi AR, Sa-

meni HR, Haghighi S (2021) Neurogenesis in the rat neonate's hippocampus with maternal short-term REM sleep deprivation restores by royal jelly treatment. Brain Behav 11(12): e2423. doi: 10.1002/brb3.2423

23. da Silva Rocha-Lopes J, Machado RB, Suchecki D (2018) Chronic REM Sleep Restriction in Juvenile Male Rats Induces Anxiety-Like Behavior and Alters Monoamine Systems in the Amygdala and Hippocampus. Mol Neurobiol 55(4): 2884–2896. doi: 10.1007/s12035-017-0547-x
24. Mahboubi S, Nasehi M, Vaseghi S, Jamaldini SH, Zarrindast MR (2019) Benefit effect of REM-sleep deprivation on memory impairment induced by intensive exercise in male wistar rats: with respect to hippocampal BDNF and TrkB. Nat Sci Sleep 11: 179–188. doi: 10.2147/NSS.S214310
25. Sharbaf Shoar N, Fariba KA, Padhy RK (2023) Citalopram. In: StatPearls. StatPearls Publishing, Treasure Island (FL). Available from: https://www.ncbi.nlm.nih.gov/books/NBK482222/
26. Nasseri S, Vaseghi S, Nasehi M, Zarrindast MR (2024) Interaction effect of crocin and citalopram on memory and locomotor activity in rats: an insight into BDNF and synaptophysin levels in the hippocampus. Naunyn Schmiedebergs Arch Pharmacol 397(1): 45–58. doi: 10.1007/s00210-023-02570-x
27. Cooke JD, Grover LM, Spangler PR (2009) Venlafaxine treatment stimulates expression of brain-derived neurotrophic factor protein in frontal cortex and inhibits long-term potentiation in hippocampus. Neuroscience 162(4): 1411–1419. doi: 10.1016/j.neuroscience.2009.05.037
28. Schaefer TL, Skelton MR, Herring NR, Gudelsky GA, Vorhees CV, Williams MT (2012) Neonatal citalopram treatment inhibits the 5-HT depleting effects of MDMA exposure in rats. ACS Chem Neurosci 3(1): 12–21. doi: 10.1021/cn2000952
29. Kukuia KKE, Ameyaw EO, Mante PK, Ofori EO, Adinortey MB (2023) Increased Brain-Derived Neurotrophic Factor and Hippocampal Dendritic Spine Density Are Associated with the Rapid Antidepressant-like Effect of Iron-citalopram and Iron-Imipramine Combinations in Mice. Neuroscience 519: 90–106. doi: 10.1016/j.neuroscience.2023.03.009
30. Carboni L, Pischedda F, Piccoli G, Lauria G, Magri C, Gennarelli M, Riva MA (2022) Chronic Trazodone and Citalopram Treatments Increase Trophic Factor and Circadian Rhythm Gene Expression in Rat Brain Regions Relevant for Antidepressant Efficacy. Int J Mol Sci 23(22): 13784. doi: 10.3390/ijms232213784
31. Gong WG, Zhang LY, Wang JW, Jia JX, Yin YL, Zhao LL, Wei EQ, Zhang LC (2017) Citalopram Ameliorates Synaptic Plasticity Deficits in Different Cognition-Associated Brain Regions Induced by Social Isolation in Middle-Aged Rats. Mol Neurobiol 54(3): 1927–1938. doi: 10.1007/s12035-016-9781-x
32. Tariq U, Khan HA, Alhazza IM, Al Bratty M, Makeen HA, Alam MS (2022) Prophylactic role of olive fruit extract against cigarette smoke-induced oxidative stress in Sprague-Dawley rats. Cell Stress Chaperones 27(5): 545–560. doi: 10.1007/s12192-022-01293-x
33. National Research Council (2011) Guide for the Care and Use of Laboratory Animals, 8th edn. National Academies Press, Washington, DC. doi: 10.17226/12910
34. Petrucci AN, Joyal KG, Purnell BS, Buchanan GF (2021) Postictal Generalized EEG Suppression is reduced by Enhancing Dorsal Raphe Serotonergic Neurotransmission. Neuroscience 453: 206–221. doi: 10.1016/j.neuroscience.2020.11.009
35. Holden JM (2023) Effects of three serotonin reuptake inhibitors on sign-tracking in male Sprague-Dawley rats. Physiol Behav 268: 114233. doi: 10.1016/j.physbeh.2023.114233
36. Kamaei AK, Vaseghi S, Nasehi M, Zarrindast MR (2023) The effect of acute crocin on behavioral changes and BDNF expression level in socially isolated rats. Naunyn Schmiedebergs Arch Pharmacol 396(7): 1489–1501. doi: 10.1007/s00210-023-02418-4
37. Sturman O, Germain PL, Bohacek J (2018) Exploratory rearing: a context- and stress-sensitive behavior recorded in the open-field test. Stress 21(5): 443–452. doi: 10.1080/10253890.2018.1438405
38. Samizadeh MA, Vaseghi S, Nasehi M, Zarrindast MR (2024) Sex difference alters the behavioral and cognitive performance in a rat model of schizophrenia induced by sub-chronic ketamine. J Psychiatr Res 178: 180–187. doi: 10.1016/j.jpsychires.2024.08.001
39. Tajabadi Farahani Z, Vaseghi S, Nasehi M, Zarrindast MR (2024) The effect of olanzapine on spatial memory impairment, depressive-like behavior, pain perception, and BDNF and synaptophysin expression following childhood chronic unpredictable mild stress in adult male and female rats. Behav Brain Res 468: 115039. doi: 10.1016/j.bbr.2024.115039
40. Ghofrani-Jahromi Z, Vaseghi S, Nasehi M, Zarrindast MR (2024) Psilocybe cubensis extract potently prevents fear memory recall and freezing behavior in short- but not long-term in a rat model of posttraumatic stress disorder. Behav Neurosci 138(1): 1–12. doi: 10.1037/bne0000580
41. Rahimi-Danesh M, Vaseghi S, Nasehi M, Zarrindast MR (2023) Sex difference affects fear extinction but not lithium efficacy in rats following fear-conditioning with respect to the hippocampal level of BDNF. Pharmacol Biochem Behav 234: 173675. doi: 10.1016/j.pbb.2023.173675
42. Farahani ZT, Vaseghi S, Nasehi M, Zarrindast MR (2024) The effect of olanzapine on spatial memory impairment, depressive-like behavior, pain perception, and BDNF and synaptophysin expression following childhood chronic unpredictable mild stress in adult male and female rats. Behav Brain Res 468: 115039. doi: 10.1016/j.bbr.2024.115039
43. Nasseri S, Vaseghi S, Nasehi M, Zarrindast MR (2024) Interaction effect of crocin and citalopram on memory and locomotor activity in rats: an insight into BDNF and synaptophysin levels in the hippocampus. Naunyn Schmiedebergs Arch Pharmacol 397(1): 45–58. doi: 10.1007/s00210-023-02570-x
44. Lahimgarzadeh R, Vaseghi S, Nasehi M, Zarrindast MR (2022) Effect of multi-epitope derived from HIV-1 on REM sleep deprivation-induced spatial memory impairment with respect to the level of immune factors in mice. Iran J Basic Med Sci 25(2): 164–172. doi: 10.22038/IJBMS.2022.60318.13376
45. Ota SM, Moreira KD, Suchecki D, Oliveira MG (2013) Lithium prevents REM sleep deprivation-induced impairments on memory consolidation. Sleep 36(11): 1677–1684. doi: 10.5665/sleep.3120
46. Azogu I, Plamondon H (2015) Acute sleep deprivation enhances avoidance learning and spatial memory and induces delayed alterations in neurochemical expression of GR, TH, DRD1, pCREB and Ki67 in rats. Behav Brain Res 279: 177–190. doi: 10.1016/j.bbr.2014.11.032
47. Luppi PH, Fort P (2019) Sleep-wake physiology. Handb Clin Neurol 160: 359–370. doi: 10.1016/B978-0-444-64032-1.00023-0
48. Boyce R, Williams S, Adamantidis A (2017) REM sleep and memory. Curr Opin Neurobiol 44: 167–177. doi: 10.1016/j.conb.2017.05.001
49. Diekelmann S, Born J (2010) The memory function of sleep. Nat Rev Neurosci 11(2): 114–126. doi: 10.1038/nrn2762
50. Rasch B, Born J (2013) About sleep's role in memory. Physiol Rev 93(2): 681–766. doi: 10.1152/physrev.00032.2012
51. Smith C, Kitahama K, Valatx JL, Jouvet M (1974) Increased paradoxical sleep in mice during acquisition of a shock avoidance task. Brain Res 77(2): 221–230. doi: 10.1016/0006-8993(74)90782-9
52. Portell-Cortés I, Martí-Nicolovius M, Morgado-Bernal I (1989) Correlations between paradoxical sleep and shuttle-box conditio-

ning in rats. Behav Neurosci 103(5): 984–990. doi: 10.1037//0735-7044.103.5.984
53. Lucero MA (1970) Lengthening of REM sleep duration consecutive to learning in the rat. Brain Res 20(2): 319–322. doi: 10.1016/0006-8993(70)90022-5
54. Sinton CM, Jouvet M (1983) Paradoxical sleep and coping with environmental change. Behav Brain Res 9(2): 151–163. doi: 10.1016/0166-4328(83)90121-6
55. Tagney J (1973) Sleep patterns related to rearing rats in enriched and impoverished environments. Brain Res 53(2): 353–361. doi: 10.1016/0006-8993(73)90218-6
56. Eydipour Z, Nasehi M, Vaseghi S, Jamaldini SH, Zarrindast MR (2020) The role of 5-HT4 serotonin receptors in the CA1 hippocampal region on memory acquisition impairment induced by total (TSD) and REM sleep deprivation (RSD). Physiol Behav 215: 112788. doi: 10.1016/j.physbeh.2019.112788
57. Zheng X, Wang Q, Li J, Zhang L, Zhang Y, Wang Z (2024) rTMS reduces spatial learning and memory deficits induced by sleep deprivation possibly via suppressing the expression of kynurenine 3-monooxygenase in rats. Behav Brain Res 456: 114704. doi: 10.1016/j.bbr.2023.114704
58. Shahveisi K, Ahmadi-Soleimani SM, Azizi H, Ghafouri S, Abareghi F, Rezayof A (2023) Role of Cannabinoid CB(1) Receptor in Object Recognition Memory Impairment in Chronically Rapid Eye Movement Sleep-deprived Rats. Chin Med Sci J 38(1): 29–37. doi: 10.24920/004155
59. Mahdavi MS, Nasehi M, Vaseghi S, Jamaldini SH, Zarrindast MR (2021) The effect of alpha lipoic acid on passive avoidance and social interaction memory, pain perception, and locomotor activity in REM sleep-deprived rats. Pharmacol Rep 73(1): 102–110. doi: 10.1007/s43440-020-00152-9
60. Norozpour Y, Nasehi M, Vaseghi S, Jamaldini SH, Zarrindast MR (2020) The effect of alpha-2 adrenergic receptors on memory retention deficit induced by rapid eye movement sleep deprivation. Iran J Basic Med Sci 23(12): 1571–1575. doi: 10.22038/IJBMS.2020.46698.10752
61. Gujar N, Yoo SS, Hu P, Walker MP (2011) Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. J Neurosci 31(12): 4466–4474. doi: 10.1523/JNEUROSCI.3220-10.2011
62. Vandekerckhove M, Cluydts R (2010) The emotional brain and sleep: an intimate relationship. Sleep Med Rev 14(4): 219–226. doi: 10.1016/j.smrv.2010.01.002
63. Armitage R (2007) Sleep and circadian rhythms in mood disorders. Acta Psychiatr Scand Suppl 433: 104–115. doi: 10.1111/j.1600-0447.2007.00968.x
64. Gottesmann C, Gottesman I (2007) The neurobiological characteristics of rapid eye movement (REM) sleep are candidate endophenotypes of depression, schizophrenia, mental retardation and dementia. Prog Neurobiol 81(4): 237–250. doi: 10.1016/j.pneurobio.2007.01.004
65. Grunhaus L, Shipley JE, Eiser A, Pande AC, Tandon R, Remen A, Greden JF (1994) Shortened REM latency PostECT is associated with rapid recurrence of depressive symptomatology. Biol Psychiatry 36(4): 214–222. doi: 10.1016/0006-3223(94)90604-1
66. Kupfer DJ, Frank E, McEachran AB, Grochocinski VJ (1990) Delta sleep ratio. A biological correlate of early recurrence in unipolar affective disorder. Arch Gen Psychiatry 47(12): 1100–1105. doi: 10.1001/archpsyc.1990.01810240020004
67. Pedrazzoli M, Benedito MA (2004) Rapid eye movement sleep deprivation-induced down-regulation of beta-adrenergic receptors in the rat brainstem and hippocampus. Pharmacol Biochem Behav 79(1): 31–36. doi: 10.1016/j.pbb.2004.06.005
68. Asakura W, Matsumoto K, Ohta H, Watanabe H (1993) Effect of alpha 2-adrenergic drugs on REM sleep deprivation-induced increase in swimming activity. Pharmacol Biochem Behav 46(1): 111–115. doi: 10.1016/0091-3057(93)90327-r
69. Crisan CA, Moca IV, Bâldea I, Vesa ȘC, Bălașa R (2023) A Narrative Review on REM Sleep Deprivation: A Promising Non-Pharmaceutical Alternative for Treating Endogenous Depression. J Pers Med 13(2): 343. doi: 10.3390/jpm13020343
70. Maturana MJ, Pudell C, Targa AD, Rodrigues LS, Noseda AC, Fortes MH, Lima MM (2015) REM sleep deprivation reverses neurochemical and other depressive-like alterations induced by olfactory bulbectomy. Mol Neurobiol 51(1): 349–360. doi: 10.1007/s12035-014-8723-8
71. Schilgen B, Tölle R (1980) Partial sleep deprivation as therapy for depression. Arch Gen Psychiatry 37(3): 267–271. doi: 10.1001/archpsyc.1980.01780160037003
72. Andrade LA, Lima JG, Tufik S, Bertolucci PH, Carlini EA (1987) REM sleep deprivation in an experimental model of Parkinson's disease. Arq Neuropsiquiatr 45(3): 217–223. doi: 10.1590/s0004-282x1987000300002
73. Kourbanova K, Alexandre C, Latremoliere A (2022) Effect of sleep loss on pain-New conceptual and mechanistic avenues. Front Neurosci 16: 1009902. doi: 10.3389/fnins.2022.1009902
74. Hakki Onen S, Alloui A, Gross A, Eschallier A, Dubray C (2001) The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. J Sleep Res 10(1): 35–42. doi: 10.1046/j.1365-2869.2001.00240.x
75. Rasheed Z (2024) Therapeutic potentials of catalase: Mechanisms, applications, and future perspectives. Int J Health Sci 18(2): 1–6. doi: 10.53730/ijhs.v18n2.14023
76. Cordiano R, Di Gioacchino M, Mangifesta R, Panzera C, Gangemi S, Minciullo PL (2023) Malondialdehyde as a Potential Oxidative Stress Marker for Allergy-Oriented Diseases: An Update. Molecules 28(16): 5979. doi: 10.3390/molecules28165979
77. Arjmandi-Rad S, Vaseghi S, Nasehi M, Zarrindast MR (2022) The role of sleep deprivation in streptozotocin-induced Alzheimer's disease-like sporadic dementia in rats with respect to the serum level of oxidative and inflammatory markers. Exp Brain Res 240(9): 2425–2435. doi: 10.1007/s00221-022-06405-8
78. Massadeh AM, Al-Mustafa AH, Al-Shudiefat AA, Al-Momany SM (2022) Assessing the Influence of Salvia triloba on Memory Deficit Caused by Sleep Deprivation in the Context of Oxidative Stress. Curr Alzheimer Res 19(6): 440–448. doi: 10.2174/1567205019666220616122429
79. Hamed MA, Ali SA, El-Rigal NS, Hetta HF (2022) Glutamine restores testicular glutathione-dependent antioxidant defense and upregulates NO/cGMP signaling in sleep deprivation-induced reproductive dysfunction in rats. Biomed Pharmacother 148: 112765. doi: 10.1016/j.biopha.2022.112765
80. Looti Bashiyan M, Nasehi M, Vaseghi S, Zarrindast MR (2021) Investigating the effect of crocin on memory deficits induced by total sleep deprivation (TSD) with respect to the BDNF, TrkB and ERK levels in the hippocampus of male Wistar rats. J Psychopharmacol 35(6): 744–754. doi: 10.1177/0269881121991567
81. Guzman-Marin R, Ying Z, Suntsova N, Methippara M, Bashir T, Szymusiak R, Gomez-Pinilla F, McGinty D (2006) Suppression of hippocampal plasticity-related gene expression by sleep deprivation in rats. J Physiol 575(Pt 3): 807–819. doi: 10.1113/jphysiol.2006.115287
82. Saadati N, Nasehi M, Vaseghi S, Zarrindast MR (2022) Synergistic antidepressant effects of citalopram and SB-334867 in the REM sleep-deprived mice: Possible role of BDNF. Pharmacol Biochem Behav 219: 173449. doi: 10.1016/j.pbb.2022.173449