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Voluntary exercise impact on cognitive impairments in sleep-deprived intact female rats

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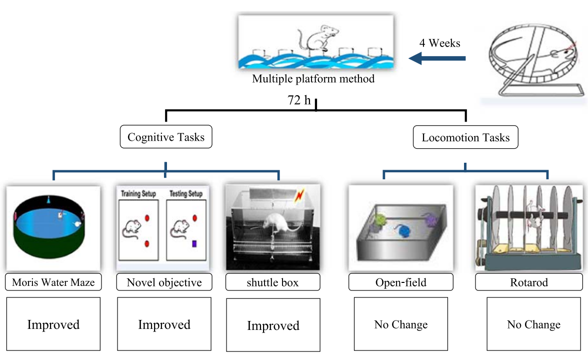
GRAPHICAL ABSTRACT



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ABSTRACT

Sleep loss is a common problem in modern societies affecting different aspects of individuals' lives. Many studies have reported that sleep deprivation (SD) leads to impairments in various types of learning and memory. Physical exercise has been suggested to attenuate the cognitive impairments induced by sleep deprivation in male rats. Our previous studies have shown that forced exercise by treadmill improved learning and memory impairments following SD. The aim of the current study was to investigate the effects of voluntary exercise by running wheel on cognitive, motor and anxiety-like behavior functions of female rats following 72 h SD.

Intact female rats were used in the present study. The multiple platform method was applied for the induction of 72 h SD. The exercise protocol was 4 weeks of running wheel and the cognitive function was evaluated using Morris water maze (MWM), passive avoidance and novel object recognition tests. Open field test and measurement of plasma corticosterone level were performed for evaluation of anxiety-like behaviors. Motor balance evaluation was surveyed by rotarod test. In this study, remarkable learning and long-term memory impairments were observed in sleep deprived rats in comparison to the other groups. Running wheel exercise ameliorated the SD-induced learning and memory impairments. Voluntary and mandatory locomotion and balance situation were not statistically significant among the different groups.

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Our study confirmed the negative effects of SD on cognitive function and approved protective effects of voluntary exercise on these negative effects.

1. Introduction

Sleep is defined as an active state characterized by reduced alertness and responsiveness that is rapidly reversible [1]. Epidemiological studies show a positive association between adequate sleep and good health [2].

Animal studies have demonstrated the positive effects of sleep on declarative and procedural memory in various behavioral tasks [3,4]. It has been shown that sleep contributes to acquisition and consolidation of memory [5,6]. “Sleep” has been considered as a time window through which the acquired information is processed without any disturbance from the sensory system [7]. It has been identified as a state that optimizes the consolidation of newly acquired information in memory, depending on the specific conditions of learning and timing of sleep. Consolidation during sleep promotes both quantitative and qualitative changes of memory representations [7]. Fragmented sleep and sleep deprivation (SD) in long period can lead to mood changes, impaired mental ability, and disturbed performance [8]. In other studies, SD showed a destructive effect on Morris water maze (MWM) [10], open field [9], novel objective recognition [11,12] and passive avoidance [13,14] tasks. Several clinical studies demonstrate that the absence of periods of sleep is closely related to occurrence of anxiety symptoms [15,16]. Widespread studies suggest that sleep facilitates several phases of learning process and memory in human and rodents while sleep deprivation impairs this process [17,18].

On the other hand, physical exercise has shown to improve learning and memory in both MWM [19,20] and passive avoidance task paradigms [21]. Physical exercise elicits functional and structural changes throughout the brain; however, its effects on the hippocampus are of particular interest as this is a brain area crucial for memory formation and spatial memory [22]. The beneficial effects of exercise on many physiological systems, including the central nervous system and brain health, are well demonstrated [22]. Exercise has been revealed to enhance hippocampus-dependent spatial memory in rodents in different paradigms such as MWM, Y maze and radial arm maze [23,24]. Running also enhances performance in tasks with low motor command such as contextual fear conditioning, passive avoidance learning, spatial pattern separation and novel object recognition [25–27].

SD has negative effects on learning and memory and it appears that exercise protects rats against these negative effects [10]. Our previous studies demonstrated that forced and regular exercise by treadmill ameliorated spatial learning and memory impairments in female sleep deprived rats [10,28]. Exercise also plays a protective role against memory impairments observed in neurodegenerative diseases such as Alzheimer's disease [29].

A recent review from the literature suggests that forced exercise and voluntary exercise have different effects on brain neurochemistry and behavior [30,31]. In contrast, either treadmill exercise or wheel running improves hippocampus-dependent spatial learning and memory [32]. It has been shown that voluntary exercise causes reductions in both dopamine neuron degeneration and behavioral deficits [33].

Considering the effect of voluntary exercise on learning and memory, in this study, we surveyed the effects of voluntary exercise on learning and memory in sleep deprived female rats.

2. Material and method

2.1. Animals

All experimental protocols and treatments were approved by the Ethics Committee of the Kerman Neuroscience Research Center. We attempted to minimize the discomfort for the animals at all stages of the study (Ethics code: KNRC-95-30). Female Wistar rats (3–4 months old, weighing 200–250 g) were used for the current study. Animals (n = 7 in each group) were caged in groups of four with ad libitum access to food and water. They were housed under controlled temperature (23 ± 1 °C) and 12-h light–dark cycle (lights on: 07:00–19:00 h). Forty-two intact rats were randomly allocated into the following subgroups: control (maintained in home cages), SD (placed on small platforms for 72 h), wide platform (Sham platform placed on large platforms for 72 h), exercise (underwent 4 weeks of voluntary exercise), wide platform/exercise (placed on large platforms after 4 weeks of voluntary exercise) and exercise/SD (placed on small platforms after 4 weeks of voluntary exercise). The rats were divided into distinct groups for open field, novel object recognition and MWM tests, which were different from the groups of rats for passive avoidance and rotarod tests. After the probe test in the MWM task, the rats were sacrificed for sampling of blood to evaluate corticosterone level (Fig. 1).

2.2. Exercise protocol

The rats in the wheel exercise group were individually placed in home cages connected with a running wheel (20 cm diameter; 9 cm width) 24 h for 4 weeks. The number of revolutions was recorded and wheel revolutions were counted irrespective of the direction of the wheel. All the rats were allowed to habituate to the experimental environment for 30 min in 2 days before the beginning of the exercise protocol to minimize nonspecific stress responses [33,34].

SD started 30 min after the last exercise session.

In the exercise group, the average amount of exercise for 4 weeks was 39,954 m between all the rats and 42,321 m in the exercise/SD group.

2.3. Induction of sleep deprivation (SD)

A multiple platform apparatus was used for the induction of SD. The apparatus (90 cm × 50 cm × 50 cm) contained 10 columns (with 10 cm height and 7 cm diameter located 2 cm above the surface of the water),

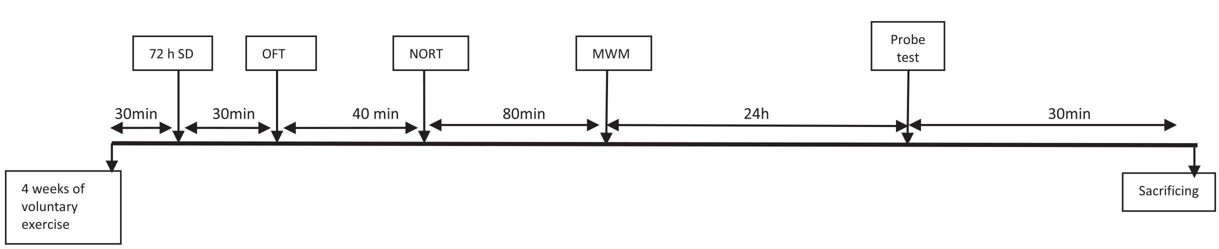

Fig. 1. Time-line diagram showing the protocol used for voluntary exercise application in animals of SD + exercise group. Also timing of behavioral tasks showed.