Behavioural Processes 119 (2015) 50–57

Contents lists available at ScienceDirect

Behavioural Processes

journal homepage: www.elsevier.com/locate/behavproc

The compensatory effect of regular exercise on long-term memory impairment in sleep deprived female rats

Maryam Salari[a,b], Vahid Sheibani[a,b,*], Hakimeh Saadati[c,**], Alimohammad Pourrahimi[a], Mohammad khaksarihadad[a,b], Khadijeh Esmaeelpour[a], Mehdi Khodamoradi[a]

[a] Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran
[b] Department of Physiology, School of Medicine, Kerman University of Medical Science, Kerman, Iran
[c] Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

ARTICLE INFO

Article history:
Received 20 April 2015
Received in revised form 20 June 2015
Accepted 25 June 2015
Available online 17 July 2015

Keywords:
Sleep deprivation
Regular exercise
Long-term memory
Morris water maze
Female rats

ABSTRACT

Previous studies have been shown that exercise can improve short-term spatial learning, memory and synaptic plasticity impairments in sleep deprived female rats. The aim of the present study was to investigate the effects of treadmill exercise on sleep deprivation (SD) induced impairment in hippocampal dependent long-term memory in female rats. Intact and ovariectomized female rats were used in the current study. Exercise protocol was 4 weeks treadmill running. Twenty four hour SD was induced by using multiple platform apparatus after learning phase. Spatial learning and long-term memory was examined by using the Morris Water Maze (MWM) test. Our results indicated that sleep deprivation impaired long term memory in the intact and ovariectomized female rats, regardless of reproductive status ($p < 0.05$) and treadmill exercise compensated this impairment ($p < 0.05$). In conclusion the results of the current study confirmed the negative effect of SD on cognitive functions and regular exercise seems to protect rats from these factors, however more investigations need to be done.

1. Introduction

Sleep plays an important role in normal physiological functions. Although its functions remain elusive, sleep may be a fundamental contributor of memory consolidation. Additionally, a key hypothesis is that post-training sleep facilitates consolidation of new information into long-term memory (Datta, 2010; Diekelmann and Born, 2010; Walker and Stickgold, 2004) .Sleep also contributes to neuronal plasticity (Cai et al., 2009; Diekelmann and Born, 2010). For example, it has been shown that sleep deprivation inhibits long-term potentiation (LTP) in the CA1 area of rat hippocampus (Davis et al., 2003). Sufficient sleep is necessary for fostering of connections in neuronal networks (Diekelmann and Born, 2010; Gais et al., 2006). Previous studies have shown that SD destroyed hippocampal dependent learning and memory (Aleisa et al., 2011). SD is widespread in various occupations and individuals, for example stressful occupations (Landrigan et al., 2004). Sleep disorders caused by various diseases and contributes to decrease in work/school efficiency in modern societies (Leconte and Bloch, 1970; Philip and Akerstedt, 2006). Most sleep studies have been performed in males; however, the effects of SD on short-term memory in females are investigated in a few studies (Alhola et al., 2005; Hajali et al., 2012). It is stated that postmenopausal women are vulnerable to cognitive deficiencies (Green and Simpkins, 2000; Hogervorst et al., 2000). Hajali et al. also indicated that female rats are more susceptible to memory impairment induced by SD than male animals (Hajali et al., 2012). Hormone replacement therapy (HRT) is a common way to treat menopausal symptoms, such as cognitive dysfunction. However it has side effects, especially the increased incidence of uterine cancer and neoplasm of the breast (LeBlanc et al., 2001; Miquel et al., 2006). In addition, because of the fluctuations of female hormone levels observed during the estrus cycle, estrus cycle phase may be an important factor when working with female animals (Colvin et al., 1968; Sell et al., 2000). Evidence indicated that physical activity, such aerobic exercise, has appeared as a promising low cost treatment to improve neurocognitive function that is available to most adults and is not involved by intolerable side effects mostly found with pharmaceutical treatments (Hillman et al., 2008). In the other hand, numerous studies have shown that exercise has beneficial

* Corresponding author at: Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran. Fax: +98 341 2264198.
** Corresponding author at: Ardabil University of Medical Sciences, Ardabil, Iran. Fax: +98 455510057.
E-mail addresses: vsheibani2@yahoo.com, v-sheibani@kmu.ac.ir (V. Sheibani), hsadat54@yahoo.com (H. Saadati).

http://dx.doi.org/10.1016/j.beproc.2015.06.014
0376-6357/

effects on memory and also on menopausal symptoms (Saadati et al., 2014a,b, 2015; Shangold, 1990). Regular physical activity has beneficial effects on cognitive function in both humans and rodents (Berchtold et al., 2005; Cotman and Berchtold, 2002). One of the most main effects of exercise is the effect on cognition, for example, it raises learning and improves memory retention (Cotman and Berchtold, 2002; Van Praag, 2009). Exercise training can increment cerebral blood volume (Cotman and Berchtold, 2002; Van der Borght et al., 2009). Several studies have reported the deleterious effects of sleep deprivation on cognitive performances and signaling molecules in the hippocampus of male rats. Meanwhile, physical exercise attenuates these impairments (Zagaar et al., 2013, 2012). Our previous studies indicated that regular exercise can improve spatial learning and memory (Saadati et al., 2015) and synaptic plasticity (Saadati et al., 2014b) impairments in sleep deprived female rats. In addition, our previous data demonstrated that exercise can reverse the decreased effects of sleep deprivation on brain-derived neurotrophic factor levels in the hippocampus of ovariectomized female rats (Saadati et al., 2014a). Therefore, our hypothesis is regular exercise has preventive effects against SD-induced spatial long-term memory impairment in intact and OVX female rats.

2. Methods

2.1. Animals

Female Wistar rats with an average weight of 200 g were used for the present study. Animals were caged in groups of four with free access to food and water. The temperature was controlled ($23 \pm 1\,^{\circ}C$) and they were also housed under a 12-h light–dark cycle (lights on: 07:00–19:00 h). Two groups of intact and ovariectomized (OVX) rats were accidentally selected, and the following subgroups were formed: control (stayed in home cages), SD, exercise, exercise/SD, sham exercise and wide platform (sham platform). A separate group of rats was also submitted as a sham surgery or sham ovariectomy (submitted to surgery without removing the ovaries) ($n = 8$ for each group). The rats of the OVX group underwent a bilateral ovariectomy. Estrus cycles of all the intact groups were synchronized by maintaining in the same cages. All procedures were performed inconformity with the National Research Council's Guide for the care and use of laboratory animals and on approval of the Ethics Committee of Kerman Neuroscience Research Center (Ethics Code: KNRC-91-33).

2.2. Surgical procedures

All of the operations were performed under general anesthesia using a mixture of ketamine and xylazine (60 mg/kg, i.p.ketamine and 10 mg/kg, i.p. xylazine). Both ovaries were eliminated by a small mid-abdominal cutting under aseptic conditions. All of the ovariectomized rats and sham surgery groups were put in a special room for one month after operation (Saadati et al., 2014b, 2015).

2.3. Treadmill exercise

For four weeks from saturday to wednesday, the exercise groups had force exercise sessions (at 0◦inclination) during the light cycle which started from 9:00 till 14:30 (they received a mild shock, 0.25 MA, while they stopped running). They were allowed to adapt to treadmill environment for 30 min during 2 successive days before the onset of the exercise protocol, this was to eliminate the possible stress of the new environment. The exercise protocol included the following steps: 30 min for the first two weeks (at 10 m/min speed), 45 min for the third week and 60 min for the fourth week (both at 15 m/min speed). Every 15 min during each session, the animals were given a 5 min break (Zagaar et al., 2012).

2.4. Induction of sleep deprivation

We used a multiple platform apparatus to induce SD (Zagaar et al., 2012; Hajali et al., 2015a,b). This apparatus (90 cm × 50 cm × 50 cm) included 10 columns (10 cm high,7 cm diameter located 2 cm above the surface of the water) which were ordered in two rows and spaced 10 cm separate (edge to edge), this was to permit rats to jump from one platform to another. The cage mates (4 rats) were put each other in a chamber to maintain social stableness. The rats had free access to clean water bottles, and food pellet baskets were always hanging from the top of the chamber. In the current research, SD was induced for 24 h. Animals were kept under standard conditions [12:12-h light–dark cycle at a controlled temperature ($23 \pm 1\,^{\circ}C$)] in the sleep deprivation period (24 h). We carried out the SD sample for 24 h after performing the last exercise session in the exercise/SD groups. The possible effects of new environmental stress were assessed by putting the control (sham platform or wide platform) groups in a similar chamber but with wider platforms (10 cm high, and 15 cm in diameter). The platforms were large enough so that the rats would not downfall into the water during their sleep period.

2.5. Morris water maze (MWM)

The MWM included of a black circular pool, 160 cm diameter, 80 cm height filled with water held at room temperature to a depth of 40 cm. The pool was geographically divided into four quadrants of equal size and starting points were designated at each quadrant as N, S, E, and W. A square platform (10 cm diameter) was invisible just below (1.5 cm) the surface of the water in the center of the northeast quadrant. The experiments were carry out in a dimly light room with different and fixed extra maze geometric images (e.g., circles, squares or triangles) attached at different points on the walls around the maze. Performances were recorded by a smart video tracing system (NoldusEthovision® system, version 5, USA) and animals could be tracked on the screen of a computer.

2.6. Spatial learning and memory

In a single training protocol each rat accomplished three blocks separated by a 30-min resting period before sleep deprivation. Each block consisted of four successive trials with 60 s duration and about 60 s inter-trial intervals. All of the experimental groups were tested ∼30 min after the end of the SD period, during the lights on phase between 8:30 and 12:00 am. On each trial, rats were randomly released into the water from one of the four quadrants of the maze with its face toward the wall of the quadrant where it was released. Each rat had 4 different releasing points. During acquisition, the location of the platform remained constant and rats were allowed to swim to the hidden escape platform. After the animal found the platform, it was allowed to remain there for 20–30 s and were then located in an animal cage to wait 20–30 s before the start of the next trial. While a rat failed to find the platform in 60 s, the experimenter guided it toward the platform. The time and distance to find the hidden platform were collected and analyzed later.

A single probe trial was given 24 h after the last training trial to test the spatial memory in the water maze after sleep deprivation. In this trial the platform was removed and rat was allowed to swim for 60 s. The time and distance spent in the target quadrant (quadrant 4) were analyzed as a measure of spatial memory retention. Following the probe trial, rats completed a visible platform test to determine any possibility of SD interference with sensory and motor coordination or motivation. In this test, the animals ability