Kerman Neuroscience Research Center
Kerman University of Medical Sciences

Effects of regular exercise on cognitive impairment induced by REM sleep deprivation in intact and ovariectomized female rats: Behavioral, electrophysiological and molecular studies.

A dissertation for the degree Doctor of Philosophy in:

Neuroscience

By

Saadati Hakimeh

PhD thesis under the supervision:

Dr. Vahid Sheibani

Advisors:

Dr. Saeed Esmaeili-Mahani, Dr. Shahrzad Mazhari

March 2015

ABSTRACT

Study Objectives: Previous evidences suggest that regular exercise can protect against learning and memory impairments in the sleep deprived male rats. In addition, previous findings demonstrate that female rats are more vulnerable to the deleterious effects of sleep deprivation on cognitive performance. The purpose of this study was to determine the effect of regular exercise and/or sleep deprivation (SD) on hippocampal dependent learning and memory, synaptic plasticity and brain-derived neurotrophic factor (BDNF) level in female rats.

Experimental Design: Intact and ovariectomiezed (OVX) female Wistar rats were used in the present study. Two sets of animals including intact and OVX were randomly allocated into the following subgroups: control, SD, wide platform (Sham platform), exercise, sham exercise and exercise plus SD. The exercise protocol was four weeks treadmill running and the multiple platform method was applied to induce 72h sleep deprivation.

We tested the effects of exercise and/or sleep deprivation using three approaches: the Morris water maze (MWM) task to test spatial learning and memory performance; electrophysiological recording in the Cornu Ammonis (CA1) area of the hippocampus to measure synaptic plasticity; also, quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) and immunoblot analysis were used to evaluate the levels of BDNF mRNA and protein in the hippocampus of female rats respectively. In addition, a plasma corticosterone level was determined in all subgroups of intact and OVX rats.

Results: Throughout behavioral investigation, significant learning impairment was observed in sleep-deprived OVX rats compared to the intact and the other OVX groups ($P<0.05$). Short term memory impairment was observed in both sleep-deprived OVX and intact groups ($P<0.05$). Physical exercise alleviated the SD-induced spatial learning and memory impairments in both intact and OVX groups. Corticosterone level was not statistically significant among the different groups. Field potential recording indicated that the induction

and maintenance of early-phase of long-term potentiation (E-LTP) in the CA1 area of the hippocampus impaired in the sleep deprived animals compared to the other groups($P<0.05$). After 72 h SD, E-LTP impairments were prevented by 4 weeks of regular treadmill exercise. In addition, protein and mRNA expression of BDNF was significantly ($P<0.05$) decreased after 72h SD in OVX female rats in compared with the other groups. Therefore, the significant down- regulation of the BDNF protein and mRNA in the sleep deprived OVX female rats was prevented by regular treadmill exercise.

Conclusions: These findings suggest that sleep deprivation impairs cognitive function and synaptic plasticity in the CA1 area of the hippocampus whereas exercise prevents these impairments. Regular exercise exerts a protective effect against sleep deprivation-induced impairment probably by inducing BDNF expression in the hippocampus of OVX - female rats. As a result, exercise-induced BDNF could contribute to the restoration of hippocampus-dependent learning and memory as well as LTP in OVX- female rats.

Keywords: Sleep deprivation, Physical exercise, Morris water maze, Long term potentiation, BDNF, Female rat