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# The effects of intensity and duration of aerobic exercise on spatial memory function in male Wistar rats

Neng Tine Kartinah,[1] Sophie Yolanda,[1] Tahyatul Bariroh[1,2]

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**Authors' affiliations:**
[1]*Department of Physiology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia,* [2]*Master Program in Biomedical Science, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia*

**Corresponding author:**
Tahyatul Bariroh
Department of Physiology, Faculty of Medicine, Universitas Indonesia, Jalan Salemba 6, Senen, Central Jakarta 10320, DKI Jakarta, Indonesia
Tel/Fax: +62-21-31930366/+62-21-31908824
**E-mail: office@fk.ui.ac.id**

**ABSTRACT**

**BACKGROUND** Memory is a vital function of the brain. Aerobic exercise has a positive effect on memory's function, but the appropriate combination of intensity and duration of aerobic exercise is still unknown. This study was aimed to investigate the effect of optimum combinations of intensity and duration of aerobic exercise on spatial memory function.

**METHODS** In this study, the authors performed *in vivo* experiment using 20 male Wistar rats (6-month-old). They were randomly divided into four groups: (1) low-intensity and short duration aerobic exercise group (L–S); (2) low-intensity and long duration aerobic exercise group (L–L); (3) high-intensity and short duration aerobic exercise group (H–S); and (4) high-intensity and long duration aerobic exercise group (H–L). The aerobic exercise treatment of each group was conducted for three weeks with a frequency of five days a week. The memory function was assessed with the help of water-E-maze on week 0, 1, 2, and 3 (a total of four times).

**RESULTS** This study indicates that the central nervous system responds to aerobic exercise as an external stimulus differently depending on the combinations of intensity and duration. Moreover, this study demonstrates that changes in memory functions are best observed in the group with low-intensity and long duration aerobic exercise.

**CONCLUSIONS** The combination of low-intensity and long duration of aerobic exercise for animal study can improve spatial memory functions better than any other combinations of intensity and duration of aerobic exercises in male Wistar rats.

**KEYWORDS** aerobic exercise, spatial memory

Memory function is known to decrease with age. The decline of memory function with increasing age is associated with decreased neuroplasticity.[1] Various research studies were conducted to develop an effective way of improving the performance of the brain's synapses in order to prevent a decline in memory function, one of which is to do physical exercise. Many studies have demonstrated that physical exercise is the most convenient, inexpensive, and effective way of improving memory functions.[2,3] Regular aerobic exercise has shown the potential to increase internal antioxidants and trigger neuroplasticity in juvenile rats and adult mice.[4] However, the appropriate type and volume of aerobic exercise have to be considered to acquire the optimum effect and avoid side effects such as oxidative stress.[5]

The volume of aerobic exercise depends on its intensity and duration. The intensity of aerobic exercise can be divided into high, moderate, and low, while the duration of aerobic exercise can be divided into short and long durations.[6] The intensity and duration of aerobic exercise have been recorded to affect hippocampal neurogenesis, brain-derived neurotrophic factor, and N-methyl-D-aspartate receptor (NMDAR) expression in normal mice, thereby indicating a change in the synaptic plasticity.[7] A study has shown that low-intensity aerobic exercise can improve spatial memory after brain ischemia.[8] Another research study has shown that high-intensity aerobic exercise can disrupt memory function.[9] The duration of aerobic exercise is also a factor that affects the plasticity of synapses. The duration of physical exercise affects the consumption of oxygen by the brain and the activation of antioxidant, which induces the growth of new nerve cells (neurogenesis) and synaptic plasticity. In addition, a study has demonstrated that long duration aerobic exercise can activate heme oxygenase-1 gene, which encodes antioxidant enzymes, better than short duration aerobic exercise.[10] This warrants a study that combines various intensities and durations of aerobic exercise in order to obtain the optimum effect, primarily to prevent the decline of memory starting at an adult age. The aim of this research study was to investigate the optimum formula of intensity and duration of aerobic exercise for improving the spatial memory function.

## METHODS

**Research design**

The authors conducted *in vivo* experiments in 20 male Wistar rats (6-months-old). The rats were randomly divided into four groups: (1) low-intensity and short duration aerobic exercise group (L–S); (2) low-intensity and long duration aerobic exercise group (L–L); (3) high-intensity and short duration aerobic exercise group (H–S); and (4) high-intensity and long duration aerobic exercise group (H–L). The aerobic exercise treatment of each group took place for three weeks with a frequency of five days a week. The memory function was assessed using water-E-maze (WEM) on week 0, 1, 2, and 3 (a total of four times). The study's design and methods were approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital (No. 849/UN2.F1/ETIK/2016).

**Animals**

Six-month-old male Wistar rats with a body weight of 150–250 g were acquired from the Department of Nutrition, Faculty of Medicine, Universitas Indonesia. The rats were housed on a 12-hours light/dark cycle. Food and water were supplied *ad libitum.* The room temperature was maintained at 25 ± 1°C. The acclimation period was vital prior to the treatment period in order to introduce the rats to the environment and research conditions. Rats were introduced to the WEM and animal treadmill. Consequently, they were placed on the WEM for not more than 3 min/day, and they ran on the animal treadmill with an incremental increase in duration and speed, but not more than 10 m/min for 10 min.

**Aerobic exercise**

With various intensities and durations assigned for each group, the rats performed aerobic exercise by running on the animal treadmill for three weeks with a frequency of five times a week. The low-intensity was considered to be 20 m/min, while the high-intensity was considered to be 30 m/min. The short duration was of 15 min while the long duration was of 30 min. Before the main exercise, rats were allowed to warm up at the treadmill at a speed of 8 m/min for 3 min.

**Water-E-maze**

The memory test was performed with the help of WEM. The ladder was employed in the maze as a motivator that was further used by the rats to save themselves and find a way out of the test device filled with water. The WEM device consists of a U-shaped main trench and three trench arms perpendicular to the main trench, two edge trenches (ti), and a middle trench (ta). WEM was filled with water until the rat cannot touch the bottom of apparatus. The M point in the middle trench is the starting point for the rats, and a ladder was laid on one edge of the trench as the target (G) for the rats in their efforts to save themselves.

The tests were performed on all the groups at the beginning and every week of treatment (week 0, 1, 2, and 3). During each test, three repetitions for each rat were performed without any intervals and lasted for not more than 2 min for each repetition. The time required to find the ladder was the parameter used to measure memory function.

**Statistical analyses**

Shapiro–Wilk test was employed to verify the data normality. For parametric variables, one-way analysis of variance (ANOVA) was utilized followed by least significant difference's post-hoc test. The significance

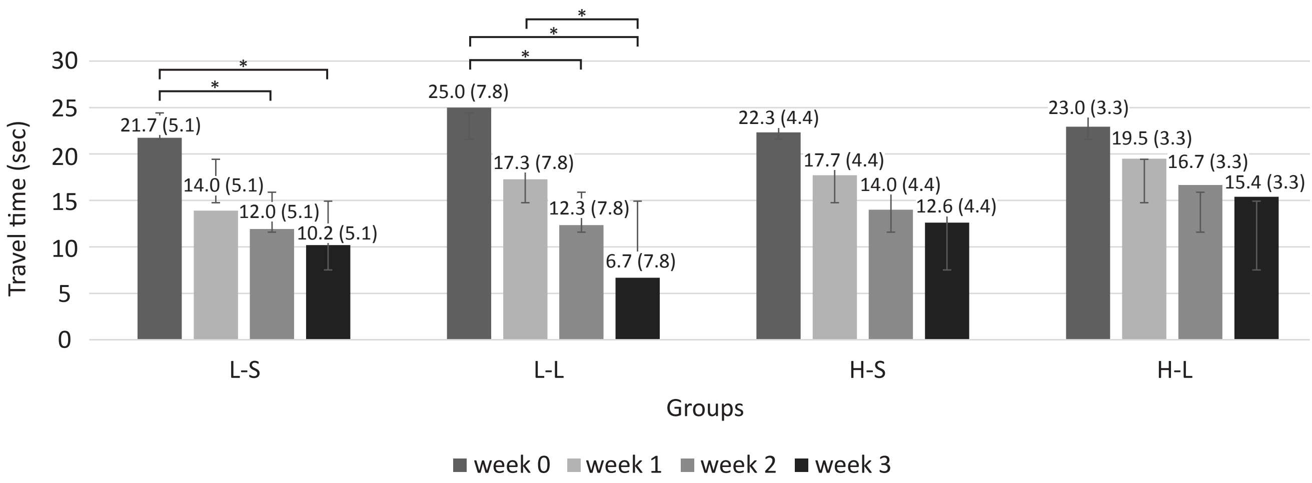


**Figure 1.** Travel time of spatial memory test results. L–S=low-intensity and short duration; L–L=low-intensity and long duration; H–S=high-intensity and short duration; and H–L=high-intensity and long duration. *$p < 0.05$

level was set at 5%, and the data were presented as the mean (standard deviation). All analyses were performed by SPSS software.

## RESULTS

The results of the memory test to determine the effect of intensity and duration of aerobic exercise on the spatial memory function are shown in Figure 1.

Figure 1 shows that the travel time decreased progressively each week. This observation suggests that the rats had learned to perform the task to achieve (reach) the target (ladder), and the spatial memory function had an exposure due to aerobic exercise with various combinations of durations and intensities. One-way ANOVA was employed to analyze the difference in the travel time for each group every week. Statistical analysis revealed that there were significant differences in travel time in L–S group on week 0 compared with that on week 2 ($p < 0.05$) and on week 0 compared with that on week 3 ($p < 0.05$). Moreover, there were significant differences in travel time in L–L group on week 0 compared with that on week 2 ($p < 0.05$), on week 0 compared with that on week 3 ($p < 0.05$), and on week 1 compared with that on week 3 ($p < 0.05$). However, there were no significant differences in travel time in H–L and H–S groups.

Figure 2 shows that the travel time decreased on post-test analysis. This observation indicates that aerobic exercise lead to an increase in spatial memory function. Statistical analysis showed that there were no significant differences of travel time between the groups on pre-test with post-test ($p > 0.05$) analysis. There was a significant difference in travel time in L–L group compared with that in H–L group.

## DISCUSSION

This study demonstrates that low-intensity aerobic exercises with short and long durations affected memory function starting from the second week,

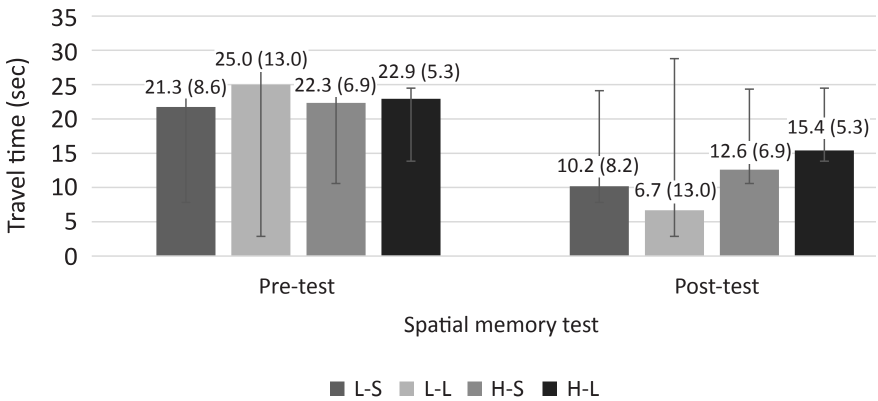


**Figure 2.** Spatial memory test results on pre-test and post-test. L–S=low-intensity and short duration; L–L=low-intensity and long duration; H–S=high-intensity and short duration; H–L=high-intensity and long duration

whereas in the high-intensity aerobic exercises with short and long durations, there were no significant changes in memory function. de Almeida et al[12] found that physical exercise affects the memory function after two weeks. This occurs due to the increased responses in the form of molecular, cellular, and structural modifications responsible for the functional plasticity characterized by the increased function of spatial memory.

The results of this study indicate that the central nervous system responds to aerobic exercise as an external stimulus differently depending on the combinations of intensity and duration. This study demonstrates that changes in memory functions are best observed in the group with low-intensity and long duration aerobic exercise (L–L), with the least improvement on the high-intensity and long duration aerobic exercise (H–L). This observation suggests that the optimum formula for the best memory function is low-intensity and long duration aerobic exercise.

Shimada et al[7] demonstrated that low-intensity is better than high-intensity in rats with middle cerebral artery occlusion. A different study revealed that low-intensity physical exercise can improve spatial memory after brain ischemia.[8] In addition, the duration of physical exercise is also a factor that affects the synaptic plasticity response. The duration of physical exercise will affect the consumption of oxygen by the brain and the activation of antioxidant, which induce the growth of new nerve cells (neurogenesis) and synaptic plasticity, including learning and memory, in this case, spatial memory. Long duration aerobic exercise is better because this duration can induce the synthesis of mitochondrial enzymes associated with metabolism process.[10]

In learning and memory, spatial function is the basis for moving. Spatial memory is formed and stored in different but coordinated frameworks, thus enabling the adaptive capacity of a well-structured movement. In adult rodents, aerobic exercise can improve performance in each task, such as spatial or non-spatial, associative or discriminatory, or procedural memory. Thus, aerobic exercise is effective in influencing the behavior and structure of brain circuits.

The improvement of spatial memory function is associated with some structural changes in hippocampal areas, and it also increases neuroplasticity. In recent study, it was observed that physical exercise can improve memory function by increasing neuroplasticity in the hippocampus.[13] Neuroplasticity is involved with some proteins in pre- and postsynaptic membranes such as synaptophysin (SYP), NMDAR, postsynaptic density protein 95 (PSD-95), and neuroligin. SYP is glutamate vesicles on the presynaptic area, which plays the role of an indicator depicting synaptic plasticity changes such as morphological changes in synapses and formation of new synapses.[14] Neuroligin and PSD-95 are adhesion molecules on postsynaptic membranes. The association between neuroligin and PSD-95 can increase the recruitment of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor and NMDAR to form long-term potentiation for learning and memory functions.[15]

Based on the results of this study, the combination of low-intensity and long duration of aerobic exercise can improve the spatial memory functions better than any other combinations of intensity and duration of aerobic exercises. This study does not provide any molecular evidence of spatial memory function. Therefore, further research is required to evaluate the proteins involved in the mechanism of spatial memory function such as SYP, neuroligin, NMDAR, and PSD-95 by the combinations of intensity and duration of aerobic exercise.

**Conflict of Interest**

The authors affirm no conflict of interest in this study.

**Acknowledgment**

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