



Original Article

Effects of aerobic and anaerobic exercise on spatial learning ability in hypothyroid rats: a pilot study

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Abstract. [Purpose] This pilot study analyzed the degradation of spatial learning ability caused by hypothyroidism using aerobic and anaerobic exercise. [Subjects and Methods] The experiments were performed on 11, four-week-old male Sprague-Dawley rats. Hypothyroidism-induced rats receiving propylthiouracil (PTU) treatment were divided into aerobic exercise, anaerobic exercise, and control groups. Each group performed exercise and rest for four weeks. Changes in lethargy, memory deterioration, and thyroid function were measured in each group by blood analysis and open field and Morris water maze tests. [Results] After four weeks, blood analysis revealed that the thyroid hormone levels had returned to normal in the aerobic exercise, anaerobic exercise, and control groups, whereas the open field and Morris water maze tests showed that the aerobic and anaerobic exercise groups had faster recovery compared to that of the control group. In addition, comparison of aerobic and anaerobic groups showed that the anaerobic exercise group had faster recovery compared to that of the aerobic group. [Conclusion] The findings of this study suggest that exercise helped to improve lethargy and deteriorated spatial learning ability caused by hypothyroidism and to recover function in rats. Anaerobic exercise was more beneficial than aerobic exercise in alleviating symptoms.

Key words: Hypothyroid, Exercise, Spatial learning ability

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INTRODUCTION

Thyroid hormone secreted from the thyroid gland is essential for maintenance of normal metabolism¹⁾. While the effects of most hormones occur in specific tissues; thyroid hormone occurs in most tissues and affects energy metabolism, heat generation, glycometabolism and lipid metabolism²⁾. Reduced thyroid hormone levels due to the insufficient production of thyroid hormone is called hypothyroidism³⁾. Hypothyroidism is a disease that progresses very slowly, and is usually not diagnosed as quickly as other diseases. Its clinical signs vary depending on the progression of the disease; however, patients generally experience fatigue, weakness, sensitivity to coldness, weight gain, lethargy, feebleness, memory deterioration, loss of appetite, muscle pain, arthralgia, and hypohidrosis⁴⁾. Quilan and others proposed that thyroid malfunction may also affect general cognitive ability⁵⁾. Thyroid hormone insufficiency especially affects neuronal differentiation and hippocampus development, leading to deterioration of memory and spatial learning ability⁶⁾. Hypothyroidism has also been implicated as a cause of reversible dementia⁷⁾. Most symptoms of hypothyroidism are permanent and patients require lifetime hormone supplementation. Most patients with hypothyroidism take oral thyroid hormones, but hormone overdose increases ventricle wall thickness and the risk of atrial fibrillation in elderly patients and may also cause osteoporosis in women after meno-

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pause⁸). Therefore, several studies have proposed exercise as a method to decrease these side effects and manage health problems associated with thyroid hormone. Both aerobic and anaerobic exercises have been suggested as effective methods to recover thyroid function^{9–11}). However, most studies lack coherence and are limited to analyzing the effects of one session of exercise^{12–18}). Although research has reported the effects of exercise on activation of energy metabolism and hormone levels, research on the effects of exercise therapy on lethargy and memory deterioration are insufficient. In this context, the current study analyzed changes in spatial learning ability deterioration and lethargy caused by hypothyroidism following aerobic and anaerobic exercise.

SUBJECTS AND METHODS

Eleven male Sprague-Dawley rats were divided into SPF (Specific Pathogen Free) animals, infected microorganism blockade clean system and green animal by using barrier system. During the purification process and pre-experimental period, they were raised in a polycarbonate box called with fixed temperature (20–22°C), relative humidity (30–70%), ventilation (10–15 times/hr), and lighting and shading cycles. They were allowed to feed freely with a maximum 60 g of solid feed (Samyang Co. Korea) with a specific amount of feed intake (daily feed consumption per rat: 15–30 g or 5–6 g per 100 g weight) and 150 ml water (daily water consumption per rat: 24–60 ml or 10–12 ml per 100 g weight). To induce hypothyroidism, 0.05 g 6-propyl-2-thiouracil (PTU, Sigma, MO, USA) was dissolved in 100 ml saline solution; 10 ml were administered to the rats daily for 6 weeks. The hypothyroid status of two normal and two rats who had received PTU were confirmed by inhalation anesthetization and blood analysis. The remaining seven rats were divided into normal (n=2) group, thyroid control (n=1), aerobic exercise (n=2), and anaerobic exercise (n=2) groups. They were made to exercise for 30 minutes, 5 days per week, for 4 weeks. Aerobic exercise was performed on a treadmill (10 m/s for 5 minutes, followed by and 25 m/s for 25 minutes for a total of 30 minutes of exercise). Anaerobic exercise consisted of climbing a 1-m ladder 8 times with a mass 50% of weight attached to their tail. The rats were given 2 minutes to rest each time they performed the exercise. The thyroid control group was left to do nothing while the rats in the other groups exercised. Lethargy and memory deterioration of white rats with hypothyroidism were analyzed using open field and Morris water maze tests. The research was approved by the Animal Test Ethics Committee of Busan Catholic University. After administration of PTU (the starting date of the experiment), weights were recorded twice weekly and analyzed according to group. The weight was measured using an electronic scale and 2–3 batches were repeated each time the weight was measured. Weights were measured in grams and in a steady state. For biochemical analysis of blood, the rats were lightly anaesthetized and the abdomen was incised. A 25-gauge syringe was used to collect 5–10 ml of blood in a heparinized tube (Franklin Lakes, NJ07417, USA). The collected blood was immediately centrifuged for 10 minutes at 3,000 rpm to collect plasma for biochemical analysis and was quickly frozen (–196 °C) in liquid N₂ gas and kept frozen until further analysis. Open field tests were performed to evaluate emotional behavior and exercise ability of the rats with induced hypothyroidism. The open equipment used in the research was a box without a lid, 78 cm wide, 78 cm long, and 30 cm tall. The boxes were monitored with a video camera set up in the middle of the box. The white rats showed exploration behavior when they were exposed to new environments. Moved or walked distances were measured as an indicator of exploration behavior. They were assessed for 5 minutes after 1 minute of adaptation time. Water maze measuring equipment and data analyzer (Kinovea 0.8.22) were used to measure spatial learning ability. A stress-reducing environment was created in a cylindrical water tank 120 cm in diameter and 50 cm tall. The tank was filled with 30 cm of water 13 °C lower (26 ± 2 °C) than the body temperature of rats (39–37.4 °C) to separate the rats from external disturbance. A circular platform 15 cm in diameter and 35 cm high was fixed and water level was adjusted so that it was not visible below 0.5 cm below the surface of water. The rats were monitored by using a video camera. The water maze was divided into four equal quadrants; northeast (NE), southeast (SE), and southwest (SW). A fixed platform was set up in the NE quadrant. A video camera was also set up in the upper middle part of the water maze ceiling to record the rats' movement and time to find the platform. As a method to train the rats during the experimental period, a visual spatial cue was artificially created around the tank and 10 practice repetitions were performed in water without coloring by making the rats start from the rest quadrants so that they could remember and find their way. The next day, harmless water coloring was dissolved to hide the surface of the fixed platform from the rats' visibility. The time for rats to reach the target point from each quadrant and the distance moved were measured.

RESULTS

First, thyroid hormone blood analysis revealed reduced initial levels of T3, T4, FT4, and thyroid hormone in the group of rats who received PTU, compared to levels in the normal group. Blood analysis after the experiment showed that thyroid hormone levels of all groups (thyroid control, thyroid aerobic exercise, and thyroid anaerobic exercise groups) were equal to those of the normal group. Weights measured before the experiment and the results of open field and Morris water maze tests after the experiment are shown in Table 1. Before the experiment, hypothyroidism-induced rats were heavier than normal rats. As a result of aerobic and anaerobic exercise in the hypothyroidism-induced rats, their weight increased compared to that of the control group, an effect more clearly seen in the anaerobic exercise group than in the aerobic exercise group. Even in the open field test, hypothyroidism-induced rats showed less movement; as a result of the exercise intervention,

Table 1. Changes in body weight (g), O.F.T (cm), and M.W.M.T (sec) before and after the experiment

		Before	After
Weight	Normal	351 ± 15.5	380.5 ± 9.9
	PTU-Control	268 ± 19.8	298 ± 5.6
	PTU-Aerobic Ex.	262.5 ± 14.8	317.5 ± 4.2
	PTU-Resistance Ex.	258.5 ± 17.6	335 ± 4.7
O.F.T.	Normal	2,269.2 ± 100.4	2,312.1 ± 120.3
	PTU-Control	1,773.1 ± 25.3	1,860.3 ± 70.3
	PTU-Aerobic Ex.	1,647.2 ± 24.4	1,920.1 ± 110.2
	PTU-Resistance Ex.	1,821.4 ± 24.6	2,439.2 ± 85.5*
M.W.M.T.	Normal	52 ± 11.1	17.1 ± 9.7
	PTU-Control	89 ± 9.6	75 ± 13.9
	PTU-Aerobic Ex.	120 ± 4.3	25.7 ± 13.4*
	PTU-Resistance Ex.	120 ± 4.5	14.7 ± 7.1*

O.F.T.: open field test, M.W.M.T.: Morris water maze test

increased movement was observed compared to the control group; this increase was more pronounced in the anaerobic exercise group. The Morris water maze test results revealed that, initially, the normal group found the platform in time, whereas hypothyroidism-induced rats either could not find the platform in time or took more than one minute to find it. However, after exercise intervention, the rats showed reduced time, with the anaerobic exercise group showing greater time reductions.

DISCUSSION

The current study determined the effect of aerobic and anaerobic exercise on rats with spatial learning ability deterioration and lethargy due to hypothyroidism. After the intervention, thyroid hormone levels had returned to normal levels in all groups. Lethargy assessed by the open field test revealed that the group of rats that performed exercise had higher measurements compared to those of the control group, with greater increases of observed in the anaerobic exercise group compared to measurements in the aerobic exercise group. Hypothyroidism results in glycometabolism and lipid metabolism malfunction. During anaerobic exercise, is performed, adenosine monophosphate-activated protein kinase (AMPK) is activated, which accelerates insulin secretion due to increased fatty acid oxidation and glucose absorption¹⁹). This seemed to have decreased lethargy. The results of the Morris water maze test, used to assess memory and learning ability, showed that the exercise group had decreased times compared to those of the control group, with greater reductions in the anaerobic exercise group compared to those of the aerobic exercise group. Exercise appeared to have a positive effect on general memory deterioration in both anaerobic and aerobic exercise groups^{20, 21}). According to Cassihans et al. in 2007, resistance exercise in white rats resulted in insulin growth factor-1 (IGF-1) secretion and improved memory²²). During aerobic exercise, brain-derived neurotrophic factor

(BDNF), tropomyosin receptor kinase B (TrkB), and beta- calmodulin-dependent protein kinase II (CaMK II) are secreted, and are also reported to improve memory²³). However, the results of the current study indicated that the effect was stronger in rats that underwent anaerobic exercise than those who underwent aerobic exercise rats; the reason for this observation may be the relationship between IGF-1 secretion induced by anaerobic exercise and memory deterioration caused by hypothyroidism. In addition, it is generally reported that, despite the normality of hypothyroidism patients, their IGF-1 blood concentration decreases^{24–26}). However, the thyroid control group that did not perform any exercise appeared to have natural recovery from the weight increase, lethargy, and memory deterioration, although the changes were much lower compared to those in the exercising groups. Both aerobic and anaerobic exercise had positive effects on lethargy and memory deterioration in induced-hypothyroidism rats, but anaerobic exercise appeared to be more effective than aerobic exercise. However, the research was performed for only eight weeks blood was analyzed only before and after the experiment; therefore, it was not possible to determine precisely when the recovery of thyroid hormone occurred. Only male rats were used for the experiment and they were fed freely; thus, the weight change could not be restricted. Even water with dissolved PTU administered freely; therefore, the doses were not standardized. This study assessed the effects of aerobic and anaerobic exercise on rats with spatial learning ability deterioration and lethargy caused by hypothyroidism. The exercises resulted in function recovery in induced-hypothyroid rats with these symptoms, and, compared to aerobic exercise, anaerobic exercise was more beneficial in alleviating the symptoms.

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