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Original Article

The Effects of Swimming on Scopolamine Induced Hippocampal Oxidative Stress in Long-Evans Rats

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Abstract

Background: *Scopolamine causes oxidative stress by accelerating the buildup of reactive oxygen species. Physical exercise, such as swimming use oxygen more efficiently, provides benefits in oxidative stress. Objective: To evaluate the effects of swimming on scopolamine induced hippocampal oxidative stress in Long-Evans rats.* ***Methods:*** *This experimental study was conducted in BMU. For this purpose, 18 Long-Evans rats aging 8 to 10 weeks and having body wt. 175±25 grams were collected from animal house of this University. On the basis of treatment, rats were divided into group I (6 rats treated with oral normal saline 5 ml/kg body wt.), group II (6 rats treated with scopolamine), and group III (6 rats treated with scopolamine and allowed to do swimming exercise) for 14 consecutive days. For estimation of hippocampal oxidative stress, reduced glutathione (GSH) & malondialdehyde (MDA) levels were measured by ELISA. Data were expressed as mean ±SEM and statistical analysis was done by using SPSS version 22. Statistical tests were carried out by ANOVA followed by Bonferroni's post hoc test. In the interpretation of results, p≤0.05 was considered as significant.* ***Results:*** *In perspective of hippocampal enzymes assay, GSH level significantly lower (p≤0.05) and MDA level significantly higher (p≥0.05) was found in group II rats when compared to group I rats. But GSH level significantly higher (p≤0.05) and MDA level significantly lower (p≤0.05) in group III rats, when compared to group-II rats. Additionally, their levels were almost similar in group III in comparison to those of group-I.* ***Conclusion:*** *Swimming can prevent scopolamine induced hippocampal oxidative stress in Long-Evans rats.*

Keywords: *Scopolamine, oxidative stress, and swimming.*

Introduction: Oxidative stress, that is increment of oxidants or decrement of antioxidants[1]. Oxidant is an oxidizing agent which removes either an electron or hydrogen atom from a chemical species which is transferred to another chemical species in biological system[2]. It causes damage to surrounding biomolecules by transferring or removing unpaired electron. The common oxidants include hydrogen peroxide (H_2O_2), superoxide anion (O_2-), hydroxyl radical (OH-) malondialdehyde (MDA) etc.[3]. On the other hand, antioxidant is the scavenging molecule that limits or prevents the harmful effects of oxygen free radicals and repairs cell damage. The common antioxidants include superoxide dismutase, catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH), vitamin E, β carotene, vitamin C, taurine, L-carnitine, coenzyme Q10 etc.[4].

The balance between oxidants and antioxidants are required for the maintenance of hippocampal function. This balance is impaired by many factors and conditions such as aging, air pollution, ionizing radiation, high calorie diet, sedentary lifestyle[5], cigarette smoke[6], and several chemical.

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To comprehend the pathophysiology of this imbalance, some of these compounds include streptozotocin, ethanol, okadaic acid, scopolamine, heavy metals, and lipopolysaccharide[7]. A muscarinic receptor antagonist called scopolamine impairs cholinergic neurotransmission, which impairs memory in rodents. According to recent research, scopolamine causes oxidative stress, which impairs memory by increasing the buildup of reactive oxygen species. Scopolamine decreases antioxidant and increases oxidant enzymes level which causes memory impairment in rat[8].

Extensive studies on human and animal suggested that physical exercise could have aids for general health and cognitive function[9]. It was also reported to improve learning ability and memory function[10]. Exercise might be voluntary as part of our lifestyle or forced during weight loss or therapeutic regimen; both types of exercise improve spatial learning and memory and this improvement is parallel to a reduction in the accumulation of oxidative damage[11]. The beneficial role of regular exercise is due to increase antioxidant capacity, repair enzymes activity, resistance to oxidative stress and lower oxidative damages compared to sedentary lifestyle. The interaction effect of exercise and antioxidant-rich diet on the brain function has been demonstrated. Both male and female ApoE4 mice benefit best from this contact in terms of spatial learning. Furthermore, a meta-analysis of the data showed that exercise might assist adults with mild cognitive impairment function better when it comes to memory[12].

Moreover, physical exercises those use oxygen more efficiently, such as swimming, running, cycling, jogging, climbing provide benefits in cognition. Among them, swimming is very cost effective and easily accessible exercise, that can be performed in naturalistic settings[13]. On the basis of this background, the present study has been designed to evaluate the effect of swimming on scopolamine induced hippocampal oxidative stress in Long-Evans rats.

MATERIALS AND METHODS

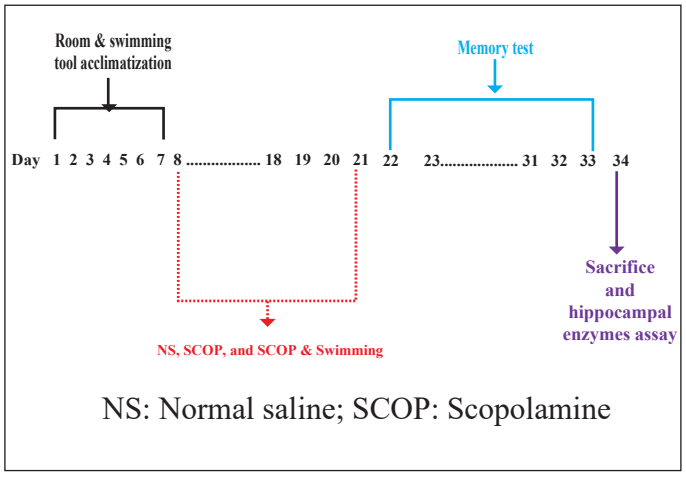
This experimental study was conducted in the KM Fariduddin animal research lab of Department of Physiology, Bangladesh Medical University (BMU) from January 2023 to June 2023. The present study protocol involving the animal subjects follow the guidelines for the Animal Experimentation Ethics Committee of icddr,b and was approved by the members of Institutional Review Board, BMU, Bangladesh.

Procurement and maintenance of animals

A total of 18 rats of 8th to 10th weeks weighing 150 to 200 gm was obtained from the central animal house of Bangladesh Medical University (BMU), Dhaka. All rats were kept in the KM Fariduddin animal research lab of the Department of Physiology, BMU and was housed in specially constructed plastic cages with 3 to 4 rats per cage under a 12/12-hour light/ dark cycle[14]. The room temperature was kept between 27^{0}C to 28^{0}C, corresponding to the thermoneutral zone for rodents[15]. All rats had access to standard laboratory food cooled boiled water ad libitum during acclimatization[16]. In order to avoid circadian influences all experiments were carried out during the day between 08:00 and 16:00 hours[17].

Experimental design

The rats were assigned randomly into three groups (n =6 rats/group): group I (rats were treated with normal saline 5 ml/kg body wt.), group II (rats were treated with intraperitoneal injection of scopolamine 2 mg/kg body wt.), and group III [rats were treated with intraperitoneal injection of scopolamine 2 mg/kg body wt. and allowed to do swimming exercise for 60 minutes daily (alternating 5 minutes swimming followed by 5 min rest) (Table I)] for 14 consecutive days (Figure 1).



NS: Normal saline; SCOP: Scopolamine

Figure 1 : Hippocampal tissue preparation

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Table I: Chemical supplementation

Chemical Agent	Collection	Dose	Route
Scopolamine	Sanofi Aventis Limited	2 mg/ kg (Ganbari et al. 2019)	Intraperitoneal (Ganbari et al 2019)
Normal saline	Beximco Pharma Limited	5 ml/ kg (Moallem, Hosseinzadeh and Farahi 2008)	
Di-ethyl ether	MERCK, Germany		
Reduced glutathione Kit	Elabscience		
Malondialdehyde Kit	Elabscience		

Procedure of swimming:

The swimming protocol was carried out using a circular pool whose diameter was one hundred fifty (150) cm and Hight was fifty (50) cm high18,19. A rat for was allowed to swim for 60 minutes per day (alternating between 5 minutes swimming followed by 5 minutes rest) for consecutive 14 days. After each 5 min swimming, the rat was placed in a cage with fresh newspaper to get dried by itself20.

Hippocampal enzymes assay

Rats were sacrificed, and brain tissue was promptly extracted in accordance with earlier research protocols21. The hippocampus was then removed from the rat's brain using the methods from earlier studies. The hippocampal tissue was then scooped, put on a petri dish, and chopped into tiny pieces22 (Figure 2). To remove extra blood thoroughly, all the pieces were washed in ice cold PBS (Phosphate Buffer solution) (0.1 M, pH=7.40). Later, the tissue pieces were weighed and homogenized in PBS according to the ratio of Weight (gm): Volume (mL) =1:4 with a glass homogenizer on ice. Then the homogenate was centrifuged for 10 minutes at 3500 rpm (revolution per minute) to get the supernatant. The supernatant was taken in a test tube and stored at -200C until hippocampal antioxidant enzymes assay23. Hippocampal total protein, reduced glutathione (GSH), and malondialdehyde (MDA) concentration in the recovered supernatant was measured using a commercially available kit purchased from Elabscience (Biotechnology Inc. 2018).

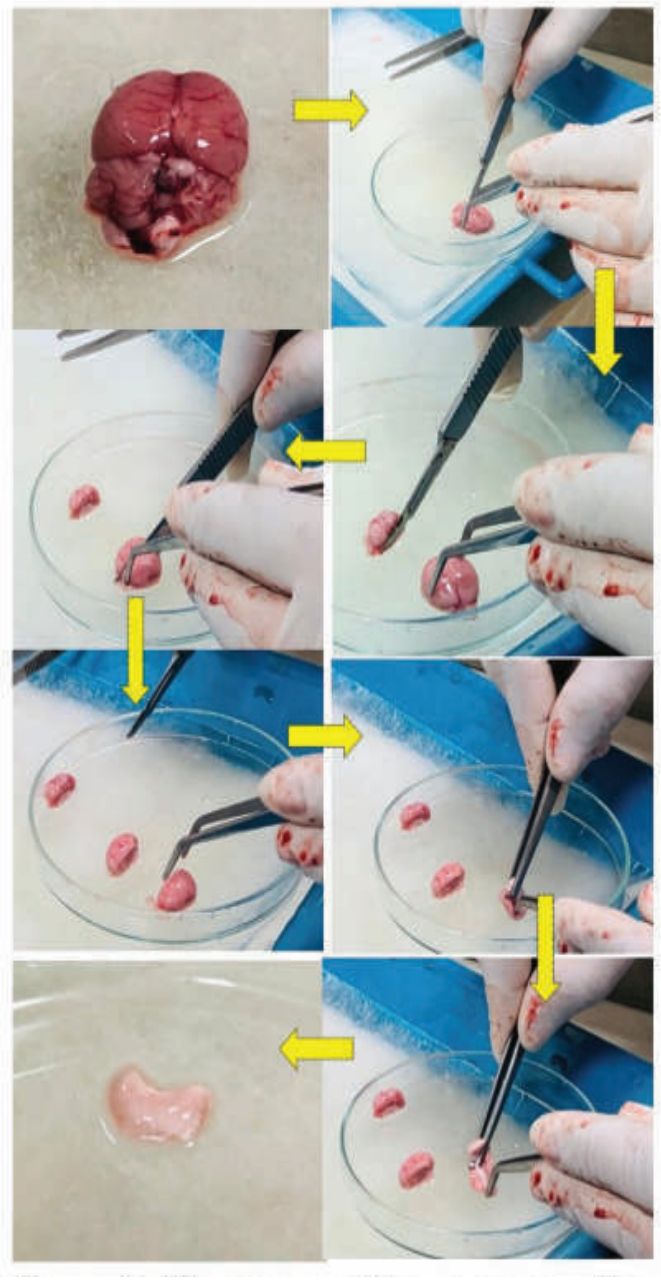

Figure 2 : Hippocampal tissue preparation

Data presentation and statistical analysis

Results were expressed as mean ± SEM (Standard error of mean) of study variables. SPSS (version 22.0) was used to carry out all statistics. Independent sample t test was used to compare means of variables between two groups to determine which group comparison is significant, where $p \leq 0.05$ was considered as statistically significant.

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Results

Effect of swimming on hippocampal reduced glutathione (GSH) and malondialdehyde (MDA)

As shown in table II, the mean value of GSH was significantly ($p \leq 0.05$) lower in group II in comparison to that of group I. Moreover, the mean values of this variable were significantly ($p \leq 0.05$) higher in group III in comparison to that of group II. However, the difference of hippocampal GSH between the group I and III was statistically non-significant on day[34].

In table II as well as, the mean value of MDA was significantly ($p \leq 0.001$) higher in group II in comparison to that of group I. Moreover, the mean values of this variable were significantly ($p \leq 0.001$) lower in group III in comparison to that of group II. However, the difference of hippocampal MDA between the group I and III was statistically non-significant on day[34].

Table II: Hippocampal enzymes in different groups of rats

Hippocampal enzymes	Groups		
	Normal saline (I)	Scopolamine (II)	Scopolamine + Swimming (III)
Reduced glutathione (µmol/mg protein)	7.30±0.54 (5.82 to 8.77)	5.33±0.23* (4.54 to 5.92)	7.07±0.44# (5.61 to 8.75)
Malondialdehyde (µmol /mg protein)	2.27±0.31 (1.39 to 3.18)	4.98±0.58*** (3.14 to 7.13)	1.74±0.24### (1.36 to 2.91)

The values represent mean±SEM of 6 rats.
* = group I vs group II, $p \leq 0.05$ was considered as significant compared to group I.
# = group II vs group III, $p \leq 0.05$ was considered as significant compared to group II.
***/### = $p \leq 0.001$.

Discussion

The current study has been assumed to evaluate the effect of swimming on scopolamine induced hippocampal oxidative enzymes. For this, scopolamine induced memory impaired Long-Evans rats were studied to detect the effect of swimming on hippocampal enzymes level. For assessing the hippocampal enzymes level, reduced glutathione (GSH) and malondialdehyde (MDA) of hippocampal tissue were estimated in the above-mentioned groups of rats.

In our study, scopolamine (2 mg/kg) caused both working and reference memory impairment in our memory impaired rats (only scopolamine treated) as evidenced by significantly higher escape latency (EL) and lower target crossings in MWM, in comparison to those of normal memory (only normal saline treated) rats. Similar results of working and reference memory deficit by scopolamine have been reported by other investigators abroad[24,25].

It is well known that normal cholinergic activity is essential for attention, learning and memory[26]. Scopolamine is an established cholinergic receptor blocker[27]. So, in our rats, scopolamine might cause memory loss due to its cholinergic receptor blocking effect by competitive antagonism in cerebral cortex which in turn reduce ACh mediated neuronal activity in prefrontal cortex (PFC) and hippocampus causing learning and memory deficit[28]. However, MDA also increased suggesting that scopolamine might also increase the oxidative activity of hippocampal tissues[29].

In our experimental rats, swimming prevented the development of scopolamine induced memory impairment and decrement of hippocampal GSH & increment of MDA, as evidenced by significantly lower EL & MDA and significantly higher target crossing (TC) & GSH in comparison to those of impaired memory rats. Similar findings of EL and TC were observed in MWM after treadmill exercise[30] and similar prevention in hippocampal GSH decrement were also observed after aerobic exercise as swimming[31,32,6].

In our study, as swimming is a type of aerobic exercise, it might activate constitutional endothelial nitric oxide synthase (eNOS) causing neuroprotection and cerebral blood flow enhancement[33]. In addition, this type of aerobic exercise also might cause increment of brain derived neurotrophic factor (BDNF)[34], a significant marker of memory and cognition. As a consequence, both of these eNOS and BDNF might activate neurogenesis, synaptogenesis[35] as well as hippocampal volume increment[36] resulted in prevention of cognition and memory impairment in our experimental rats. Besides, these 14 days swimming might increase the GSH and decrease MDA level in hippocampus of our experimental rats directly[32].

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Moreover, in this study, the restoration of memory was close to normal memory status as evidenced by similar EL, TC, GSH, and MDA in our experimental rats to those of normal memory rats. Similar observations in EL and TC after treadmill exercise[30] and in GSH after swimming exercise[33] were found by other researchers abroad.

CONCLUSION

This study concluded that swimming can prevent scopolamine induced hippocampal oxidative stress in Long-Evans rats.

Limitations:

This experiment was done with two enzymes from hippocampus.

Acknowledgments

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Conflict of interest

There are no conflicts of interest between us.

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