Golestan University of Medical Sciences

Jorjani Biomedicine Journal

Online ISSN: 2645-3509

The Effects of Exercise and Folate Nano-Liposomes on D1 and D2 Receptor Gene Expression in the Brain of Alzheimer's Rats

Farah Nameni[1*], FatemeFiroozmand[2]

1. Department of Sport Physiology, Varamin Pishva Branch, Islamic Azad University, Varamin, Iran
2. MSc. of Sport Physiology, Varamin Pishva Branch, Islamic Azad University, Varamin, Iran

Article Type:

Original article

Article History:

Received: 30 Jan 2022
Revised: 15 May 2022
Accepted: 21 May 2022
Published: 31 May 2022

Correspondence:

Farah Nameni,

Department of Sport Physiology, Varamin Pishva Branch, Islamic Azad University, Varamin, Iran

nameni@iauvaramin.ac.ir

DOI: 10.29252/jorjanibiomedj.10.2.36

Abstract

Background and objectives: Alzheimer's is a neurodegenerative disorder characterized by memory loss and cognitive dysfunction. Research has shown that blood metal levels and physical activity may be crucial to injury and possibly Alzheimer's treatment. This study aimed to evaluate the effects of high-intensity interval training (HIIT) and folate Nano liposomes on the expression of D1 and D2 genes in the hippocampal tissue of Alzheimer's rats.

Material and Methods: Thirty-five male Wistar rats at eight weeks of age were randomly divided into five groups (healthy control, Alzheimer's control, Alzheimer's + HIIT, Alzheimer's + Nano-liposome folate, Alzheimer's + HIIT + Nano-liposome folate). After Alzheimer's induction, exercise program protocol and folate Nano liposomes were performed as supplements in the groups. After the last training session, the mice were anesthetized, and the hippocampus was examined. D1 and D2 receptor gene expression were examined by the Real-time-PCR method.

Results: The results showed that the highest increase in D1 and D2 receptor gene expression was in the Alzheimer's group, and the lowest growth was in the Alzheimer's+HIIT+ Nano liposome group ($P<0.05$).

Conclusion: Resistance training and Nano-liposome folate decreased D1 and D2 receptor gene expression after Alzheimer's induction. This reduction may be due to the modulatory effects of physical activity and Nanomedicines in preventing or reducing pathological conditions.

Keywords: Exercise [MeSH], Dopamine [MeSH], Dietary Supplements [MeSH], Immune System [MeSH]

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]

© The Authors.

Publisher: Golestan University of Medical Sciences.

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]

Highlights

- The use of Nano-drugs and exercise can regulate and reduce the spread of Alzheimer's disease. In this experimental study, the synergistic effects of folate Nano-liposomes and HIIT reduced the expression of dopamine D1 and D2 receptor genes.

Introduction

Neurological and mental illnesses are major causes of cognitive disorders that affect millions of people. Various drugs have been introduced to treat these disorders, but no effective treatment has yet been found. One treatment is the use of nanoparticle systems. Nanoparticles can improve drug delivery and have been introduced to reduce and overcome Alzheimer's. Regular exercise can positively affect depression, anxiety, and other cognitive disorders (1). Physical inactivity is one of the most substantial risk factors for dementia and Alzheimer's Disease (AD) (2). High-Intensity Interval Training (HIIT) is a training protocol with short periods of intense or explosive anaerobic training with short and intermittent recovery periods. The protocol relies on the anaerobic energy release system to prevent or delay many diseases (3). Alzheimer's disease is a common type of dementia with progressive neuronal degeneration (4). There are five types of dopamine receptors, D1-D5. D1 receptors bind to adenylate cyclase, and when activated, cyclic Adenosine Monophosphate (AMP) is produced as a secondary messenger (5). Unlike D1, D2 receptor gene expression does not positively correlate with adenylate cyclase and inhibits this enzyme (6). However, activation of D1 and D2 receptor gene expression increases the release of acetylcholine in the hippocampus (7). The biological use of nanoparticles has been emphasized as a new therapeutic approach in treating diseases and lesions of the nervous system. Exercise for physiological reasons can also be effective in synergizing these effects (8). Exercise plays an essential role in preventing neuroinflammation and improving memory by increasing dopamine D2 and D1 receptor gene expression and acetylcholine in the hippocampus (9). Physical activity and exercise increase blood flow throughout the body and brain (10). Kabir et al. (2020) showed that combination therapy was effective for AD, including the concomitant use of memantine and a cholinesterase inhibitor (11, 12). Natural compounds such as chelertin, chalcone, coumarin, hoprin, berberine, and resveratrol derivatives have shown such potential and necessitate further studies for the development of AD (13). Investigation of anti-amyloid genic and antioxidant properties of biosynthesized silver nanoparticles using leaf extract to lemon showed that with increasing the concentration of the extract, the antioxidant properties of these nanoparticles increased, and the most inhibition of amyloid filament production at 2 mg/ml and 96 Percent were observed (14). Nano-liposomes enable conjugation and increase the uptake of nanoparticles in the treatment of Alzheimer's disease. Increasing ferritin reduces fat peroxidation in the hippocampus, weakens the immune system, and reduces cognitive perception (15). Direct delivery of the drug from the nose to the brain in the formulation of nanoparticles for the treatment of neurological disorders has also been introduced. Drug delivery was, therefore, more efficient and targeted. However, more preclinical studies are needed to confirm non-toxicity and their beneficial effects (16). In most studies, only nanoparticles were used, and no exercise was used. There were also examples of human research. But in this study, controlled animal samples and regular exercise activities were used. Many treatments are limited in effectiveness, have side effects, and have not shown significant changes in AD (17). Nano-liposomes seem to eliminate lipid deficiencies of metals such as folate by combining lipid molecules in an aqueous solution (18, 19). Of course, plant-based diets and folate-rich fish are resistant to AD (20). Folate deficiency is one of the factors affecting homocysteine, cognitive disorders, and Alzheimer's (21). Iron nanoparticles can be magnetized and pass through

the microvascular endothelial cells of the brain and be used to treat neurological and cerebral diseases (22). Dopamine, which acts as a neurotransmitter and hormonal agent in the brain (23), controls the locomotors system and destroys dopaminergic neurons or dysfunction (24). Only supplements (drugs) or only exercise were used in previous studies. But in this study, both variables were examined simultaneously, and so far, genes and this exercise protocol have not been used. This study aimed to evaluate the effects of High-Intensity Interval Training (HIIT) and folate Nano liposomes on the expression of D1 and D2 genes in the hippocampal tissue of Alzheimer's rats.

Materials and Methods

Thirty-five male Wistar rats with a mean age of 8weeks±4days and a mean weight of 250±20g were obtained. All stages of the research were carried out by the rules of ethics in research and the Helsinki Declaration, under the supervision and getting a code of ethics. All the rats' living, feeding, and sleeping facilities were provided. The experimental steps were performed without using a shocker in a standard laboratory by a technician and an animal specialist. Rats were kept in the Physiology and Pharmacology animal laboratory under controlled light conditions (12 hours of light and 12 hours of darkness), the temperature of 22°C, and humidity of about 45%. Three-five rats in Plexiglas cages with netting and dimensions of 25×27×43 cm in storage had free access to standard water and food.

2.1. Grouping

After three days of familiarity with the environment, the rats were introduced to the treadmill and how to run on it for 10 minutes five times a week. After 48 hours of rest from the last familiarization session, the rats were tested for measurement of maximal exhaustion test, and the maximum oxygen consumption was predicted using the maximum velocity during exhaustion (25). Rats were randomly divided (for random sampling, the names of 5 groups were first recorded on a sheet and then folded into a container. Then, a rat and a leaf were taken out of the container). According to the group's name, the rat was in that group. The sheet of each group was taken out of the container after completing the number) Five groups and seven rats were placed in each group (control, Alzheimer control, Alzheimer+HIIT, Alzheimer+Folate Nano liposomes, HIIT+Alzheimer+Folate Nano liposomes).

2.2. Alzheimer's induction

To prepare the peptide, in the first step, beta-amyloid was dissolved in the buffer solution until its pH reached 7.4. The resulting solution was incubated at 37°C for three days. Then at -70°C, a dense beta-amyloid was formed. The animal physician and technician then anesthetized the rats by intraperitoneal injection of ketamine and xylazine. The animals' heads were then fixed in a stereotaxic device, and by creating a longitudinal incision in the posterior part of the skull, the injection cannulas were inserted into the lateral ventricles in the rear position of the Bergma 0.8, 1.5 mm on either side of the longitudinal incision and 2.5 mm lower. The surface of the skull was placed, and the beta-amyloid injection into the hippocampus (one microliter on each side) was performed with a Hamilton syringe. Dye was first injected into the rats' heads to ensure the correct injection site in the brain. The rats were sacrificed after the study period, and the injection site was examined. In the sham group, all laboratory steps were the same as in the beta-amyloid injection group, except that in the sham group, one microliter of DMSO buffer was injected into each of the hippocampi (26).

2.3. Exercise protocol

The training protocol was a combination of high-intensity repetitions and active rest. High-Intensity Interval Training (HIIT) included two minutes of running on a treadmill with a maximum intensity of 80% in the first week. The training program was performed from the second to the fourth week with 110-90% of the ultimate power. Active rest also included two minutes of running, completed with 40% of maximum intensity in the first to the third week. It continued in the fourth week with a maximum of 30%

[Downloaded from goums.ac.ir on 2023-12-11]
[DOR: 20.1001.1.26453509.2022.10.2.3.3]
[DOI: 10.52547/jorjanibiomedj.10.2.36]

maximum. The number of repetitions was determined according to the intensity of the rats' training sessions. So in the first week, two repeats, in the second week 4 repetitions, and from the beginning of the third week 6 repetitions were designed in the sections. Rats were monitored during all training sessions and were encouraged to continue running by manipulating the sponge (23).

2.4. Supplementation

Consumption of Folate Nano-liposomes was injected intra-peritoneal as a supplement for 6 weeks and 5 days a week using a dose of 80µmol/kg. To determine the status of Alzheimer's, Maurice Blue Maze memory and spatial learning tests, Probe test, and visible platform tests were used.

2.5. Laboratory Measurements of D1 and D2 receptor gene expression

Three days after the last training session; Mice were rapidly anesthetized by intraperitoneal injection of ketamine (90mg/kg) and xylazine (10mg/kg). The hippocampus was frozen and refrigerated for analysis at -80°C. D1 and D2 receptor gene expression were examined by the Real-time-PCR method. The RNA extraction method was performed according to the kit protocol. cDNA was synthesized by Prime Script TM RT reagent (catalog number#RR037A), and according to the kit instructions. For each reaction, the kit instructions were used to prepare and add ingredients. The mixture was then incubated at 37°C for 15 minutes and then the tubes were heated at 85°C for five seconds to stop the reaction. In the beginning, the optimal cDNA concentration and the primers related to each gene were determined separately for each using a serial concentration test so that the lowest dimer and the best Ct were observed (22) (Table 1).

Table 1. Sequence of primers

Gene	Forward primer 5´-3´	Reverse primer 5´-3´
D1	AAGCTGAAAGTCAACAAATGACAGTT	TGGACTGTCTGCCCATTGG
D2	ACTTGCATTGCTGATTGCTG	TTGAATAGGCCAGGGTTTTG
18S	GCAATTATTCCCCATGAACG	GGCCTCACTAAACCATCCAA

2.6. Data analysis

The Shapiro–Wilk test results also showed the normal distribution of data. Using the Leven test, the homogeneity of variances was investigated and confirmed. One-way ANOVA was used to determine intergroup differences after Alzheimer's induction. The results were analyzed by the Bonferroni post hoc test ($P<0.05$). The test hypotheses were one-sided.

Results

3.1. Effects of Folate Nano liposomes and HIIT on D1 and D2 receptor gene expression

Descriptive information was reviewed and recorded. A comparison of D1 and D2 receptor gene expression showed the most significant increase in the Alzheimer's group. Increased expression of the D1 and D2 receptor gene was lower in Alzheimer's + HIIT + folate Nano-liposome group than in the Nano-liposome folate, Alzheimer's, and HIIT groups (Figure 1 and 2) ($P<0.001$)

.

[Downloaded from goums.ac.ir on 2023-12-11]
[DOR: 20.1001.1.26453509.2022.10.2.3.3]
[DOI: 10.52547/jorjanibiomedj.10.2.36]

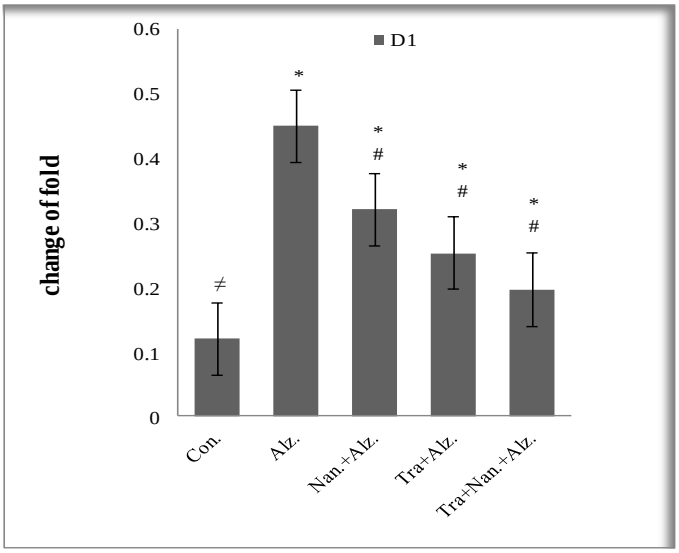

Figure1. Comparison of gene expression values and significant D1changes between five experimental groups in male rats

*:P≤0.05, significant difference between the control group and another group

#:P≤0.05, a significant difference between Alzheimer's group and another group

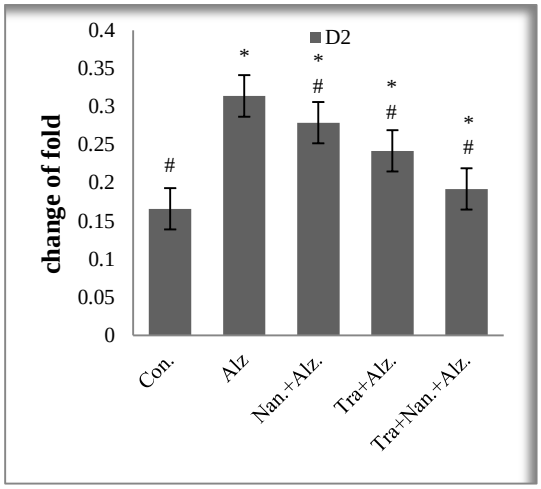

Figure 2. Comparison of gene expression values and significant D1changes between five experimental groups in male rats

*:P≤0.05, significant difference between the control group and another group

#:P≤0.05, a significant difference between Alzheimer's group and another group

Discussion

The results showed that HIIT and folate Nano liposomes reduced the expression of dopamine D1 and D2 receptor genes in rats. One possible mechanism is that HIIT increases blood flow to the brain, improving brain function, nervous system, and muscle coordination, which is consistent with Burger et al. (2010) (27). Folate Nano-liposomes have also acted as an antioxidant against the beta-amyloid peptide, apoptosis, Alzheimer's disease, and improved neurotransmitter function, in line with Farioli et al. (2015) results (28). Taval et al. (2021) had

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]

similar results to the findings of this study and confirmed the effect of physical activity on brain function (29). Cholinergic neurotransmitters may be produced by physical activity, which reduces the activity of Aβ plaques and improves learning, memory, and nerve tissue formation (30). Thus, exercise may increase dopamine D2 receptor and acetylcholine secretion in the hippocampus, enhance the function of the memory cholinergic system, and stop the release of acetylcholine release in the hippocampus, preventing memory impairment (31).

Exercise's potential effects on dopamine include increased urinary dopamine, increased availability of dopamine D2/D3 receptor, increased dopamine secretion in the caudal nucleus, the release of dopamine in the intra-abdominal striatum, and increased blood plasma dopamine. But some studies did not show significant changes in dopamine concentrations after exercise. Contradictory results were found in studies in which the administration of dopamine inhibitors, in combination with dopamine inhibitors, positively affected performance and reduced fatigue at maximum speed. However, blocking dopamine receptors appears to be harmful, and a significant positive correlation was observed between dopamine-related gene expression and regular exercise (32). The differences between the training protocol, the research sample, and the lack of supplementation have caused contradictions.

Piri et al. (2011) stated that activation of presynaptic nicotinic receptors could also increase glutamate secretion and positively affect memory. Thus, the activity of dopaminergic receptors D1 and D2 increases proliferation, differentiation of neurons and dopamine receptors gene expression, and brain growth (33). Exercise increases calcium concentration in the cell and is therefore effective in dopamine secretion (34). The magnetic properties of folate Nano liposomes appear to be involved in information storage, and the accumulation of these particles has also been observed in Alzheimer's disease. Magnetic iron oxide nanoparticles and residues in the axons of neurons can interact magnetically, which is essential for the transmission and storage of brain data. However, as these nanoparticles accumulate in the brain, this interaction is disrupted, and the nanoparticles attach to microtubules and tau proteins, leading to the instability of microtubular polymers. Petzinger (2015) also confirmed this mechanism (35). This study seems that the results are due to the synergistic effects of exercise and supplementation. Cordero (2017) also believed that iron plays a significant role in oxygen transport and physical activity, and its deficiency causes fatigue and irritability. Therefore, consumption of folate and exercise Nano liposomes increased access to oxygen and increased dopamine secretion, positively affected cognitive status, and improved Alzheimer's disease (36). In humans, compounds such as tacrine (a cholinesterase inhibitor) have been used to stop the progression of Alzheimer's but have been limited due to toxic liver side effects. Donepezil, rivastigmine, and galantamine are also widely used. The dose of donepezil and memantine should be increased with increasing dose but may not work after several months of treatment and should be discontinued. Of course, they have conduction effects and abnormalities and may not affect them. These drugs are the best drugs available to stop and treat AD. But they have a relatively moderate effect and do not change the course of the underlying nerve damage (37). The differences between the results of the present study and these findings are: subject, exercise, medication, disease progression, and type of drug combination. The critical point of this study was to investigate the simultaneous effects of exercise and supplementation and the use of animal samples. These effects have been shown to reduce nerve damage and improve brain function by activating blood flow, synergizing the impacts of iron absorption and exercise.

Conclusion

The present study showed that high-intensity interval training with folate Nano-liposomes modulates the D1 and D2 gene expression in rats. We suggest that further research is needed to confirm the results.

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]
[DOI: 10.52547/jorjanibiomedj.10.2.36]

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]

Conflict of Interests

There is no conflict of interest between the authors

Ethical Approval

The code of ethics has been obtained by the Faculty of Medicine of the Islamic Azad University, Varamin Branch, with the number: IR.IAU.VARAMIN. REC.1399.041.

Funding/Support

This article is an excerpt from a student dissertation, and the authors have borne all costs.

References

1. Guszkowska M. Effects of exercise on anxiety, depression and mood. Psychiatry Pol. 2004; 38:611-620. [Google Scholar]

2. Chaddock L,Pontifex MB, Hillman CH, Kramer AF.A review of the relation of aerobic fitness and physical activity to brain structure and function in children.J Int Neuropsychol Soc.2011; 17:975-985. [view at publisher] [DOI] [PMID] [Google Scholar]

3. Shigenori Ito. High-intensity interval training for health benefits and care of cardiac diseases - The key to an efficient exercise protocol.Published online 2019 ;26. [DOI] [PMID] [PMCID] [Google Scholar]

4. Ngowi EE, Wang Y-Z, Qian L, Helmy YASH, Anyomi B,Li T, et al. The Application of Nanotechnology for the Diagnosis and Treatment of Brain Diseases and Disorders. Front. Bioeng. Biotechnol.2021. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

5. Siddappaji KK, Gopal S. Molecular mechanisms in Alzheimer's disease and the impact of physical exercise with advancements in therapeutic approaches. AIMS Neurosci.2021;8(3): 357-389. [DOI] [PMID] [PMCID] [Google Scholar]

6. Ayano G. Dopamine: Receptors, Functions, Synthesis, Pathways, Locations and Mental Disorders: Review of Literatures. J Ment Disord Treat 2016; 2:120. [DOI] [Google Scholar]

7. Baranowski BJ, Marko DM, Fenech RK, Yang AJ, MacPherson RE. Healthy brain, healthy life: a review of diet and exercise interventions to promote brain health and reduce Alzheimer's disease risk. Applied Physiology, Nutrition and Metabolism. 2020;45(10):1055-65. [view at publisher] [DOI] [PMID] [Google Scholar]

8. Soluki M, Mahmoudi F, Abdolmaleki A, Asadi A. The Protective Effects of Nanoparticles in the Treatment of Nervous System Injuries: A Narrative Review. J Rafsanjan Univ Med Sci.2021; 20(9):1027-48. [view at publisher] [DOI] [Google Scholar]

9. Laura M , Meng VY, Xhima K, Lipsman N, Hamani C, Aubert I. The Neuroprotective Effects of Exercise: Maintaining a Healthy Brain throughout Aging. Brain Plast. 2018;4(1):17-52. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

10. Bherer L, Erickson KI, Liu-Ambrose T. A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. 2013;657508.doi: 10.1155/ 2013/ 657 508. Epub 2013 Sep 11. [view at publisher] [Google Scholar]

11. Kabir MT, Uddin MS, Mamun AA, Jeandet P, Aleya L, Mansouri RA, et al. Combination drug therapy for the management of Alzheimer's disease. Int. J. Mol. Sci.2020;21:3272. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

12. Mirmiran P, Bahadoran Z, Golzarand M, Rajab A, Azizi F. Ardeh (Sesamum indicum) could improve serum triglycerides and atherogenic lipid parameters in type 2 diabetic patients: A randomized clinical trial. Arch Iran Med. 2013;16(11):652 - 656. [Google Scholar]

13. Gong C-X, Dai C-L, Liu F and Iqbal K. Multi-Targets: An Unconventional Drug Development Strategy for Alzheimer's Disease. Front. Aging Neurosci.2022;14:837649. [DOI] [PMID] [PMCID] [Google Scholar]

14. Saffari M, Lotfi Z, Arasteh A. Investigation of anti-amyloid genic and antioxidant properties of biosynthesized silver nanoparticles using leaf

extract to lemon. First National Conference on Medicinal Plants, Entrepreneurship and Commercialization. 1400. https:// civilica. com/ doc/13 53801 [Google Scholar]

15. Kwon O,Woo Y,Lee J,Kim K. Effects of task-oriented treadmill-walking training on walking ability of stokes patients. Top Stroke Rehabil. 2015 Dec; 22(6):444-52. 16. [DOI] [PMID] [Google Scholar]

16. Assadpour S,Shiran MR,Akhtari J. Nose-to Brain Direct Delivery of Nanodrug Formulations in Treatment of Neurological Disorders: A Review Study. Journal of Mazandaran University of Medical Sciences Thirty-first period .1400;195:173 -156. [view at publisher] [Google Scholar]

17. Cho DK, Choi DH, Cho JY. Effect of treadmill exercise on skeletal muscle autophagy in rats with obesity induced by a high-fat diet. J Exerc Nutrition Biochem. 2017;21(3):026-034. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

18. Gonçalves NB, Bannitz RF, Silva BR, Becari DD, Poloni CG, Patrícia MF, et al. α-Linolenic acid prevents hepatic steatosis and improves glucose tolerance in mice fed a high-fat diet. Clinics (Sao Paulo).2018;73,e150. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

19. Rosa-Caldwell ME,Lee DE, Brown JL, Brown LA, Perry RA, Greene ES, and et al. Moderate physical activity promotes basal hepatic autophagy in diet-induced obese mice. Appl. Physiol. Nutr. Metab. 2017;42:148-156. [view at publisher] [DOI] [PMID] [Google Scholar]

20. Yang J, Sáinz N ,Soriano EF, Gil-Iturbe E, Castilla-Madrigal R, Fernández-Galilea M, et al. Effects of Long-Term DHA Supplementation and Physical Exercise on Non-Alcoholic Fatty Liver Development in Obese Aged Female Mice.Nutrients.2021;13:501.19. [DOI] [PMID] [PMCID] [Google Scholar]

21. Dalibalta S,Majdalawieh AF,Manjikian H. Health benefits of sesame on cardiovascular disease and its associated risk factors. Saudi Pharmaceutical Journal.2020;28(10):1276-1289. [DOI] [PMID] [PMCID] [Google Scholar]

22. Melling CW, Thorp DB, Milne KJ, Krause MP, Noble EG. Exercise mediated regulation of Hsp70 expression following aerobic exercise training. Am J Physiol Heart Circ Physiol.2007; 293:3692-3698. [view at publisher] [DOI] [PMID] [Google Scholar]

23. Srivastava1 K, Narang R, Bhatia J, Saluja D. Expression of Heat Shock Protein 70 Gene and Its Correlation with Inflammatory Markers in Essential Hypertension. PLoS ONE.2016;11(3): e0151060. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

24. Kim WS,Ghassemi Nejad J,RohSG, Lee HG. Heat-Shock Proteins Gene Expression in Peripheral Blood Mononuclear Cells as an Indicator of Heat Stress in Beef Calves. Animals. 2020;10:895. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

25. Krüger K, Reichel T, Zeilinger C. Role of heat shock proteins 70/90 in exercise physiology and exercise immunology and their diagnostic potential in sports. J Appl Physiol.2019;126:916-927. [view at publisher] [DOI] [PMID] [Google Scholar]

26. Zeidabadi R, Ameri A, Naghdi E, Blurry B, Effect of long and short-term and very low intensity physical activity on learning and spatial memory of rat mice. Motion behavior.2014; (15):172-55. [Google Scholar]

27. Burger C. Region-specific genetic alterations in the aging hippocampus: implications for cognitive aging. Frontiers in aging neuroscience.2010;2.140. [DOI] [PMID] [PMCID] [Google Scholar]

28. Farioli-Vecchioli S, Tirone F. Control of the cell cycle in adult neurogenesis and its relation with physical exercise. Brain Plasticity.2015;1(1):41-54. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

29. Toval A, Garrigos D, Kutsenko Y, Popović M, Do-Couto BR, Morales-Delgado N, et al. Dopaminergic Modulation of Forced Running

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]

Performance in Adolescent Rats: Role of Striatal D1 and Extra-striatal D2 Dopamine Receptors. Mol Neurobiol.2021;58(4):1782-1791. [DOI] [PMID] [PMCID] [Google Scholar]

30. Russo-Neustadt A, Beard RC, Cotman CW. Exercise, antidepressant medications, and enhanced brain derived neurotrophic factor expression. Neuropsycho pharmacology.1999;21 (5):679-82. [DOI] [Google Scholar]

31. Matta R, Tiessen AN, Choleris E. The Role of Dorsal Hippocampal Dopamine D1-Type Receptors in Social Learning, Social Interactions, and Food Intake in Male and Female Mice. Neuro psychopharmacology. 2017 Nov; 42(12): 2344-2353. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

32. Marques A, Marconcin P, Werneck AO,Ferrari G, Gouveia ÉR,Kliegel M,et al. Bidirectional association between physical activity and dopamine across adulthood A systematic review. Brain Sci.2021;11:829. [DOI] [Google Scholar]

33. Piri M, Zarrindast MR. Nitric oxide in the ventral tegmental area is involved in retrieval of inhibitory avoidance memory by nicotine. Neuroscience.2011;175:154-61. [DOI] [PMID] [Google Scholar]

34. Sahab Negah S, Khaksar Z, Kazemi H, Aligholi H, Safahani M, Modarres Mousavi M et al. The role of dopamine receptors during brain development. Shefaye Khatam.2014;2(3):65-76. [DOI]

35. Petzinger GM, Holschneider DP, Fishera BE, McEwena S, Hallidaya KM. The Effects of Exercise on Dopamine Neurotransmission in Parkinson's disease: Targeting Neuroplasti- city to Modulate Basal Ganglia Circuitry. Brain Plasticity.2015;1:29-39. [DOI] [PMID] [PMCID] [Google Scholar]

36. Cordeiro LMS, Rabelo PCR, Moraes MM,Teixeira-Coelho F,Coimbra CC,Wanner SP. Physical exercise induced fatigue: the role of serotonergic and dopaminergic systems. Brazilian. J.Med.Biol.Res.2017;50(12):e6432. [DOI] [PMID] [PMCID] [Google Scholar]

37. Briggs R, Kennelly SP, O'Neill D. Drug treatments in Alzheimer's disease. Clin Med (Lond). 2016;16(3):247-253. [DOI] [PMID] [PMCID] [Google Scholar]

How to cite:

Nameni F, Firoozmand F. The Effect of Exercise and Folate Nano-Liposomes on D1 and D2 Receptor Gene Expression in the Brain of Alzheimer's Rats. *Jorjani Biomedicine Journal*. 2022; 10(2):36-44.

[Downloaded from goums.ac.ir on 2023-12-11]

[DOR: 20.1001.1.26453509.2022.10.2.3.3]

[DOI: 10.52547/jorjanibiomedj.10.2.36]