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Research Article

The Effect of Panouol Herbal Supplement Consumption on RBM24 Gene Expression in a Mouse Model of Parkinson's Disease Following Aquatic Exercise

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Abstract

Introduction: RBM24 is an RNA-binding protein involved in neuronal differentiation, RNA stability, and adult neurogenesis. Dysregulation of RBM24 has been associated with impaired neural regeneration and enhanced neurodegenerative processes, which are key pathological features of Parkinson's disease. Considering the neuroprotective effects of exercise and herbal antioxidants, this study aimed to investigate the combined effects of aquatic exercise and Panoeol herbal supplementation on RBM24 gene expression in a mouse model of Parkinson's disease.

Methods: For this research and case study, we chose two autistic children, from a rehabilitation center in Tehran. This selection was made through the A-B-A method, considering their HFA and IQ scores (60-90). The participants were a 12-year-old boy with an IQ score of 67 and an 11-year-old girl with an IQ score of 60. Following their parents' approval, they agreed to take part in the study. Subsequently, they completed a pre-test before beginning the rehabilitation exercises, which were designed to last for 12 weeks, totaling 36 sessions of 60 minutes each. To enhance the precision and success of the targeted exercise program, we employed a single-subject research approach. The assessments were conducted prior to the start of the intervention, followed by the completion of the targeted exercises over 12 weeks (36 sessions) of 60 minutes each, divided into two 30-minute segments with a 10-15 minute break in between. To enhance the precision and efficiency of the targeted training program, a single-subject research approach was employed. Following 18 training sessions and throughout the follow-up period, the participants underwent assessments, and a comprehensive evaluation was conducted at the conclusion and post-training. The (EMS) emotional Development questionnaire were utilized to measure the impact of the targeted training program on the improvement of emosional abilities.

Findings: Parkinson's induction significantly decreased RBM24 gene expression compared to the healthy control group. Both aquatic exercise and Panoeol supplementation independently increased RBM24 expression; however, the greatest increase was observed in the combined intervention group ($p < 0.05$).

Conclusion: The combination of aquatic exercise and Panoeol supplementation effectively increases RBM24 gene expression in a Parkinson's disease mouse model. These findings suggest that RBM24 may play a key mechanistic role in the neuroprotective effects of exercise and herbal supplementation and could serve as a potential therapeutic target for slowing neurodegeneration in Parkinson's disease.

Keywords:
Aquatic Exercise, Panouol Herbal, RBM24 Gene, Parkinson's Disease

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1. Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative disorders in adults, characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta and the onset of motor symptoms such as tremor, muscle rigidity, bradykinesia, and postural instability(1). In addition to motor deficits, patients with PD exhibit widespread molecular and cellular alterations, including neuroinflammation, oxidative stress, disturbances in trophic signaling, changes in gene expression, and dysregulation of RNA post-transcriptional processing(2). These molecular alterations can accelerate disease progression and reduce the efficacy of conventional pharmacological treatments, highlighting the importance of identifying novel molecular targets for therapeutic interventions(3). Accumulating evidence indicates that regular physical exercise, particularly aquatic exercise or hydrotherapy, exerts multiple beneficial effects on brain function and neuronal health. Aquatic exercise not only improves physical performance and motor function but also enhances neuronal plasticity and survival by modulating inflammatory and oxidative stress responses and activating protective molecular pathways(4). Previous studies have shown that regular exercise can increase the expression of neurotrophic factors, reduce levels of pro-inflammatory cytokines, and improve cognitive performance in both animal models and humans(2). In parallel, supplementation with plant-derived compounds exhibiting antioxidant and anti-inflammatory properties, such as Panoeol, has emerged as a potential adjunctive strategy for mitigating neuronal damage and promoting neuronal function.

Such supplements may synergistically enhance the neuroprotective effects of physical exercise and modulate molecular pathways associated with neuronal survival and plasticity(5). The combined intervention of aquatic exercise and herbal supplementation may therefore produce additive or synergistic effects on neuronal protection and molecular regulation(6).

RBM24 (RNA-binding motif protein 24) is an RNA-binding protein involved in the regulation of post-transcriptional processes, including mRNA stability and splicing. While previous studies have predominantly focused on its role in muscle and cardiac tissues, its expression and function in the brain, particularly in neurodegenerative conditions such as PD, remain largely unexplored(7). Given that RBM24 is less connected with well-characterized inflammatory and neuroplastic pathways, investigating its role provides an opportunity to uncover novel molecular mechanisms underlying neuronal responses to exercise and herbal supplementation(8). Therefore, the present study aims to investigate the role of RBM24 in the molecular response to aquatic exercise and Panoeol supplementation in a mouse model of Parkinson's disease. We hypothesize that these interventions may significantly alter RBM24 expression in key brain regions, including the substantia nigra and striatum, potentially contributing to neuroprotective mechanisms and modulation of cellular responses. This study may provide new insights into the impact of combined physical and dietary interventions on understudied RNA-binding proteins and their potential as targets for neuroprotection in PD.

2. Materials and Methods

In this experimental study, 30 male C57BL/6 mice, aged 8–10 weeks and weighing between 20 and 25 grams, were obtained from the Laboratory Animal Breeding and Propagation Center at Isfahan Royan Center. Following transfer to a specialized laboratory, the animals were allowed a one-week acclimation period to adapt to the new environment. Throughout the entire study, the mice were maintained under standard laboratory conditions, including a 12-hour light–dark cycle, ambient temperature of 20–22°C, relative humidity of 55%, and free access to food and water. All experimental procedures were conducted in accordance with ethical guidelines for the use of laboratory animals and the principles of the Helsinki Declaration, and the study protocol was approved by the Ethics Committee of Islamic Azad University, Isfahan (Khorasgan).

Induction of Parkinson's disease

To induce a Parkinson's disease model, male C57BL/6 mice were administered MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), a neurotoxin widely used to induce dopaminergic neuron degeneration. MPTP was injected intraperitoneally at a dose of 30 mg/kg per day for five consecutive days(9).

Grouping and research design

A total of 30 mice were randomly divided into five groups: Parkinson's, aquatic exercise + Parkinson's, Panoeol supplementation + Parkinson's, aquatic exercise + Panoeol supplementation + Parkinson's. It is worth noting that, to evaluate the effect of Parkinson's induction, 5 healthy mice were included in the healthy control group.

Aquatic Exercise Protocol

The aquatic exercise protocol consisted of 8weeks of swimming in a circular rodent pool with a diameter of 1 meter, water depth of 50 cm, and temperature maintained at 25 ± 2°C. Each session lasted 50 minutes at moderate intensity, with three sessions per week. Prior to each session, the animals were allowed 1 minute of acclimation in the water to familiarize themselves with the environment and perform a warm-up. During the main exercise, mice were released from a fixed section of the pool and, while swimming, navigated to a hidden platform acting as a safety refuge. The platform was 10 cm in diameter, made of transparent plexiglass, and positioned 1 cm below the water surface. As soon as a mouse reached the platform, its position was changed to ensure continuous swimming and active exercise throughout the session. This protocol ensured that mice performed moderate-intensity aerobic exercise while minimizing stress and allowing for consistent engagement during each session.

Panoeol Supplementation Protocol

Panoeol was administered to the mice via drinking water at a dose of 1 gram per mouse every **12** hours (twice daily) for 56 days (8 weeks). The supplement consisted of a mixture of three probiotic bacterial strains: *Lactobacillus acidophilus* (ATCC 4356), *Lactobacillus fermentum* (ATCC 9338), and *Bifidobacterium lactis* (DSM 10140), combined in equal proportions. Each strain was added at approximately 10^10 colony-forming units (CFU) per 334 mg of water solution.The probiotic strains were prepared in a water-soluble formulation and purchased from Zist-Takhmir Company (Tehran, Iran).

This protocol ensured consistent intake of the probiotic mixture along with drinking water throughout the intervention period(10).

Molecular Analysis of brain Tissue by Real Time PCR

The Real Time PCR method was used to determine the expression level of the RBM24 gene. In this procedure, 50 mg of brain tissue was first isolated, and RNA extraction was carried out for all experimental groups according to the manufacturer's protocol (Qiagen, Germany).To evaluate RNA quality, the samples were first electrophoresed on an agarose gel and then assessed for purity by measuring optical absorption at a wavelength of 260 nm using a Sigma PicoDrop device (USA).

Statistical analysis

To analyze the data in this study, the Shapiro–Wilk test was first applied to assess the normality of the data distribution. After confirming that the findings followed a normal distribution, a one-way analysis of variance (One-way ANOVA) was employed to compare the groups.

3. Results

The results of one-way analysis of variance indicated that RBM24 gene expression in the brain tissue of Parkinsonian mice differed significantly among the various groups (P=0.001). Tukey's post hoc test showed that RBM24 expression in the Parkinson's group was significantly decreased compared to the control group (P=0.05). Moreover, the aquatic exercise group (P=0.001), Panouel supplement group (P=0.001), and the combined aquatic exercise plus Panouel supplement group (P=0.001) showed a significant increase in RBM24 expression compared to the Parkinson's group, with the combined exercise and supplement group exhibiting the greatest increase among all groups.

Table 1. RBM24 Gene Expression Levels in Brain Tissue Assessed by One-Way Analysis of Variance

	Sum of squares		df	average of squares	F	P
between groups	.299		4	.072	92.794	.0001
within the group	.019		25	.001		
Total	.309		29			

3. Discussion

The results of this study showed that Panouel supplement consumption and aquatic exercise led to a significant increase in RBM24 gene expression in the Parkinson's group, and this increase was greatest in the combined aquatic exercise and Panouel supplement group. Parkinson's disease has a wide range of complications, the most important of which are neuromuscular impairments and cognitive/motor dysfunction. Studies have shown that certain positive lifestyle changes, such as a healthy diet and exercise, can improve neurological disorders and complications of Parkinson's disease through various mechanisms (2, 11). The aim of this study was to investigate the effect of eight weeks of aquatic exercise combined with Panouel supplement consumption on RBM24 gene expression in the brain tissue of Parkinsonian mice. According to the results obtained, Parkinson's induction caused brain dysfunction and a decrease in RBM24 gene expression.(8). After eight weeks of aquatic exercise and Panouel supplement consumption, RBM24 gene expression increased in the Parkinson's group compared to the control group. The reduction of RBM24 expression in the Parkinson's group may be attributed to neuronal dysfunction and damage to nerve cells in Parkinson's disease. The possible mechanisms underlying the effect of aquatic exercise and Panouel supplementation on increasing RBM24 expression include improved neuronal metabolic function, enhanced neurotrophic support, increased neural plasticity, and reduced oxidative stress(12, 13). These results indicate that the combination of aquatic exercise and Panouel supplementation has a synergistic effect and produced the greatest increase in RBM24 expression compared to the other groups(8, 14). RBM24 is an important protein involved in neuronal function and the regulation of neural gene expression, playing a crucial role in maintaining neuronal stability and protecting neurons from damage(15).

In this study, RBM24 expression was found to be reduced in the Parkinson's group, while aquatic exercise combined with Panouel supplementation led to an increase in its expression in Parkinsonian mice.(16, 17). Wang and colleagues demonstrated that RBM24 is a tissue-specific splicing factor that plays a critical role in the differentiation and regeneration of adult muscle cells. Deletion of RBM24 in mice leads to impaired muscle regeneration and delayed repair. This gene regulates a network of alternative splicing events involved in myogenesis, muscle regeneration, and hypertrophy. The study results indicate that RBM24 is essential for adult tissue regeneration and may serve as an important target for improving cellular repair under injury or disease conditions.(8, 18) Overall, recent studies indicate that RBM24 plays a key role in neural stem cells and adult neurogenesis, particularly in the subventricular zone, and its reduction or deletion is associated with impaired neurogenesis and the emergence of Parkinson's-like phenotypes(15). Evidence also suggests that RBM24 can modulate regulatory pathways related to cell survival or death in various tissues and is involved in the regulation of apoptosis, although this role is tissue-dependent and, in some cancers, has even been associated with increased apoptosis. On the other hand, long-term aerobic exercises, such as swimming, in neurodegenerative models (including mouse models of brain diseases) have been shown to enhance antioxidant capacity, reduce ROS levels and oxidative stress markers, and improve cognitive and motor functions.(19, 20). These effects are generally associated with activation of antioxidant pathways (such as Nrf2/Keap1/GPX4) and reduced cell death. Based on this evidence, references can be used in your discussion regarding the role of RBM24 in neurogenesis and Parkinson's disease, its role in apoptosis regulation, and the antioxidant and neuroprotective effects of exercise (particularly swimming) on the brain and Parkinsonian models(8, 21).

The combination of aquatic exercise and Panouel supplementation has a synergistic effect: aquatic exercise provides a protective environment and activates neurotrophic pathways, while Panouel supplementation adds antioxidant effects and enhances gene regulatory pathways(1). This combination leads to a significant increase in RBM24 expression in the brains of Parkinsonian mice, thereby contributing to improved neurogenesis and neuronal regenerationThe combination of aquatic exercise and Panouel supplementation has a synergistic effect: aquatic exercise provides a protective environment and activates neurotrophic pathways, while Panouel supplementation adds antioxidant effects and enhances gene regulatory pathways(22). This combination leads to a significant increase in RBM24 expression in the brains of Parkinsonian mice, thereby contributing to improved neurogenesis and neuronal regeneration(23-26).

4. Conclusion

The results of the present study showed that aquatic exercise and Panouel supplementation increased RBM24 gene expression in the brains of Parkinsonian mice, indicating an improvement in neuronal regeneration and central nervous system function. Furthermore, the combined administration of aquatic exercise and Panouel supplementation had the greatest effect on increasing RBM24 expression and reducing neuronal damage. Overall, periodic aquatic exercise together with Panouel supplementation, through its antioxidant and neuroprotective effects, contributes to enhanced neurogenesis and neuronal regeneration in the Parkinsonian model.

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Compliance with ethical standards

Conflict of interest None declared.

Ethical approval the research was conducted with regard to the ethical principles

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: Z AM, Kh.J,SH.R, F.T; Methodology: Z AM, Kh.J,SH.R, F.T; Software: Kh.J, M. Z AM, F.T; Validation: Z AM, Kh.J,SH.R, F.T; Formal analysis: A Z AM, Kh.J,SH.R, F.T; Investigation: Z AM, Kh.J,SH.R, F.T; Resources: Kh.J, Z AM; Data curation: Z AM, Kh.J,SH.R, F.T; Writing - original draft: Z AM, Kh.J,SH.R, F.T; Writing - review & editing: Z AM, Kh.J,SH.R, F.T; Visualization: Z AM, Kh.J,SH.R, F.T ; Supervision: Z AM, Kh.J,SH.R, F.T; Project administration: Z AM, Kh.J,SH.R, F.T; Funding acquisition: : Z AM.

References

1. Aarabi, M. A., Abdi, K., Khanjani, M. Saeid Using of Rehabilitation Services, The Main Concern of Autism Spectrum Disorder: What Can Be Done?. *Journal of Rehabilitation Sciences & Research*, 2020; 7(4): 189-190. doi: 10.30476/jrsr.2020.89004.1121

2. Homayounnia Firouzjah M, Majidi Yaeichi N, Hematinia R. The Effectiveness of Sensory-Motor Integration Exercises on Social Skills and Motor Performance in Children with Autism. J Autism Dev Disord. 2025 May;55(5):1902-1909. doi: 10.1007/s10803-024-06325-2. Epub 2024 Apr 3. PMID: 38565778.

4. Asgharzadeh N. The effect of eight weeks of ball games on the communication skills of children with autism. Master's thesis in physical education of Azad University of research Sciences; 2018.

5. Association Ap. Diagnostic statistical manual of disorders (DSM-50): American Psychiatric pub; 2014.

6. Boon-Yasidhi V, Jearnarongrit P, Tulayapichitchock P, Tarugsa J. Adverse effects of risperidone in children with autism spectrum disorders in a naturalistic clinical setting at siriraj hospital, Thailand. Psychiatry J. 2014;2014:136158. doi: 10.1155/2014/136158. Epub 2014 Feb 3. PMID: 24790986; PMCID: PMC3979146.

6. Darvishi S, Abolmaali K, Rafiepoor A, Dortaj F. (2023). The efficacy of social emotional skill training on improving theory of mind in children with autism. *Journal of Psychological Science*. *22*(126), 1069-1082. doi:10.52547/JPS.22.126.1069.URL: http://psychologicalscience.ir/article-1-1798-en.html.

7. Grigory Payne, V. Larry D. Khalji, H. khagawi, D. translators. Human motor development, a Life Long approach. Arak university publications, 2006.

8. Hambrick M.E. Sport communication research: A social network analysis. Sport management review.2017, 20: 170-183.

8. Hosseinzadeh K, Gamari S, Askari A, Abdizadad K. The effect of games in teaching social skills of autistic children. www.irijournals.com.2022,322-332.

9. Hosseinzadeh K, Gamari S, Askari A, Abdizadad K. The effect of games in teaching social skills of autistic children. www.irijournals.com.2022,322-332.

9. Khosrotash, P., Abolmaali Alhosseini, K., & Hashemian, K. (2019). Studying The effectiveness of integrative instruction in the executive function, and the collaborative for academic, social and emotional learning on the general mathematical performance: A case study of female students with mathematical learning disability. Psychology of exceptional Individuals, 13(1), 107-132. http://ijpb.ir/article-1-264-fa.html.

10. Khosrotash, P., Abolmaali Alhosseini, K., & Hashemian, K. (2019). Studying The effectiveness of integrative instruction in the executive function, and the collaborative for academic, social and emotional learning on the general mathematical performance: A case study of female students with mathematical learning disability. Psychology of exceptional Individuals, 13(1), 107-132. http://ijpb.ir/article-1-264-fa.html.

11. Li, HJ., Chen, CY., Tsai, CH. *et al.* Utilization and medical costs of outpatient rehabilitation among children with autism spectrum conditions in Taiwan. *BMC Health Serv Res* **19**, 354 (2019). https://doi.org/10.1186/s12913-019-4193-z.

12. Liao, Y., Dillenburger, K, He, W, Xay & Cai, H. A systematic review of applied behavior analytic interventions for children with autism. in main Land china. Review Journal of Autism and Developmental Disorders. 2020. 7(4), 333-351.

13. Miller A, Vernon T, Wu V, Russo K. Social skill group interventions for adolescents with autism spectrum disorders: A systematic review. J Autism Dev Disorder, 2014; 1(4): 254-65.

14. Noferesti A. Hassan abadi H. Data analysis in single case experimental design studies. Journal roish psychology.2019, 7, 12-33, March 13.

15. Pashazadeh Azari Z, Hosseini SA, Rassafiani M, Samadi SA, Hoseinzadeh S, Dunn W. Contextual Intervention Adapted for Autism Spectrum Disorder: An RCT of a Parenting Program with Parents of Children Diagnosed with Autism Spectrum Disorder (ASD). Iran J Child Neurol. 2019 Fall;13(4):19-35. PMID: 31645864; PMCID: PMC6789080.

16. Rooh Parvar (2015). Presenting an applied program for the emotional-social development of preschool children. The first national conference on modern studies and research in the field of educational sciences and psychology in Iran.

17. Sarabi R, Hashemi Razini H, Abdallahi M. Comparing parental stress, Parenting styles, and social problem solving in mothers of Children with autism Spectrum disorder and typically developing Children quartely journal of children mental helth, 2019. 4(4), 165-79.

18. Soleimani S. et al . The effect of rhythmic games on the social skills of preschoal children with attention deficit / hyperactivity disorder. Scientific journal of Gorgan university of medical sciences. 2016,Volume 18. 12. 45.

19. Stevenson, B. S, & Correa V.I. Applie Behavior Analysis, Students with Autism, and the Requirement to provide a free Appropriate public Education. Journal of Disability policy Studies. 2019, 29(4), 206-215.

20. Syriopoulou-Delli CK, Gkiolnta E. Review of assistive technology in the training of children with autism spectrum disorders. Int J Dev Disabil. 2020 Jan 20;68(2):73-85. doi: 10.1080/20473869.2019.1706333. PMID: 35309695; PMCID: PMC8928843.

21. Tabatabai S, Shabazi M, Bagherzade F. The relationship between motor development and Social development in children 6 to 20 years in Mashhad. Sports of Motor Development and Learning Journal; 2017. 2 (8).

22. Taziki T, Hasanzadeh S, Afrour Gh, Chobari Bonab B. Ghasem zadeh S. The effectiveness of intervention using pets and pets on the cognitive, social, and behavior of children in autism spectrum. Behavioral Sciences reasearch Journal. 2013.15: 125-143.

23. Tonge BJ, Bull K, Brereton A, Wilson R. A review of evidence-based early intervention for behavioural problems in children with autism spectrum disorder: the core components of effective programs, child-focused interventions and comprehensive treatment models. Curr Opin Psychiatry. 2014 Mar;27(2):158-65. doi: 10.1097/YCO.0000000000000043. PMID: 24452070.

24. Varogiz, T. Teaching and using signs of social communication for minors with autism spectrum disorders and similar problems. Translated Sajjadian M, Shahrivar. Z. Tehran. Arjmand. 2017.

25. Vakilizade N, Malekpour M, Faramarzi A. Investigating the effect of joint attention training on the degree of social initiation responding of children with autism spectrum disorder : single-subject research. The journal of paramedical science and rehabilitation. 2016, 6(3): 68-79.