# Comparison of the effects of perceptual-motor exercises, vitamin D supplementation and the combination of these interventions on decreasing stereotypical behavior in children with autism disorder

**Hadi Moradi[1], Mehdi Sohrabi[1], Hamidreza Taheri[1], Ezzat Khodashenas[2], and Ahmadreza Movahedi[3]**

[1]Department of Motor Behavior, Faculty of Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran
[2]Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[3]College of Sport Sciences, University of Isfahan, Isfahan, Iran

Objectives: The aim of this study was to examine the combined effects of perceptual-motor exercises and vitamin $D_3$ supplementation on the reduction of stereotypical behavior in children with autism spectrum disorder (ASD).
Methods: In this study, 100 eligible children with age ranging from 6 to 9 years were randomly selected and divided into four groups: Group A—perceptual-motor exercises ($n = 25$); Group B—25-hydroxycholecalciferol (25 (OH) D) ($n = 25$); Group C—perceptual-motor exercises and 25 (OH) D ($n = 25$); and Group D—control ($n = 25$).
Results: The stereotypes decreased from elementary level, 17% in Group A, 13% in Group B and 28% in Group C among the participants. There was no change in the stereotypical in the control group during the interventions. Also, the stereotypes in Group C showed the highest decrease, compared to the other three groups.
Conclusions: We concluded that combination of perceptual-motor exercises and vitamin $D_3$ supplementation in children with ASD leads to significant reduction in their stereotypic behaviors.

**Keywords:** Stereotypical, perceptual-motor exercises, vitamin $D_3$, autism spectrum disorder

## Introduction

Stereotypical behaviors are one of the main symptoms in individuals with autism disorder (American Psychiatric Association 2013). Patients with autism show a variety of stereotypical behaviors. It seems that stereotypical movements aim to provide sensory input and hence are considered self-stimulating (Schmitz *et al*. 2017). The stereotypical movements are known as very constant, repetitive, non-flexible, abnormal, strange, and uncanny behaviors, performed mainly without a specific purpose (Berkson and Davenport 1962, Rapp *et al*. 2004).

The stereotypical behavior in individuals with autism disorder causes significant disruptions in learning process (Schmitz *et al*. 2017), self-disturbing behaviors (Bodfish *et al.* 2000), behavioral problems (Gabriels *et al.* 2005), and delayed response to environmental stimuli (Lovaas *et al*. 1971). The movements often take almost the entire attention of the child, so that he/she is unable to follow and respond to other stimuli, and they are highly resistant to treatment (Bodfish *et al*. 2000). Therefore, stereotypical behaviors are a major problem for parents and doctors associated with these children, so paying attention to these behaviors and implementing appropriate methods to decrease these behaviors is of great importance.

Despite the deficits and its effects on individuals with autism, research has shown that the use of appropriate interventions can have a positive effect on these deficits. Various treatment methods have been reported

Correspondence to: Mehdi Sohrabi, Department of Motor Behavior, Faculty of Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran. Email: sohrabi@um.ac.ir


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by researchers to improve deficits in individuals with autism disorder, such as physical activities (Bahrami *et al.* 2016), nutrition (Amminger *et al*. 2007), social stories (Gray and Garand 1993), games, and verbal behavior training (Yoder 2006). Studies on physical activities have confirmed the effect of these interventions on improving the children's academic skills, perceptual function, social skills, self-harm behaviors, and aggression (Allison *et al*. 1991, Movahedi *et al*. 2013, Hilton *et al*. 2014, Pan *et al*. 2016). Research indicates that the motor skills of young children with autism spectrum disorder (ASD) are significantly delayed and of poor quality (Green *et al*. 2009). Low levels of physical activity can lead to an unhealthy body composition and increased morbidity (Janssen and LeBlanc 2010), thus potentially placing individuals with ASD at greater risk for negative health outcomes. It is possible that low levels of motor-skill proficiency may be one of the contributing factors, in conjunction with social factors, to the physical inactivity in children with ASD (Bremer and Lloyd 2016). Therefore, the improvement of motor skills may be crucial for children with ASD because it enables them to share physical activity with their peers and allows them to benefit from the benefits of physical activity (Bremer and Lloyd 2016). Children with autism have deficiencies in perceptual-motor processes (Jepsen and VonThaden 2002). So it is very important for children to have a rich and strong background of perceptual motor experiences as a base of the motor and nervous systems (Piek *et al.* 2006). The efficiency of exercise-based interventions on stereotypic behaviors in individuals with autism has rarely been studied. Investigators have not yet empirically studied the role played by perceptual-motor exercises on reduction of stereotypic behaviors in children with autism spectrum disorders, in the present study our main goal was to determine whether perceptual-motor exercises to children with autism disorder lead to reductions in their stereotypic behaviors.

Another factor that may play a role in children's development in the first years of life is the nutritional effects at early ages. Neural structures are sensitive to environmental and nutritional factors like vitamin D, which play an important role during this period (Harms *et al.* 2011). Vitamin D has been found to have a potential role in brain homeostasis and development, such as neuronal differentiation, neurotransmission, and synaptic function (Cannell 2017, Wang *et al*. 2016). Vitamin D deficiency is reported to be widespread worldwide (Palacios and Gonzalez 2014). Low levels of vitamin D induce negative changes on anxiety and social behavior (Pan *et al*. 2014), immune system (Hewison 2010), and degradation of cognitive function (Grung *et al*. 2017). Vitamin D deficiency is also involved in the incidence of autism disorder (Wang *et al*. 2016). Majority of studies have conclude that vitamin D level in children with ASD is significantly lower than that in healthy individuals (Du *et al*. 2015, Fernell *et al*. 2015, Saad *et al*. 2018). We can deduce that low vitamin D level is common and an ongoing condition in children with ASD, even evolving toward the adult period (Jia *et al*. 2018).

The brain of individuals with autism spectrum disorder has significantly lower concentrations of serotonin compared to those without autism (Chugani *et al*. 1999). The disruption of the serotonergic system is one of the most consistent observations associated with autism (Zafeiriou *et al.* 2009). Investigators have shown that serotonin plays a major role in autism (Kane *et al*. 2012, Yang *et al.* 2012, Boccuto *et al*. 2013b, Patrick and Ames 2014). Researchers have shown that the disturbances of brain key neurotransmitters including serotonin play a role in the maintenance of stereotypic behaviors (Schoenecker and Heller 2001). However, further reduction of brain serotonin in individuals with autism is exacerbated by the acute reduction of tryptophan and symptoms such as repetitive behaviors and face recognition patterns, which revealed the continued need for serotonin to modulate these behaviors (Daly *et al*. 2012). Though vitamin D supplementation might improve symptoms in children with autism spectrum disorder, yet, study in this area is limited (Saad *et al*. 2016a, 2016b). Therefore, previous studies suggest more studies to be carried out (Patrick and Ames 2014).

Despite evidence that shows delay in motor skills and inadequate levels of vitamin D as the main indicators for diagnosis of autism spectrum disorder, few researches have evaluated their impact as interventions on the deficits of children with autism disorder. To our knowledge, studies on stereotypical behaviors have been conducted more in case studies or small research projects (Jia *et al*. 2015). In addition, no study has examined various combinations of interventions on children with autism. Therefore, this study is one of the first studies to examine the combination of vitamin $D_3$ and perceptual-motor activities on reducing the stereotypical behavior of children with autism disorder. Given that children with autism suffer from a wide range of disorders, the cause of which has remained unknown to date, the researchers suggest using a combination of interventions to address the deficiencies in individuals with this disorder. Hence, the present study sought to examine two important interventions and combine these two interventions on children with autism. Finally, the main aim of this study was to compare the efficacy of perceptual-motor exercises and vitamin $D_3$ supplementation and the combination of these two interventions on reducing stereotypical behavior in children with autism disorder. The results of this study provided beneficial empirical evidence for perceptual-motor exercises and vitamin $D_3$ supplementation and combining these two interventions to improve stereotypical behavior in individuals with autism disorder.

## Methods

### *Participants*

Participants were students ranging in age from 6 to 9 years (M = 7.62 years, SD =1.15) from one of three specialized institutions for youth with ASD who were selected randomly to participate in the present study (see Table 1 for additional demographic information and baseline ASD-specific symptom severity). The children were living with their own families, and attended one of three institutions for students with autism. Each participant had been formerly diagnosed as having ASD using the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition, Text Revision (DSM-5) (American Psychiatric Association 2013). Participants were screened by an experienced physician and were found eligible to participate in the study. Participants were 100 children with ASD whom were selected from a sample of 250 children with autism. All participants were in a good nutritional state. In total, 139 children with ASD were excluded as they did not meet the inclusion criteria. A total of 11 participants were also excluded as their families declined to participate in the study.

The inclusion criteria for this study are an autism diagnosis confirmed by a psychologist along with a medical team and based on diagnostic criteria DSM-5, obtaining consent from parents, vitamin D serum level less than 30 ng/ml, chronological age between six and nine years, IQ more than 70, sound sense of sight and hearing, lack of orthopedic and respiratory disorders, and lack of seizure attacks in the last two years. Participants who had associated gastrointestinal problems, children with feeding problems or malnutrition, genetic disorders, autoimmune disorders, anemia, neurological diseases, and metabolic disorders, children with known endocrine, cardiovascular, pulmonary, and liver or kidney disease, history of severe head trauma or stroke, as well as any subjects receiving vitamin D-containing preparations and drugs that may affect vitamin D levels were excluded.

None of the participants had officially received physical activity and vitamin D interventions in the last six months. In addition, they were all following identical treatment strategies at the autism center. All subjects had a good nutritional status; children with feeding problems or malnutrition were excluded from the study. Then the participants were randomly assigned into four groups: Group A–perceptual-motor exercises ($n = 25$); Group B–vitamin $D_3$ supplementation ($n = 25$); Group C–perceptual-motor exercises and vitamin $D_3$ supplementation ($n = 25$); and Group D– p

\\lacebo ($n = 25$). Table 1 provides the characteristics of the participants, including their chronological age, gender, IQ, and the level of Vitamin D before the interventions. This study has been carried out in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. All procedures are approved by the Ethical Committee of Ferdowsi University of Mashhad, Iran. Informed consent had been obtained from parents of all participants prior to their inclusion.

### *Experimental interventions*

I. Group A: Perceptual-motor exercises

The motor activities for this study were taken from *Perceptual–motor activities for children* by Johnstone and Ramon (2011). In designing this protocol, attempts were made to use previous studies carried out in this field (Kurtz 2007). The activities, content, and goals of the intervention are listed in Table 2.

II. Group B: Vitamin $D_3$ supplementation

Group A consisted of 25 patients who were randomly allocated to receive vitamin $D_3$ drops, 300 IU/kg/day not to exceed 5000 IU/day (Saad *et al*. 2016a, 2016b) for 3 months.

**Table 1. Participants' characteristics (age, sex, autism severity, IQ, and 25 (OH) D levels) at the pre-intervention time.**

| | Group A *M* ± *SD* | Group B *M* ± *SD* | Group C *M* ± *SD* | Group D *M* ± *SD* | *p* Value |
|---|---|---|---|---|---|
| ASD | 25 | 25 | 25 | 25 | |
| Age (years) | 1.03 ± 7.64 | 0.97 ± 8.04 | 1.22 ± 7.60 | 1.25 ± 7.20 | 0.08 |
| Sex (male/female) | male | male | male | male | |
| Autism severity | 12.94 ± 53.20 | 14.96 ± 56.64 | 19.54 ± 55.68 | 19.58 ± 58.16 | 0.77 |
| IQ | 7.38 ± 91.92 | 6.96 ± 91.52 | 8.06 ± 92.84 | 6.45 ± 93.40 | 0.79 |
| 25 (OH) D levels (ng/ml) | 5.02 ± 11.88 | 4.61 ± 12.60 | 4.79 ± 13.04 | 4.87 ± 11.52 | 0.67 |

Abbreviations: Group A: perceptual-motor exercises; Group B: vitamin $D_3$ supplementation; Group C: perceptual-motor exercises and vitamin $D_3$ supplementation; Group D: Placebo; M: mean; SD: standard deviation

Autism severity: Sum of the GARS-2 (Gilliam Autism Rating Scale-Second Edition) three subscales (stereotypy, communication and social interaction) raw scores

ANOVA test were used to check if there are differences between the 4 groups. Significant differences between the 4 groups were illustrated as $p < 0.05$.

Significant: $p < 0.05$

**Table 2. Perceptual-motor exercises protocol.**

| Physical exercises | Length (min) | Contains | Target |
|---|---|---|---|
| Warm up | 10 | Jogging, stretching | Warm up and stretching |
| Perceptual-motor exercises | 45 | 1. Jumping: Such as jumping back and forth on the squares (30 x 30 cm), jumping succession, crosswise jumping (a jump to the right and a jump to the left), etc.<br>2. Hopping: Such as hopping back and forth, opping in succession, crosswise hopping (a hop to the right and a hop to the left), etc.<br>3. Static and dynamic balance: Such as standing with the dominant foot on a hard surface, walking on a balance beam with eyes opened, etc.<br>4. Hitting ball with feet: Such as walking alongside blue and red balls and hitting the red ones, etc.<br>5. Throwing ball to the target by hand: Such as throwing a ball into the basket from a distance of one meter or 1.5 meters, etc.<br>6. Throw and receive ball: Such as throwing a plastic ball to a wall at a distance of one meter and catching it by hand, etc. | Improvement of: Stability skills, Locomotor skills, Manipulative skills, dynamic balance, static balance, motor planning, motor coordination, eye–hand coordination, eye–foot coordination, gross motor coordination, body awareness, tracking skills, transference, arm-leg strength, body awareness, directionality, throwing accuracy, precision, spatial awareness, Kinesthetic awareness, tactile awareness, Unilateral movement |
| Cool down | 5 | Walking slowly, stretching | Cool down and recovery |

**Table 3. Vitamin D levels in ASD patients before and after vitamin $D_3$ supplementation.**

| | Group | Before vitamin D therapy (M ± SD) | After vitamin D therapy (M ± SD) | *p* Value (paired samples test) |
|---|---|---|---|---|
| | A | 5.02 ± 11.88 | 4.56 ± 12.04 | 0.61 |
| Vitamin D levels (ng/ml) | B | 4.61 ± 12.60 | 6.48 ± 24.36 | 0.01* |
| | C | 4.79 ± 13.04 | 5.76 ± 24.04 | 0.01* |
| | D | 4.87 ± 11.52 | 3.95 ± 11.08 | 0.28 |

Group A: perceptual-motor Exercises; Group B: vitamin $D_3$ supplementation; Group C: perceptual-motor exercises and vitamin $D_3$ supplementation; Group D: Placebo.
M: mean; SD: standard deviation
*: Significant at $p < 0.05$.

III. Group C: Perceptual-motor exercises and Vitamin $D_3$ supplementation

This involved performing a combination of Perceptual-motor Exercises and taking Vitamin $D_3$ for 3 months (Table 3).

IV. Group D: Placebo

Group D consisted of 25 patients who received a matching placebo drops with the same taste and color of vitamin $D_3$ drops for 3 months. The placebo consisted of a combination of polysorbate 20, which is the same fragrance ingredient used in vitamin D drops in addition to glycerin, disodium edetate, and b-cyclodextrin in purified water.

## Materials

a. Gilliam Autism Diagnostic Inventory-Second Edition (GARS-2)

We used the stereotypy behavior subscale of Gilliam Autism Rating Scale-2 (GARS-2) to evaluate changes in participants' stereotypy behavior intensity (Gilliam 2006). Gilliam Autism Rating Scale-Second Edition has been widely used in research studies and educational program (Worley and Matson 2011). The stereotypy subscale of GARS-2 contains 14 items that describe specific, measurable, and observable stereotyped behaviors. It incorporates observations, parent or teachers interviews, and questions completed by the examiner according to their interpretation. The items of the subscale ask caregivers how often a child: 1. Avoids establishing eye contact, looks away when eye contact is made; 2. Stares at hands, objects, or items in the environment for at least 5 seconds; 3. Rapidly flicks fingers or hands in front of eyes for periods of 5 seconds or more; 4. Eats specific foods and refuses to eat what most people will usually eat; 5. Licks, tastes or attempts to eat inedible objects; 6. Smells or sniffs objects; 7. Whirls, turns in circles; 8. Spins objects not designed for spinning; 9. Rocks back and forth while seated or standing; 10. Makes rapid lunging, darting movement when moving from place to place; 11. Walks on tiptoes; 12. Flaps hand or fingers in front of face or at sides; 13. Makes high-pitched sounds; and 14. Slaps, hits, or bites self or attempts to injure self in other ways. Parents and teachers are asked to rate the individual based on the frequency of occurrence of each stereotyped behavior under ordinary circumstances in a 6-h period. The current study concentrated on the total raw score in the stereotypy subscale of GARS-2. The

**Table 4. Vitamin D levels in ASD patients before and after vitamin $D_3$ supplementation.**

| Group | Pre-intervention | Intervention | Post-intervention (3 months) |
|---|---|---|---|
| A | Stereotypy was assessed | Participants were instructed Perceptual-motor Exercises for 36 sessions | Stereotypy was assessed |
| B | Stereotypy was assessed | Vitamin $D_3$ supplementation (300 IU/kg/ day not to exceed 5,000 IU/day) | Stereotypy was assessed |
| C | Stereotypy was assessed | Participants were instructed Perceptual-motor Exercises for 36 sessions + Vitamin $D_3$ supplementation (300 IU/kg/ day not to exceed 5,000 IU/day) | Stereotypy was assessed |
| D | Stereotypy was assessed | received placebos (matching placebo drops with the same taste and color of vitamin $D_3$) | Stereotypy was assessed |

Abbreviations: Group A: perceptual-motor exercises; Group B: Vitamin $D_3$ supplementation; Group C: perceptual-motor exercises and Vitamin $D_3$ supplementation; Group D: control

subscale is both reliable and valid and has high psychometric properties (Worley and Matson 2011).

B. Evaluation of the level of Vitamin D by the Elecsys method

Serum 25(OH) D is considered to be adequate if it is $\geq$30 ng/mL, inadequate if it is between $<$30 and $>$10 ng/mL, and deficient if it is $\leq$10 ng/Ml (Mostafa and Al-Ayadhi 2012). After sampling the blood from the participants, the Elecsys 2010 device made in the German Roche Company was used to evaluate the levels of Vitamin D. Investigators have found a debate about values of the normal levels of vitamin D; if the value should be equal to, or more than, 20 ng/ml, 30 ng/ml, or higher even still (Holick *et al*. 2011, Stubbs *et al*. 2016). Based on this technology and combined with well designed, specific and sensitive immunoassays, Elecsys delivers reliable results (Connell *et al*. 2011). Children whose Vitamin D serum levels were less than 30 ng/ml had the inclusion conditions to enter the study. Serum Vitamin D levels were measured before and 3 months after treatment (Table 4).

C. Raven IQ test

This test is comprised of abstract images which create a logical sequence and is administered separately (Raven *et al*. 1996). This test has a high level of validity (0.80) and can be administered to groups (Raven *et al.* 2008). This tool in the study was used to screen and homogenize the general intelligence level of children with autism.

## Procedure

Each child who qualified to participate in this study had been previously diagnosed with ASD by a clinician or school psychologist according to the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013). At the initial assessment, all parents completed a supplemental information form in order to provide demographic data and a brief developmental history of their child.

We administered stereotypical behavior subscale of GARS-2 before intervention (pre-intervention) and post-intervention (3 months) via interview with the participants' parents, care givers and teachers and by child direct observation. We organized a separate formal meeting where we asked the participants' parents, caregivers, and teachers to read over the statements grouped with each number in the subscale. Then we asked them to compromise and agree on the statement within each group that best describes the way they have been feeling about the child during the previous week.

In Group Perceptual-motor Exercises (Group A), to ensure quality in program implementation, the physical activity intervention was implemented as prescribed and supervised by the primary researcher for each session. The researcher received help from an instructor at the Center of Autism. This instructor had 10 years of experience with autistic children. If the instructor did not implement the instructional sequence of each component of the intervention as intended, the primary researcher intervened to assist the instructor. If any participant engaged in off-task behavior during the program, the instructor managed the behavior, and the primary researcher assisted the instructor when required. The sessions were carried out in a therapy room located at the Center of Autism. The course lasted for 3 months and the sessions were thrice a week. Each session was 60 minutes long. They included stretching and jogging (10 minutes), main perceptual-motor Exercises (45 minutes), and cool down (5 minutes) (Table 2).

Children with ASD in Group Vitamin $D_3$ supplementation (Group B), under the control of the researcher, consumed Vitamin $D_3$ tablets (300 IU/kg/day not to exceed 5000 IU/day (Saad *et al*. 2016a, 2016b) for 3 months). In Group C, both interventions of Groups A and B were conducted for 3 months (The protocol of Perceptual-motor Exercises was 36 sessions (3 months) at 12 weeks and three sessions per week, with each session lasting 60 minutes + receive vitamin $D_3$ drops, 300 IU/kg/day not to exceed 5000 IU/day for 3 months). Children with ASD in Group D also received a matching placebo drops with the same taste and color of vitamin $D_3$ drops for 3 months. The rate of changes in the severity of stereotypical behavior was evaluated using the stereotypical subscale of GARS-2 before and after the intervention (Table 3).

## *Statistics*

We used a Kolmogorov–Smirnov test to assess the normality of distribution of the data. To study the changes in stereotypy severity before and after the intervention, paired *t*-test was used. Then, an analysis of covariance (ANCOVA) test and a Bonferroni follow-up test were used to determine the differences between the four groups. For all statistical analyses, $p \leq 0.05$ was considered to indicate statistical significance. The data were also presented as mean (±) and standard deviation (SD).

## Results

Table 5 presents descriptive information about the groups at the pretest and post-test stages.

First, *t*-test was used to determine whether the groups have been affected by interventions over the course of time. The results showed significant differences in the severity of stereotypy severity in the experimental groups during interventions ($p = 0.01$) and stereotypy severity significantly improved after the intervention. However, in the control group, the difference was not statistically significant ($p = 0.51$) (Table 5).

Table 6 provides the results of the ANCOVA test, indicating a significant difference between the groups.

To carefully investigate the difference between the four groups in the variable stereotypy severity, the Bonferroni test was used. Here the estimations were as follows: The severity of stereotypy severity in the three experimental groups (group-A, B, and C) had a significant difference compared with the control group ($p = 0.01$). No significant difference was observed between perceptual-motor exercises groups and the group with vitamin $D_3$ supplements in the severity of stereotypy severity ($p = 1.00$). The severity of stereotypy severity in the perceptual-motor exercises group and the group with vitamin $D_3$ supplements was significantly different from the other three groups ($p = 0.01$). This represents a significant improvement in stereotypy severity in the combination group, compared to the other three groups (Table 6).

## Discussion

The aim of this study was to compare the effects of perceptual-motor exercises and vitamin $D_3$ supplementation and the combination of these interventions on the improvement of stereotypical behaviors in children with autism disorder. The findings showed a significant reduction in the stereotypical behavior of ASD children in the three experimental groups after the end of the interventions. The stereotypical behavior reduced from the elementary level 17% in the group of perceptual-motor exercises, 13% in the group of vitamin $D_3$ supplementation and 28% in the combined group of perceptual-motor exercises and vitamin D supplementation among participants. There was no significant change in the reduction of stereotypical behavior in children with autism disorder in the control group. The results also showed that stereotypical behaviors in the combined group (perceptual-motor exercises and vitamin $D_3$ supplementation) significantly improved compared to the other three groups.

The usefulness of physical interventions for improving the symptoms of children with autism disorder has been confirmed in several studies (Brand *et al.* 2015, Bremer and Lloyd 2016, Ketcheson *et al.* 2017). Regarding the use of physical activities in improving the stereotypical behavior, studies on these

**Table 5. Results of the stereotypy subscale of GARS-2 in response to intervention.**

| | Group | PRI (baseline) | POI (12 weeks) | Magnitude of change | Paired samples test |
|---|---|---|---|---|---|
| | A | 3.44 ± 15.84 | 2.69 ± 13.08 | 2.53 ± 2.76 | 0.01* |
| SSGARS-2 | B | 3.88 ± 17.08 | 2.80 ± 14.76 | 2.07 ± 2.32 | 0.01* |
| | C | 3.47 ± 17.40 | 2.82 ± 12.36 | 2.42 ± 5.04 | 0.01* |
| | D | 3.19 ± 16.28 | 4.01 ± 15.92 | 2.69 ± 0.36 | 0.51 |

Abbreviations: SSGARS-2, stereotypy subscale of Gilliam Autism Rating Scale-Second Edition; Higher scores indicate a higher level of stereotypy.
Group A: perceptual-motor exercises; Group B: Vitamin $D_3$ supplementation; Group C: perceptual-motor exercises and Vitamin $D_3$ supplementation; Group D: control
PRI: pre-intervention; POI: post-intervention.
Data are mean ± SD.
*: Significant at $p < 0.05$.

**Table 6. Summary of analysis of covariance.**

| | Source | Sum of squares | d.f | Mean square | *F* | Sig. | Effect size |
|---|---|---|---|---|---|---|---|
| SSGARS-2 | Pretests | 507.72 | 1 | 507.72 | 111.58 | 0.01* | 0.54 |
| | Group | 238.09 | 3 | 79.36 | 14.44 | 0.01* | 0.35 |
| | Error | 432.27 | 95 | 4.55 | | | |

Abbreviations: SSGARS-2: stereotypy subscale of Gilliam Autism Rating Scale-Second Edition.
*: Significant at $p < 0.05$.

interventions have shown that these interventions can play a significant role in reducing the stereotypical behavior in children with autism disorder (Bahrami *et al.* 2012, Schmitz *et al.* 2017). These findings show the importance of physical activities and the formulation of such programs in improving the deficits of children with autism disorder. From the results of these studies, it can be concluded that physical exercises not only improve the physical status but also decrease the incompatible patterns of autism behavior (Lancioni and O'Reilly 1998).

Considering the effect of perceptual-motor exercises on the improvement of stereotypical behavior in children with autism disorder, several mechanisms can be expressed. The first mechanism is related to the similarity of motor activities and stereotypical behaviors. According to some researchers, physical activities, as an effective tool, is effective in reducing strain behaviors by providing a similar sensory feedback, through a more appropriate way (Watters and Watters 1980). Stereotypic behaviors are often hypothesized to occur because the behavior itself produces pleasant internal consequences for the individual (Rapp *et al.* 2004). This interpretation justifies the emergence and maintenance of stereotypical movements in children with autism disorder. Based on this justification, stereotypical movements are maintained through sensory feedback produced after these movements and these movements may be replaced or destroyed by movements that create a similar feedback (Berkson 1983). Therefore, the more trained movements overlap with mold movements, the more the effect of these movements will be in reducing or eliminating mold movements (Watters and Watters 1980). In this regard, Lang *et al.* (2010) argued that, as a result of the similarity of physical activities by physical exercises with the stereotypical behaviors performed by patients with autism disorder, the targeted activities replace untargeted stereotypical activities in these individuals (Lang *et al.* 2010). Hence, perceptual-motor exercises and the involvement of children with autism disorder in activities such as throwing, receiving, coordination and balancing movements will reinforce their intrinsic needs, so that they no longer need to participate in performing stereotypical behavior for them.

The second mechanism can be viewed from a neurological point of view. Studies on patients with autism disorders have reported abnormal levels of neurotransmitters such as serotonin and dopamine in these individuals (Volkmar and Anderson 1989). Serotonin plays a major role in autism, as a neurotransmitter (Boccuto *et al.* 2013a, Yang *et al.* 2012). According to animal studies, a decrease in the level of serotonin results in excessive growth of the cerebral cortex and behavioral features which are similar to autism (Boylan *et al.* 2007, Hohmann *et al.* 2007). Such an evolutionary defect in individuals with autism suggests that inadequate serotonin concentration prevents normal growth of the brain in these individuals (Boylan *et al.* 2007, Rokade 2011) . Researchers have also shown that disturbances in neurotransmitters such as serotonin and dopamine play a role in the stereotypical behavior of children with autism disorder (Schoenecker and Heller 2001). There is a large amount of evidence that links stereotypy to the synthesis and metabolism of dopamine and serotonin. Hyperserotoninaemia has been shown to have negative correlations with declarative abilities and self-injuries behaviors in individuals with autism disorder (Lanovaz 2011). However, it has been shown that participation in physical activities can have a significant effect on dopaminergic and serotoninergic systems and thus, improve the synthesis of serotonin and dopamine (Meeusen and De Meirleir 1995) and improve deficits such as reduction of stereotypical behavior in children with autism.

Concerning vitamin D supplementation, the results showed that the application of vitamin D supplementation for 12 weeks significantly decreased stereotypical behavior in children with autism disorder. The consistent reduction of stereotypic behaviors of the participants of the vitamin D supplementation group in our study may also be explained from a neurochemical point of view. Vitamin D activates tryptophan hydroxylase 2 (TPH2) in the brain and suppresses the transcription of tryptophan hydroxylase 1 (TPH1) in the tissue outside the blood–brain barrier. In normal subjects, TPH2 was greater than TPH1, but the levels of TPH1 were higher than autism, which increases gastrointestinal inflammation, weakens the immune system, serotonin neurotransmission and abnormal social behavior in these individuals. Based on animal studies, lack of TPH2 in rats' brain serotonin synthesis presented behavioral symptoms such as autism, including disruptions in social behavior and communication and tendency to stereotypical behaviors (Huang and Santangelo 2008, Kane *et al.* 2012, Yang *et al.* 2012, Boccuto *et al.* 2013b, Patrick and Ames 2014). In patients with autism, as well, the further reduction of brain serotonin is exacerbated by the acute reduction of tryptophan, leading to symptoms such as repetitive behaviors and facial recognition patterns that reveal the continued need for serotonin to modulate these behaviors (McDougle *et al.* 1996, Daly *et al.* 2012). Researchers have shown that disturbances of brain key neurotransmitters including serotonin play a role in the maintenance of stereotypic behaviors (Schoenecker and Heller 2001). However, recent experimental studies have shown that vitamin D can regulate the synthesis and response to serotonin via TPH2, which can help improve deficits in children with autism disorder (Patrick and Ames 2014). In the present study, vitamin D supplementation may have also increased the levels of TPH2, which in turn results in more neurotransmission of serotonin in the brain and improves symptoms, such as stereotypical behavior in children with autism disorder. These data provide strong and convincing evidence for a causal role of tryptophan-derived serotonin in regulating many stereotypical behavior and support the proposal that supplemental interventions affecting the serotonin pathway may lead to improvements in a wide range of stereotypical behavior in ASD (Patrick and Ames 2014). For these reasons, dietary intervention with vitamin D would boost brain serotonin concentrations and help prevent and possibly ameliorate some of the symptoms associated with ASD without side effects.

Finally, the results of the study showed that a combination of perceptual-motor exercises and vitamin D supplementation in comparison to each of the groups alone, led to a further reduction in stereotypical behavior. In relation to the effects of the combination of perceptual-motor Exercises and the consumption of Vitamin D, several possible mechanisms could be mentioned. having adequate levels of Vitamin D may improve neuromuscular function and ultimately improve motor performance (Dhesi *et al*. 2004, Lanteri *et al.* 2013). Adequate levels of Vitamin D lead to the creation of better morphological compliance of the muscles through calcium absorption. This would lead to better muscular function and activity (Todd *et al.* 2015). In this way, it could help in the perceptual-motor Exercises of children with autism. Also, the use of vitamin D in combined group in the present study has led to better functioning of children in Motor activities to perform exercises better and this can be effective in improving the stereotypical behavior of children with autism disorder. By the interpretation of the superiority of the combined interventions, it can be stated that, on the one hand, the effects of vitamin D supplementation increased TPH2 and consequently increased neurotransmission of serotonin in the brain (Patrick and Ames 2014), as well as the role of vitamin D in neurotransmitter factors (Kalueff and Tuohimaa 2007). This vitamin D-mediated production of serotonin would be critical to produce serotonergic signals during neurodevelopment, thus shaping the developing brain, and throughout adulthood, where it plays a critical role in regulating a variety of brain functions including stereotypical behavior. In addition, adequate vitamin D hormone levels would suppress TPH1 expression, which has important implications for lowering inflammation and keeping autoimmunity at bay. Vitamin D could also regulate the synthesis and response to serotonin and oxytocin, as well as the response to vasopressin, which could help improve social functioning and stereotypical behavior in children with autism disorder, as well. For these reasons, dietary intervention with vitamin D would boost brain serotonin concentrations and help prevent and possibly ameliorate some of the symptoms associated with ASD without side effects.

On the other hand, Vitamin $D_3$ supplementation also increased the effects of motor activities on neurotrophic (Kalueff and Tuohimaa 2007) factors and increased the learning of different skills (Pilc 2010, Griffin *et al.* 2011) such as motor coordination, balance and throwing skills, as well as the replacement of motor activities with stereotypical behaviors to relieve intrinsic feelings in children with autism disorder, and improve stereotypical behaviors in children with autism disorder.

Although this study provides valuable information about the effects of motor activity and vitamin D on stereotypic behaviors of children with autism, some of the limitations of this study should be considered. Although we did not take any neurochemical and physiological data in the present investigation, we speculate that the perceptual-motor exercises and vitamin $D_3$ supplementation may improve the synthesis and metabolism of brain key neurotransmitters and consequently may consistently decrease the stereotypic behaviors in children with ASD. However, for more precise conclusion in this context, it's better to investigate neuropsychological and physiological factors using accurate tools in future. We used fixed vitamin $D_3$ dosing, but it may be more appropriate to titrate vitamin D dosing based on baseline 25(OH) D levels and/or body size. Although we analyzed results based on age (ranging from 6 to 9 years), vitamin $D_3$ treatment effects have been reported to be more pronounced in younger children with ASD (Feng *et al*. 2017) leading to the suggestion that vitamin $D_3$ supplementation should start in early infancy or during gestation (Stubbs *et al.* 2016). In this context, it is possible that there is a window of opportunity for adequate vitamin $D_3$ to provide neuroprotection and that we included older children in whom neuronal networks are established and therefore less likely to benefit from supplementation. In this study, groups B and D were blinded, but regarding to the type of perceptual-motor activities intervention, blinding in groups A and C was not possible. Finally, it is possible that a higher dose of vitamin D would produce a greater change in children with ASD stereotypical behavior.

## Conclusion

ASD is a severe, lifelong disorder with serious social and financial consequences. Insufficient vitamin D due to genetic and environmental factors is common in children with autism spectrum disorder and may be a risk factor for developing ASD. The results showed that the combination of perceptual-motor exercises and vitamin $D_3$ supplementation has a double effect in comparison with any of the interventions alone on reducing the stereotypical behavior of children with autism disorder. Hence, the use of combined intervention can be an ideal strategy to decrease stereotypical behavior in children with autism disorder. Vitamin $D_3$ supplementation can be a worthwhile effort to reduce symptoms in ASD with low vitamin levels. In addition, vitamin $D_3$ supplementation during pregnancy may be preventive as a preventive means for children with ASD or a measure to reduce the prevalence of ASD. Supplementation of vitamin $D_3$, which is a confident and cost-effective form of treatment, may significantly improve outcome in some children with ASD, especially in younger children. However, the exact mechanism how vitamin $D_3$ contributes to the etiology and treatment of ASD needs further study. This study would suggest that when children with ASD receive direct instructions on targeted perceptual-motor exercises delivered within an evidence-based framework, the results are positive. However, considering all the facts in relation to the roles of Vitamin $D_3$ and perceptual-motor exercises in autism, further research is needed to provide a definitive statement on this issue and a clarification of more precise mechanisms.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## ORCID

Mehdi Sohrabi http://orcid.org/0000-0002-4820-3486

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