1-1-2022

Is exercise effective in improving the cognitive and behavioral executive functions in children diagnosed with ADHD?

Cara Scatena
Philadelphia College of Osteopathic Medicine

Is exercise effective in improving the cognitive and behavioral executive functions in children diagnosed with ADHD?

Cara Scatena, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 17, 202

ABSTRACT

Objective: The objective of this selective EBM review is to determine "Is exercise effective in improving the cognitive and behavioral functions in children diagnosed with ADHD?"

Study Design: A systematic review of three randomized control trials (RCTs). All three of these studies were published between 2011 and 2016.

Data Sources: All three of the RCTs were found using PubMed. All of the studies were published in English in peer-reviewed journals and selected based on their relevance to the clinical question.

Outcome Measured: The outcome measured in these studies is the measurable improvement in executive functions related to the effects of exercise in ADHD. In the study by Memarmoghaddam et al., cognitive and behavioral inhibitions were measured using the Stroop Test and Go-No-Go Tests. In the study by Ziereis et al., working memory was measured with Digit span and the letter-number sequencing test of HAWIK-IV. In the study by Change et al., attention, cognitive and behavioral inhibitions were measured using the Stroop and Wisconsin Card Scoring Test (WCST).

Results: In the RCT by Memarmoghaddam et al., there were significant differences in the experimental exercising group in comparison to the control group who did not exercise. The p-value of $p = 0.000$ indicates statistical significance with a large treatment effect. In the RCT led by Ziereis et al., there was a significant improvement in executive functions in the experimental group compared to the control group as indicated by $p < 0.001$. In the RCT led by Chang et al., the improvement in executive functions was significant as seen with the p-values of $p<0.01$ in the Stroop test and $p<0.05$ in WCST.

Conclusions: All three of the RCT's showed that participation in exercise programs led to improvement in executive functions in children with ADHD as evidenced by F-score and p-values. These studies suggest that structured exercise programs are effective in improving the executive functions in children with ADHD. Further studies should explore exercise in comparison to pharmacologic agents, should include bigger samples sizes and explore different means of exercise therapies.

Key Words: ADHD, children, exercise, executive functions

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder most often diagnosed in childhood. In 2016 it was reported that 6.1 million children (9.4%) aged 2-17 were diagnosed with ADHD.[2] Children diagnosed with ADHD report trouble with attention, over-activity and controlling impulsive behaviors. ADHD is diagnosed with the DSM-5 criteria; symptoms must be present before 12 years old, and symptoms of inattention and/or hyperactivity must interfere with daily functioning.[1]

Evaluating and treating ADHD is common under the scope of a physician assistant's practice. The prevalence of ADHD has allowed for extensive research and healthcare education on the signs/symptoms, diagnosis and treatment. On the contrary the etiology of ADHD is not well understood, yet there is a known genetic risk in families. The roll that neurotransmitters such as norepinephrine and dopamine play in the brains of those with ADHD is continuously being studied. Those with ADHD have decreased levels of norepinephrine, but it is not known if there is a deficiency in the precursor dopamine or in the norepinephrine.[2] Depending on where in the brain norepinephrine is deficient will result in different symptoms for that child. [2]

The standard treatment approach to children with ADHD is multi-modal including a variety of behavioral therapy and pharmacotherapy. Children with ADHD have 1.6x more outpatient primary care visits each year, and 9.9x more outpatient therapists and mental health visits.[3] Additionally, they have 3.4x more pharmacy fills each year as compared to children who do not have ADHD. [3] The necessity of increased medical visits and prescriptions coupled with many indirect financial burdens for families, leaves children with ADHD with significantly higher costs than non-ADHD children. In 2001, the expected annual cost per child with ADHD was $1465/year to cover medications and treatment costs, in comparison to an expected annual cost of $690 in a child without ADHD. [3] The indirect costs of the child's behaviors and the burden on caregivers was $15,035 over the course of the child's development. [4] This number is three times that of comparable costs to a child without ADHD. [4]

Co-treatment of pharmacologic and behavioral therapy is highly encouraged, however pharmacological management is predominant. This is also seen in Europe, where an analysis showed that more than 56% of patients were initially treated with methylphenidate.[5] Stimulants, which include various levels of amphetamine and methylphenidate, are the first line medication used to treat ADHD. These work to increase levels of dopamine in the brain. Examples of common stimulants are Adderall, Ritalin and Vyvanse.[1] Non-stimulants, such as atomoxetine is a newer option, as well as clonidine and guanfacine as a secondary use.[1] Psychotherapy, CBT, behavior therapy and parent behavior management training are essential to the comprehensive and long-term treatment of ADHD. While pharmacotherapy has shown to be very effective, it is associated with negative side effects such as decreased appetite and adolescent dependence.

The brains of children with ADHD require structure, variety, the ability to incorporate new skills and a system to measure outcomes. Exercise programs provide structured workouts to help build a daily routine as they offer a variety of movements and training styles.[6] Exercise programs teach new skills and build upon old skills, and they allow for a specific and measurable goal to be set that can be attained.[6] Exercise stimulates the release of norepinephrine and dopamine, the neurotransmitters that are decreased in the brain of a child with ADHD.

This selective EBM evaluates the use of exercise as a part of the treatment regimen to help control the behaviors of children with ADHD which requires the utilization of their cognitive function. The goal is to improve the behaviors of children with ADHD while lessening their dependence on pharmacological therapy.

OBJECTIVE

The objective of this selective EBM review is to determine "Is exercise effective in improving the cognitive and behavioral functions in children diagnosed with ADHD?"

METHODS

For this systematic review, the studies that were incorporated were chosen based on their relevance, credibility and significance to the objective. Three randomized control trials (RCTs) using the criteria listed below were chosen for this systematic review.

The search was conducted through PubMed using keywords "children," "ADHD," "exercise," and "executive functions." The studies used in this review are RCTs published in English and published in 2012 or later. Further criteria used to select relevant studies were the review and incorporation of patient-oriented outcomes, using PICO (population, intervention, comparison and outcomes). This ensures relevance to both the practitioner and the patient. The *population* criteria used to fulfil the search were school-aged children diagnosed with ADHD. The *intervention* used in the studies were the children's participation in an exercise program. The *comparison* was the use of control groups: two of the studies in this review utilized control groups who did not participate in any exercise, while in the third study, the control group watched an exercise-related video. The *outcome* assessed was change in executive functions.

The inclusion criteria for this search were studies published 2012-present, RCT's and in the English language. The exclusion criteria for this search were adult population, secondary studies, studies before 2010, and studies that did not use a standard method of measuring executive function. The statistics used to calculate the significance of the results in the RCT's were p-value, F-score, lambda (λ) and $\eta 2$. Table 1 seen below, shows the demographics and characteristics of included studies.

OUTCOMES MEASURED

The outcome measured in the studies was the improvement in executive functions in children with ADHD. Each of the selected studies utilized different subjective measurement scales to measure the change in executive function.

Memarmoghaddam et al., and Chang et al., utilized the Stroop Test to measure cognitive inhibition. The first stage of the Stroop test shows only consistent stimuli, the second stage shows only inconsistent stimuli, and the third stage uses both consistent colored words and inconsistent colored words.[7] The third stage was the focus of effect analysis in these RCT's. Additionally, the RCT lead by Memarmoghaddam et al. used the Go-No-Go to measure behavioral inhibition. The "Go" stimuli requires the participant to react within 2 seconds, while the "No Go" tests the ability to not respond. In addition to the Stroop test, the study lead by Chang et al., used the Wisconsin card scoring test (WCST). The WCST measures executive function as well as strategic planning, set shifting and impulse responding.[9] WCST requires participants to sort response cards according to the stimulus cards and the instructor's feedback.

In the study lead by Ziereis et al., verbal working memory was measured using the digit span task and letter-number-sequencing task of HAWIK-IV.[8] In the digit span task, number sequences were presented to the participant; the participant was then required to repeat the sequence back in the correct order both forwards and backwards.[8] The letter number test worked similarly, however the participant recalled the letters back alphabetically and the numbers back in ascending order. [8]

ADHD is considered to be an executive function deficit disorder. [2] Children with ADHD are typically far behind their peers in developing executive functions.[2] This can ultimately cause age-related setbacks that if continued into adulthood can reduce their quality of life. The outcomes measured in these studies look to focus on the patient's improvement in executive functions which if implemented early when the child is diagnosed with ADHD can improve success both in the classroom, at home and in their future careers.

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/d	Interventions
Memarmoghaddam[7]	RCT	40	7-11	Males with ADHD, primary school students (age 7-11)	IQ score below 70, children with autism, and other mental disorders and health problems	4	Participation in an exercise program
Ziereis[8]	RCT	43	7-12	Children diagnosed with any predominant type of ADHD, age 7-12	IQ score below 85, children with gross sensory or motor problems, children with the diagnosis of mental retardation rather than the diagnosis of autism, schizophrenia, epilepsy or the history of other neurological problems	10	Either a sports program focusing on specific skills or in a group focused on more generalized physical activity
Chang[9] (2011)	RCT	40	8-15	Children 8-15 y/o, ADHD dx by a psychiatrist; free of intellectual disability, brain injury, and disease; children who meet the criteria assessed of the Physical Activity Readiness Questionnaire	Adults, children not diagnosed with ADHD	0	Participate in moderate intensity aerobic activity

RESULTS

The RCT lead by Memarmoghaddam et al., included 40 boys aged 7-11 from the sixth educational district who were diagnosed with ADHD.[7] The students were randomly divided into two groups. A pre-test for both the Stroop test and Go-No-Go were distributed to both groups at the initiation of the study. The experimental group was enrolled into an 8-week exercise program consisting of three 90-minute sessions each week.[7] The exercise programs were designed to improve executive functions. The program was structured with 25 for goal-directed exercise, 10 minutes of station training, 15 minutes on the treadmill, 15 minutes for ball games and 25 minutes for the warm-up and cool down.[7] The control group did not participate in any activity including exercise. After the training sessions, post-tests were distributed to both groups.

Memarmoghaddam et al., used mean and standard deviations (SD) to measure the statistical data throughout the study. For the Stroop test, MANCOVA analysis determined there was statistical significance with a large treatment effect for the exercise group as seen with λ = 0.140, p-value = 0.000 and $\eta 2$ = 0.86.[7] Further analysis with ANCOVA was used to evaluate the effectiveness of exercise on each factor of the Stroop test. The Stroop test analysis considered error number, no response, true number, and response time (RT). These results showed that the most significant impact on was with regard to RT.[7] Specifically, the $\eta 2$ values indicate large effect size ($\eta 2$ = 0.68, $\eta 2$ = 0.64) and p-value= 0.000 indicates significance.[7] Values for effects on RT in the Stroop test are seen in Table 2 below.

Table 2. Stroop Test Changes in RT from Pre-test to Post-test After 8 Weeks. (Mean ± SD)

	Consistent RT pre-test	Consistent RT post-test	Mean Change	Inconsistent RT pre-test	Inconsistent RT post-test	Mean Change
Experimental Group	135 ± 90.26	1106.57 ± 65.77	971.57	1344.26 ± 81.51	1168.89 ± 92.76	-175.37
Control Group	1367.76 ±89.65	1324.52±115.76	-43.24	14.17 ±75.18	1410.17±97.80	1,396

The MANCOVA analysis was utilized to determine the statistical significance of the Go-No-Go test, using the same statistical measures. The results indicated that there was significance on the scores of those in the exercise group as compared to the control group with a large treatment effect as seen with λ = 0.297, P = 0.000, $\eta 2$ = 0.703.[7] Further analysis with ANCOVA showed that the exercise program had the largest influence on the No Go-True number and the No Go-Error number.[7] The $\eta 2$ value of 0.45 indicates large effect size and p-value= 0.000 for both No Go -True and -Error indicate statistical significance.[7]

Values for effects on No-Go from Go-No-Go are seen in Table 3 below.

Table 3. Changes in No Go Values from Pre-Test to Post-Test After 12 Weeks. (Mean ± SD)

	No Go- True pre-test	No Go- True post-test	Change	No Go- Error pre-test	No Go- Error post-test	Change
Experimental Group	21.42 ± 2.81	24.68 ± 2.53	3.26	8.57 ± 2.81	5.31 ± 2.53	-3.26
Control Group	21± 2.76	22.11 ±3.14	1.11	9 ± 2.76	7.88 ± 3.14	-1.12

The RCT lead by Ziereis et al., was comprised of 43 children, both male and female that were 7-12 years old and diagnosed with ADHD.[8] The children were randomly assigned to one of two experimental groups or to a control group for a 12-week program.[8] Participants in the first experimental group focused on specific skills such as ball handling and balance while participants in the second control group were trained without any specific focus.[8] The study analyzed the impact of exercise on working memory (WM) and motor performance using digit span and letter-number sequencing of HAWIK-IV. For the purpose of this systemic review, motor performance measures and outcomes were omitted. The WM assessments were distributed at the beginning of the study, after the first training session (post-test-1), and one week following the last session (post-test-2).[8]

The statistical data used to interpret the effects in executive function was presented as the mean, SD, F-score and p values. Assessments compared from the pre-test and post-test-1 only showed significant improvement in one variable; catching and aiming, with values of $F=8.197$ $p<0.05$ and $\eta2 = 0.23$.[8] The long-term effects were interpreted using the results from post-test-2 at the conclusion of the study. Both the digit-span score and the letter-number score were converted into individual age-adjusted index-scores, these scores were totaled to calculate the overall WM index-score.[8] The results were statistically significant with a large effect size for all three variables. The WM index-score demonstrated $F=17.800$, $p<.001$, $\eta2 = .35$.[8] The digit-span was statistically significant with $F=24.261$, $p< .001$, $\eta2 = .43$.[8] Letter-number sequencing was significant with $F= 5.851$, $p<.05$ and $\eta 2 = .15$.[8] The mean and SD for the WM index-score is summarized in Table 4 below.

Table 4. Changes in Index-Score WM from Baseline to Follow-up. (Mean ± SD)

	Pre-Test Score (Baseline)	Post-Test Score (After 12 weeks)	Mean Difference
EG 1 (specific)	96 ± 13	109 ± 15	13
EG 2 (general)	100 ± 12	108 ± 10	8
Control	103 ± 13	100 ± 12	-3

Chang et al. conducted a randomized control trial with 40 children to understand the effect of exercise on executive functions in children with ADHD.[9] The population of this study were children ages 8-13 diagnosed with ADHD who were randomly divided into two groups: the experimental group who participated in moderate aerobic activity, and the control group who watched an exercise-related video.[9] The experimental group ran on a treadmill for thirty minutes.[9] Throughout the exercise, the heart rate reserve (HRR) of each child was monitored. Their speed/intensity was adjusted in order to maintain 50-70% HRR.[9] The exercise-related video used for the control group was created with the intention to manipulate stable arousal.[9] This RCT was performed on one day and lasted around 100 minutes from start to completion.[9] The post-test for both groups was initiated within one minute of finishing treatment.[9]

Improvement in selective attention and inhibition after exercise were assessed using the Stroop test in this study. The Stroop Color-Word test was the focus of the studies review. The mixed ANOVA used p-value and F score. Significant effects on time in the post-test were shown when compared to the pre-test with the calculated values of $F= 62.51$, $p < .01$ and $\eta 2 = 0.62$.[9] However, with the control group, there was no significance relative to the pre-test between groups with values of $F =0.5$ and $p > .05$.[9] Further analysis showed that both groups had shorter durations during the post-test with significant value as seen with $F= 3.30$ and $p = .08$.[9] However, time change in the exercise group was more significant with an effect size of 1.26 compared to 0.58.[9] The values for the Stroop Color-Word test are summarized in Table 5 below.

Table 5. Changes in Stroop Color-Word from Baseline to Follow-up. (Mean ± SD)

	Pre-Test Score (Baseline)	Post-Test Score (After 100 minutes)	Mean Change	Effect Size
Control Group*	66.76 ± 17.13	57.30 ± 15.64	-9.46	-0.58
Exercise Group*	67.13 ± 16.98	49.94 ± 9.15	-17.19	-1.26

* Lower scores represent better performance

The WCST assesses total correct, perseverative responses, perseverative errors, non-perseverative errors, conceptual level response and categories completed.[9] While all categories showed significant effects on time, non-preservative errors and categories completed showed the most improved performance.[9] The effect on time was significant in non-preservative errors for the exercise group, calculated as $F=9.62$, $p <.005$ & $\eta 2 = 0.34$.[9] This significant effect was not seen in the control group as evidenced by $F=0.01$ and $p >.05$.[9] Comparable findings were seen in categories completed where the exercise group had a significant effect on time with $F= 8.24$, $p <.01$ & $\eta 2 = 0.3$, while the control group did not, $F=0.24$ and $p >.05$.[9] The mean, SD and ES for the non-preservative errors and categories completed of the WCST is summarized in Table 6 below.

Table 6. Changes in WCST from Baseline to Follow-up. (Mean ± SD)

	Control Group	**Exercise Group**
Non-preservative errors* Pre-Test (baseline)	18.95 ± 14.53	29. 55 ± 17.12
Non-preservative errors* Post-Test (After 100 minutes)	18.90 ± 15.90	17.85 ± 14.52
Effect Size	0.00	- 0.74
Categories Completed ** Pre-Test (baseline)	4.75 ± 1.77	3.60 ± 2.16
Categories Completed** Post-Test (After 100 minutes)	4.85 ± 1.92	4.70 ± 2.07
Effect Size	0.05	0.52

* Lower scores represent better performance // ** Higher scores represent better performance

DISCUSSION

The first line treatment of pharmacologic treatment for ADHD is nearly universal. These medications work to increase levels of dopamine and norepinephrine in the brain which lead to increased levels of energy, attention and concentration. While these medications have well-known efficacy, they are also known for their long list of adverse side effects and addictive nature that worsen with increased time on these medications.

This comprehensive review evaluated the efficacy of utilizing exercise in children with ADHD to help improve their executive functions. All three of the studies in this review found statistically significant improvement in executive functions after physical activity using multiple different testing modalities. All of the studies showed large effect sizes with statistically significant p-values and F scores in comparison to their pre-study baselines. The studies researched prove that there is an increase in productivity, concentration and inhibition after structured exercise compared to the control groups. The results from these studies help to further emphasize the correlation between neurotransmitters involved in exercise and stimulant medications which if utilized can lead to an improvement in quality of life.

Implementing exercise as an adjunctive treatment to delay or lessen the onset use of stimulants could have substantial positive effects. Benefits of implementing physical activity include decreasing dependence on the medications and the side effects associated with stimulants. Increasing cardiovascular movement in childhood has well-studied, long-term benefits beyond the control of ADHD symptoms. Families should experience lower overall costs managing ADHD in their children. However, exercise as a treatment option for ADHD in children does come with some limitations. Structured exercise programs may have a cost, be time-consuming, and may require the supervision of an adult during the program.

All of these studies in this review had some limitations. The control groups could not be blinded as there was no activity for them as compared to the exercise group. Another limitation was the small sample sizes of less than 40 participants in each study, which is not statistically significant relative to the population of children with ADHD. Further, the Memarmoghaddam et al. study was limited given that they only studied male participants. Noteworthy was the fact that each of the studies attempted to study the "pure effect" of exercise on ADHD and therefore did not allow any of the children to use medications for their ADHD during the duration of the study.

CONCLUSION

The statistical evidence of the studies by Memarmoghaddam et al., Ziereis et al., and Chang et al., are initially conclusive indicators that physical activity may be an effective treatment to improve the cognitive and behavioral executive functions in children with ADHD.

The exact mechanism of improvement in brain function and its relationship to exercise is not perfectly understood, however, this review provides greater evidence that exercise may have correlations with neurotransmitters. The dopamine and norepinephrine released during exercise can mimic the inhibition of reuptake of these neurotransmitters similar to the use of stimulants.

Future studies should utilize larger groups of participants for greater statistical significance. Furthermore, they should add a third group comprised of non-exercising children who are using ADHD medications to measure against the exercise group without the aid of medications; both groups would be compared to their control groups. Using these three groups with more participants would allow for correlating data across multiple variables and could help to definitely determine the efficacy of exercise versus the use of pharmacological agents. In conclusion, future studies are required to further prove the efficacy of exercise as is necessary to help improve the quality of life and the financial implications of children living with ADHD.

REFERENCES

1. Centers for Disease Control and Prevention. What is ADHD? National Center on Birth Defects and Developmental Disabilities website. Updated September 23, 2021. Accessed October 2, 2021. https://www.cdc.gov/ncbddd/adhd/

2. Silver, Larry. The ADHD brain – ADHD neuroscience 101. Additudemag. Updated March 2, 2021. Accessed October 4, 2021. https://www.additudemag.com/adhd-neuroscience-101/

3. Guevara J, Lozano P, Wickizer T, Mell L, Gephart H. Utilization and cost of health care services for children with attention-deficit/hyperactivity disorder. *Pediatrics* 2001;108 (1): 71–78. doi.org/10.1542/peds.108.1.71

4. Zhao, X., Page, T.F., Altszuler, A.R. *et al.* Family burden of raising a child with ADHD. *J Abnorm Child Psychol* **47,** 1327–1338 (2019). doi.org/10.1007/s10802-019-00518-5

5. Hodgkins P, Setyawan J, Mitra D, et al. Management of ADHD in children across Europe: patient demographics, physician characteristics and treatment patterns. Eur J Pediatr. 2013;172(7):895-906. doi:10.1007/s00431-013-1969-8

6. Lara M. Attention Magazine: The exercise prescription for ADHD. CHADD website. Published June 2012. Accessed October 4, 2021. https://chadd.org/wp-content/uploads/2018/06/ATTN_06_12_Exercise.pdf

7. Memarmoghaddam M, Torbati HT, Sohrabi M, Mashhadi A, Kashi A. Effects of a selected exercise program on executive function of children with attention deficit hyperactivity disorder. *J Med Life*. 2016;9(4):373-379. Accessed January 3, 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5141397/.

8. Ziereis S, Jansen P. Effects of physical activity on executive function and motor performance in children with ADHD. *Res Dev Disabi*l. 2015;38:181-191. doi:10.1016/j.ridd.2014.12.005

9. Chang YK, Liu S, Yu HH, Lee YH. Effect of acute exercise on executive function in children with attention deficit hyperactivity disorder. *Arch Clin Neuropsychol*. 2012;27(2):225-237. doi:10.1093/arclin/acr094