

Efficacy of Medication and Nonmedication Methods on Working Memory of Children With Attention Deficit and Hyperactivity Disorder

Mohammad Ahmadpanah,¹ Mohammad Haghghi,¹ Ali Ghaleiha,¹ Leila Jahangard,¹ Marzieh Nazaribadie,¹ and Amineh Akhondi^{2,*}

¹Behavioral Disorders and Substances Abuse Research Center, Hamadan University of Medical Sciences, Hamadan, IR Iran

²Hamadan Educational Organization, Ministry of Education, Hamadan, IR Iran

*Corresponding author: Amineh Akhondi, Hamadan Educational Organization, Ministry of Education, Hamadan, IR Iran. Tel/Fax: +98-8138271066, E-mail: m1_ahmad2000@yahoo.com

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Abstract

Background: Working memory is the ability to keep and manipulate information in a short time. Children with attention deficit and hyperactivity disorder (ADHD) are among the people suffering from deficiency in the active memory, and this deficiency has been attributed to the problem of frontal lobe. This study utilized a new approach with suitable tasks and methods for training active memory and assessment of its effects.

Objectives: This study aimed to investigate the effectiveness of medicinal and behavioral therapies on working memory of children with attention deficit and hyperactivity disorder.

Patients and Methods: The children participating in this study were 7-15 years old, and were diagnosed with ADHD by the psychiatrist and psychologist based on DSM-IV criteria. The intervention group comprised 8 boys and 6 girls with the average age of 11 (± 2) years, and the control group comprised 2 girls and 5 boys with an average age of 11.4 (± 3). Three children in the test group and 2 in the control group were under medicinal therapy.

Results: Training of working memory significantly improved the performance in nontrained areas as visual-spatial working memory as well as the performance in Raven progressive tests which are a perfect example of nonverbal, complicated reasoning tasks.

Conclusions: The performance of working memory improved through training, and these trainings extended to other areas of cognition functions not receiving any training. Trainings resulted in the improvement of performance in the tasks related to prefrontal area. They had also a positive and significant impact on the movement activities of hyperactive children.

Keywords: Attention Deficit and Hyperactivity Disorder, Memory in Children, Drug Therapy

1. Background

Research has shown that the children with attention deficit and hyperactivity disorder (ADHD) are likely to show behaviors which indicate disorder in working memory 4 times more than the other children with the same age. Working memory refers to our ability to remember and process information in the short time. We save information in an irregular form in our mind for both remembrance and process of information. For example, we use this memory for remembering the name and phone number of a certain person, or directions while driving. Without this memory, we probably get lost rapidly. Or we may not know how to go to a new conference and will forget the names and telephone numbers of people.

Working memory is of special significance with respect to doing different activities at school, from complicated activities like studying, comprehension, mental calculations, and memorizing words to simple activities such as making notes and walking around. Working memory grows significantly in childhood. It is shown in the literature that how memorable information will grow in size as individual grows up.

For example, at the average age of 5, two issues are kept in a child's memory, while at about the average age of 10, three or four issues are kept in the child's memory. Therefore, working memory is a cognition system, responsible for the preservation and manipulation of temporary information, and plays a significant role in maintaining behaviors requiring concentration in learning (1). Deficiency in working memory is observed in the people with attention deficiency and hyperactivity (2,3). This memory is composed of a central executive system responsible for attention control, 2 reservoirs for maintaining and manipulation of verbal and visual-spatial information, and a part for integration of multidimensional representation. All these components bring about special neuronal activities. Attention deficiency along with hyperactivity is a known disorder, including attention deficiency or impulsivity, or a combination of both. This disorder is seen in performing functions and affects high level processes which are essential for doing targeted behaviors. Physiological surveys indicate that this disorder involves mostly the frontal lobes. One of its most important characteristics is inhibition

or damage in inhibitions (2, 4, 5) and working memory (3, 6), especially in visual-spatial subjects (3, 7).

Stimulants like methylphenidate and amphetamines are prescribed as a preliminary medication for reducing ADHD behavioral symptoms. Some research results indicate that these medicines have improved the visual-spatial working memory level (8). Nonmedicinal and behavioral interventions have recently attracted attention, and some study results show the impact of these interventions on the improvement of behavioral problems such as the salient feature of ADHD children and working memory. These interventions comprise intervening programs, including several short sessions to teach a series of memorable lessons (which require maintaining and manipulating a chain of verbal or visual-spatial information). Research shows that behavioral intervention has improved the working memory of children with ADHD who have not received medication (9), children with weak working memory (10), and adults with mental injuries resulting from heart attack (11). Studies related to brain scanning have shown that behavioral intervention has a positive effect on neuron activities in middle frontal gyrus and parietal and superior cortexes, i.e., areas associated with working memory (9, 12, 13).

The objective of the present study was to examine the effect of medicinal and behavioral intervention on the working memory of children with ADHD. Therefore, the question this study attempts to deal with is whether non-medicinal therapies (training the skills associated with short-term memory) conducted along with medication contributes to the promotion of the working memory of children with ADHD. Taking the manifold behavioral and educational problems of these children into consideration, the first line of therapy in Iran is medicinal therapy, whereas research results suggest two methods of therapy. On the other hand, no research has been conducted in this subject, and the fact that some children do not respond to medicinal therapy has frustrated parents and psychiatrists. If this research proves the efficiency of behavioral exercise on memory, one of the most problematic areas in these children, i.e., working memory, will boost and relative improvement in other areas will be observed subsequently.

2. Objectives

This study aimed to examine the effect of medicinal and behavioral therapies on the working memory of the children with ADHD.

3. Patients and Methods

This study is of experimental type with pretest and post-test model and control group. Before starting up, the preliminary coordination with Hamadan's psychiatrists was done, and the work process was described for them. They were requested to refer patients aging 6 to 14 with ADHD for memory assessment. Before starting the main task, all children took Raven intelligence as well as memory verbal and numeral tests. After matching them, they were placed

in two groups: medicinal therapy and medicinal therapy plus behavioral therapy. In the second stage, one group of children continued the medicinal therapy with the same method and the other group received a training program of working memory training model for 25 sessions during 25 training days in addition to medicinal therapy. In the third stage, which started 20 days after working memory training program, all the children took an exam from each aspect of working memory. Tests were conducted with fixed sequence, and regular break intervals were given to reduce the effect of fatigue on results. Finally, the two groups' differences were compared. At the psychiatrists' discretion, the people with other mental illnesses were excluded from the intervention program. Considering the previous foreign studies, the sample volume in this test comprised 20 girls and 20 boys.

The ability of keeping and manipulating information in the short-term memory is associated with prefrontal cortex. This capacity is the basis of many cognitional skills like logical reasoning and problem solving (9, 10, 14).

In addition, working memory has been considered as the specific and fixed character of the people in question, especially as this capability have always been associated with general intelligence (14).

Children with ADHD have been characterized with inattention, impulsivity, and hyperactivity. Among cognition disorders in this group, working memory injury is of higher importance (14) and this disorder is assumed to be associated with a problem in frontal lobe (2).

If working memory deficiency is considered as the central core of cognition problems in children with hyperactivity and inattention, improvement in working memory will result in the reduction of ADHD symptoms. Previous attempts at improving working memory have had some success. In the previous tests, working memory tasks were repeatedly done without coordinating their difficulty level with individuals' ability level. In such a condition the speed and time of reaction is reduced but no increase in working memory capacity is provided. In training retention methods to children with learning inability some success has been achieved. There are also case studies which show those who had learnt the strategies of keeping a lot of digits in mind were successful in this task (15).

However, in these studies the trained strategies did not have a significant impact in other cognition functions of the people under study. Also, strategies did not improve the general capacity of the working memory. In this investigation, we considered two issues. First, we wondered if the capacity of the active memory improves through a new type of computerized cognition training program. Second, we wanted to know if these trainings will result in the reduction of motional activities of ADHD. In this study, the previously proved methods used in the promotion of the capacity of sensory distinction were applied which induce cortex plasticity in sensory and motional parts.

Trainings were conducted in a way to match each person's capability, and were progressing step by step; also their proportion or disproportion was examined and verified through repeated tests. Each session, held daily, lasted 15 - 25 minutes. There were

4-6 sessions per week and they lasted at least 5 to 6 weeks.

A computerized program was used which was already prepared based on these principles. Children with ADHD performed working memory tasks in visual-spatial areas. We used memory backward version of the span of working memory numbers and tasks in the area of verbal-spatial. Verbal and visual feedback was incorporated in the process of tasks for better acceptance and cooperation. The pseudo-form or less dose of computer program was also used; it was similar to intervention program with the difference that the two previous considerations were not applied to them, and their training time was at most 10 minutes. The study was designed in a way that children, parents, and the psychologist were not aware of groupings before and after intervention.

A series of cognition tasks were given to children before and after the intervention program for the assessment of working memory's capacity and prefrontal functions. These tests were consisted of progressive matrixes of Raven for children (16)(colorful) comprised complex and progressive reasoning task used for the measurement of prefrontal performance and general intelligence ability. According to the assessments, the performance in this test was about $r^2 = 0.09$ (14).

Stroop test was used for the measurement of impulsivity in which children with ADHD have shown problems. According to previous studies, good and bad performance in this test is associated with good or bad functional performance of prefrontal cortex (17).

For the assessment of motional activities and capabilities before intervention program, the level of children's head movements was measured in a continuous 15-minute task by means of a computer. The method used in this study for the measurement of movements had shown in previous studies to have a good correlation with behavioral marking scales in the area of hyperactivity of ADHD children (18).

In later supplementary tests, we investigated whether normal teenagers (with no problem in working memory and ADHD) benefit from these tests designed for children with ADHD.

The children participating in this study were 7-15 years old. They were diagnosed as hyperactive and attention deficit based on DSM-IV criteria by the psychiatrist and psychologist. The intervention group was consisted of 8 boys and 6 girls with the average age of $11 (\pm 2)$ years, and the control group was consisted of 2 girls and 5 boys with an average age of $11.4 (\pm 3)$. Three children in the test group and 2 in the control group were under medicinal therapy.

There was no significant difference between the groups with regard to age. Also, there was no significant difference with regard to cognition performance marks or head movement in pretest. The study was conducted in Farshchian Medical Center and the work process was approved by the Ethics Committee of the university.

Tests utilized in pretest and posttest are as follows:

3.1. Taking 5 Cognition Tests

1) The trained version of visual-spatial working memory test: Some circles were shown in a 4x4 table, and after a short pause, participants would locate each as they were

shown. The test went on like this till the participant made two consecutive mistakes. Marking was based on the maximum number of the remembered circles.

2) Course block striking test: 10 blocks were put in order in an irregular form before the child. The participant offered them in backward and forward form, and he/she was asked to remember them in the same training form. Marking was done as with the first test.

3) Stroop test: words describing colors were printed with a color other than the color of the words, and participants were asked to immediately identify the color of the typed words.

4) Raven progressive matrices: Children were asked to establish a logical relationship among a series of nonverbal reasoning tasks. This test is also used as an assessment of general nonverbal mental ability.

5) Selective reaction time tasks: Visual stimulants were appeared on the computer's monitor. Separate serial response boxes were used for collecting responses. Yellow circles were appeared on the left or right part of the screen. The participant was asked to press the enter key once the yellow circle appeared on the screen. The yellow color often appeared after green color. At first, participants were exposed to the simple form of reaction time. The reaction time gradually grows more complicated as more choices appear on the screen. Responses were registered within 15 minutes. Stimulants were presented every two seconds, and 5% of the presented stimulants were targets.

4. Results

As we can see in Tables 1 and 2, the test and retest changes in the intervention group were compared with the test and retest changes in control group. The comparison of results showed a significant difference in the exercises of visual-spatial working memory and course block striking tasks. Participants in the course test remembered the location of small cubes in a pseudorandom way. A noticeable improvement for all children was observed in course test, and inter-group difference was significant ($P < 0.001$). A wealth of evidence indicative of significant changes in Raven progressive matrices marks was also observed.

All testing group children in this part showed progress. A significant improvement was also observed in the performance of the children in Stroop test. Only in reaction time test, a weak and irregular difference was observed.

The number of head movements was significantly reduced in the study group. It means that significant changes were observed among all participants. The number of head movements in the control group increased by 6% compared to the initial test; this result was in agreement with the previous study results which had shown an increase of 8% (17).

Test and retest results and the comparison between testing and control groups were significant in 4 tests of course test trained working memory program, Raven progressive matrices, Stroop's exactness, and head movements.

The correlation analysis of test/retest differences showed that improvement in two working memory tasks was significantly related with each other.

Table 1. Comparison of the Performance of Experiment and Control Groups in Tests Before and After Interventions

Visual-Spatial Working Memory	Medication Group			Control Group		Group Differences ^a
	After intervention	Before intervention	P value ^b	After intervention	Before intervention	
Course test of striking cubes						
Stroop test	6.70 (0.38)	5.03 (0.18)	0.0008	5.11 (0.18)	5.32 (0.19)	0.0007
Speak (at most 60 s)	6.83 (0.31)	4.80 (0.16)	0.0001	4.75 (0.25)	4.34 (0.41)	0.001
Completion time, s	58.9 (0.5)	54 (1)	0.04	54/1 (1.99)	55 (0.7)	0.02
Raven progressive matrices	89.3 (6.85)	99 (7.1)	0.19	84.3 (14.2)	79 (5.8)	0.14
Selective reaction time tasks	31.2 (1.8)	25.9 (1.3)	0.001	28.95 (1.2)	18.3 (0.7)	0.001
Hidden reaction time, ms	294	280	0.30	339	311	0.37
One-two selection	75	149	0.06	76	89	0.05
Reaction time standard deviation	94	105	0.20	115	126	0.53
Head movements	330	1011	0.002	1840	1485	0.00008

^aTest/retest difference in the medication group before and after intervention (t-way t test).

^bComparison of test/retest, i.e., medication group and control group.

Table 2. Correlation Between Test-retest Differences in Medication Group^a

	Training working Memory	Course Blocks	Raven Matrix	Head Movements
Course blocks	0.85			
Raven test	0.76	0.54		
Head movements	0.75	0.55	0.71	
Stroop test	0.42	0.60	- 0.19	0.21

^aP < 0.05.

5. Discussion

The present study showed that targeted, precise, and computerized training of working memory gradually influences the amount of information children can keep in their mind. This improvement occurs gradually over training, and affects gradually in motional and perceptual skills of the children as well.

The positive results of working memory trainings may also indicate that these trainings improve normal children's working memory too.

Performance improvement was observed in both trained and untrained working memory and visual-spatial areas, i.e., training impacts extend from one area to others.

Nonidentical impacts were observed only in reaction time test; however, this is consistent with previous study results. Previous studies had shown that cognition tasks result in more improvement through training compared to tasks associated with attention area.

These trainings have also had a significant impact on tasks associated with reasoning. Due to the impact of the training providing process in the course cube striking test, the assessment of training impacts is not a simple job. But improvement in reasoning test results is indica-

tive of the fact that training impacts extend to other non-trained aspects, since trainings did not include such subjects as problem solving and reasoning.

This argue holds true for Stroop test as well. Improvement in test results is indicative of the fact that working memory trainings positively impact working memory, and working memory itself has been the fundamental basis of the reasoning. In summary, the results of progressive matrixes show noticeable changes, in other words, both working memory and reasoning have a common mental origin. The key and fundamental common feature in working memory tasks, Raven progressive matrices, and Stroop test is that all are based on the performance of prefrontal cortex.

Another finding of this study is that working memory tasks reduce head movements. That is, the better the working memory marks, the more the head movements showed reduction. Now the question is how cognition deficiency, impulsivity, symptoms, and movements in ADHD are related to one another. Perhaps a cause and effect relationship can be established between them. The fact that the capacity of working memory, including reasoning ability is remarkably influenced by trainings,

and that Raven matrices ignore fixed cognition abilities and do not cover all cognition areas indicate the existence of conflicts and contradictions in this area, thus requiring the use of cognition tests which address dynamic and static cognition capabilities. Although more studies are required regarding the impacts of these trainings in the everyday life of hyperactive children, the results of the present study showed that the trainings associated with working memory has influenced the cognition performance of these children, and these impacts are significant.

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Footnotes

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References

- Kane MJ, Brown LH, McVay JC, Silvia PJ, Myin-Germeys I, Kwapił TR. For whom the mind wanders, and when: an experience-sampling study of working memory and executive control in daily life. *Psychol Sci*. 2007;**18**(7):614–21. doi: 10.1111/j.1467-9280.2007.01948.x. [PubMed: 17614870]
- Barkley RA. *ADHD and the nature of self-control*. New York City: Guilford Press; 1997.
- Martinussen R, Tannock R. Working memory impairments in children with attention-deficit hyperactivity disorder with and without comorbid language learning disorders. *J Clin Exp Neuropsychol*. 2006;**28**(7):1073–94. doi: 10.1080/13803390500205700. [PubMed: 16840237]
- Nigg JT. Is ADHD a disinhibitory disorder? *Psychol Bull*. 2001;**127**(5):571–98. [PubMed: 11548968]
- Willcutt EG, Pennington BF, Olson RK, Chhabildas N, Hulslander J. Neuropsychological analyses of comorbidity between reading disability and attention deficit hyperactivity disorder: in search of the common deficit. *Dev Neuropsychol*. 2005;**27**(1):35–78. doi: 10.1207/s15326942dn2701_3. [PubMed: 15737942]
- Castellanos FX, Sonuga-Barke EJ, Milham MP, Tannock R. Characterizing cognition in ADHD: beyond executive dysfunction. *Trends Cogn Sci*. 2006;**10**(3):117–23. doi: 10.1016/j.tics.2006.01.011. [PubMed: 16460990]
- Barnett R, Maruff P, Vance A, Luk ES, Costin J, Wood C, et al. Abnormal executive function in attention deficit hyperactivity disorder: the effect of stimulant medication and age on spatial working memory. *Psychol Med*. 2001;**31**(6):1107–15. [PubMed: 11513378]
- Bedard AC, Jain U, Johnson SH, Tannock R. Effects of methylphenidate on working memory components: influence of measurement. *J Child Psychol Psychiatry*. 2007;**48**(9):872–80. doi: 10.1111/j.1469-7610.2007.01760.x. [PubMed: 17714372]
- Klingberg T, Fernell E, Olesen PJ, Johnson M, Gustafsson P, Dahlstrom K, et al. Computerized training of working memory in children with ADHD—a randomized, controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2005;**44**(2):177–86. doi: 10.1097/00004583-200502000-00010. [PubMed: 15689731]
- Holmes J, Gathercole SE, Dunning DL. Adaptive training leads to sustained enhancement of poor working memory in children. *Dev Sci*. 2009;**12**(4):F9–15. doi: 10.1111/j.1467-7687.2009.00848.x. [PubMed: 19635074]
- Westerberg H, Jacobaeus H, Hirvikoski T, Clevberger P, Ostensson ML, Bartfai A, et al. Computerized working memory training after stroke—a pilot study. *Brain Inj*. 2007;**21**(1):21–9. doi: 10.1080/02699050601148726. [PubMed: 17364516]
- McNab F, Varrone A, Farde L, Jucaite A, Bystritsky P, Forsberg H, et al. Changes in cortical dopamine D1 receptor binding associated with cognitive training. *Science*. 2009;**323**(5915):800–2. doi: 10.1126/science.1166102. [PubMed: 19197069]
- Olesen PJ, Westerberg H, Klingberg T. Increased prefrontal and parietal activity after training of working memory. *Nat Neurosci*. 2004;**7**(1):75–9. doi: 10.1038/nn1165. [PubMed: 14699419]
- Engel PMJ, Santos FH, Gathercole SE. Are Working Memory Measures Free of Socioeconomic Influence? *J Speech Language Hear Res*. 2008;**51**(6):1580. doi: 10.1044/1092-4388(2008/07-0210).
- Thorell LB, Lindqvist S, Bergman Nutley S, Bohlin G, Klingberg T. Training and transfer effects of executive functions in preschool children. *Dev Sci*. 2009;**12**(1):106–13. doi: 10.1111/j.1467-7687.2008.00745.x. [PubMed: 19120418]
- Raven JC, John HC. *Raven's progressive matrices and vocabulary scales*. Oxford: Oxford Psychologists Press; 1998.
- Clark JF, Ellis JK, Bench J, Khoury J, Graman P. High-performance vision training improves batting statistics for University of Cincinnati baseball players. *PLoS One*. 2012;**7**(1):e29109. doi: 10.1371/journal.pone.0029109. [PubMed: 22384222]
- So YK, Noh JS, Kim YS, Ko SG, Koh YJ. The reliability and validity of Korean parent and teacher ADHD rating scale. *J Korea Neuropsychiatr Assoc*. 2002;**41**(2):283–9.