Original Article

A Comparison of Effectiveness of Regulation of Working Memory Function and Methylphenidate on Remediation of Attention Deficit Hyperactivity Disorder (ADHD)

Mohammad Reza Mohammadi, MD[1]
Ali Akbar Soleimani, PhD[2]
Zahra Farahmand, MSc[3]
Samira Keshavarzi, MSc[4]
Nastaran Ahmadi, Msc[1]

1Tehran University of Medical Science, Psychiatry & Psychology Research Center, Tehran, Iran
2 University of Science and Culture, Faculty of Humanities, Tehran, Iran
3 Tehran University of Medical Sciences, Department of Psychology, Roozbeh Hospital, Tehran, Iran
4 No.372, Children Mental Health Clinic, Dastgerdi St, Valiasr Ave, Tehran, Iran

Corresponding author:
Soleimani Ali Akbar, PhD
University of Science and Culture, Faculty of Humanities, Ashrafi Esfahani Blv, Park St, Bahar St, No. 38, Tehran, Iran
Tel: +98 (21) 44238171
Email: soleimani@usc.ac.ir

Abstract: Attention Deficit/Hyperactivity Disorder (ADHD) is a prevalent and serious disorder affecting such key cognitive components as working memory. Working memory serves to facilitate and check attention in any individual and to focus on those affairs that need to be retained in mind. This study examines whether a combination of the two therapeutic methods of working memory training and Methylphenidate might be more effective in treating ADHD in children aged 6 to 12 years of age than when methylphenidate is applied alone.

Method: Subjects of the study are 48 children suffering from ADHD. They were selected by random sampling. The experimental group included 23 children with ADHD who received a combination of working memory training and Methylphenidate, and the control group which included 25 children with ADHD received Methylphenidate only. To check the effects of the intervention, Conners' Parent Rating Scale (CPRS-48) was applied before and after the intervention. After intervention, data were collected from the remaining samples in the two groups. Data were examined both through descriptive statistical methods and analytic statistical methods, including T-student test and Quantile-Quantile Plots diagram .

Results: The study demonstrated that a combination of the cognitive intervention of working memory training and methylphenidate is more effective in alleviating ADHD symptoms rather than when methylphenidate is applied in isolation. In the CPRS pre-test and post-test, the mean difference of the experimental and the control group was 8.39 and 1.88 respectively, indicating that the working memory group has improved more than the control group.

Conclusions: The study reveals that the ADHD symptoms were more contained in the test group than the control group due to working memory training .

The cognitive intervention through working memory training may be effective in alleviating the severity of disorder measured in the pre-test.

Keywords: *Attention Deficit Hyperactivity Disorder (ADHD), working memory function, Methylphenidate.*

Iran J Psychiatry 2014; 9:1: 25-30

Attention Deficit Hyperactivity Disorder (ADHD) usually occurs in children and adolescents and shows such sustainable symptoms as inattentive, hyperactivity and impulsive behaviors. Children suffering from the disorder face more educational problems than their peers and might be driven away from the community or suffer antisocial behavior during school years and face numerous behavioral problems after school (1).

ADHD disorder is identified with such behavioral symptoms as inattention, hyperactivity and impulsivity though these children may also suffer from cognitive disorders that may affect their daily living activities at school or home. Children usually show deficiency in executive functions (for example in planning or sustained working), data processing speed (they prove slower than their peers) and working memory function that is usually considered as an executive function (1).

The three processes actually interact with one another in that working memory problems may either affect executive function or further lower the already low speed of data processing in children when they try to recover and organize specific data (2).

Working memory is an executive function, and it serves as a reference for 'mental working space' where a transfer of information takes place in the long term memory for a short moment (in a matter of seconds) for the purpose of a cognitive activity(3). Working memory serves to facilitate and check attention in any individual and helps to focus on those affairs that need to be retained in mind (4).

The notion of working memory disorder has been very helpful in explaining many cognitive and psychological problems faced by children due to Attention Deficit/Hyperactivity Disorder (ADHD) (5, 6 and 7). Neuropsychologists have compared the tasks of working memory with other tasks assigned to children and found that ADHD children face more problems in tackling with the working memory tasks (8).

A meta-analysis research based on 465 studies has indicated that working memory's dysfunctions are to blame for ADHD disorder. The research has shown that the dysfunctions largely affect the visual-spatial function of mind (9). Verbal working memory is essential for comprehension of long sentences so that the capacity of verbal working memory can help predict the probable performance of an individual in answering questions in the comprehension section of a Scholastic Aptitude Test (SAT) (10). Moreover, working memory plays a significant role in controlling attention and retaining relevant information during the problem solving process. It is generally stated that working memory serves as the sole and significant factor in determining the general ability of mind (11). Individual differences in terms of working memory capacity may provide clues to determine individual differences concerning levels of non-verbal Intelligence Quantity (IQ). Additionally, researchers have recently discovered a strong relationship between the capacity of working memory and the ability of mind to steer away from irrelevant information or distraction (factor disrupting concentration) (12).

Further, a significant research demonstrated poor performance in executive functions and attention on the part of children suffering from neuropsychological/ developmental learning disabilities. Seidman and Biederman have cited several significant studies indicating that neuropsychological disorders, including deficiency in performing executive functions or attention in pre-school children may linger until older ages, causing them serious problems in performing school duties or personal affairs. Therefore, it is imperative to identify and diagnose the sort of problems in preschoolers before it is too late so that early interventions are planned (13 and 14).

The findings of these psychological researches comply with neurological studies, showing that children who enjoy higher working memory capacity are less likely to store irrelevant information. The prefrontal cortex of the brain performs a major function in preparing the organ for filtering irrelevant information. Children with higher working memory capacity show more activities in their prefrontal cortex and subsequently act more successfully in filtering disruptors of concentration (15). Researchers nowadays have identified working memory as the cerebral platform to blame for Attention Deficit/Hyperactivity Disorder (ADHD) and for the same reason, it has been examined extensively. Studies initially indicated that working memory training may improve mental impairment in children suffering from Attention Deficit/Hyperactivity Disorder (ADHD). Ever since, researchers across the world embarked to apply working memory training in teenagers and adults suffering from Attention Deficit/Hyperactivity Disorder (ADHD).

A Swedish team at the credible Karolinska center for the first time showed that working memory may be improved through computer-based training. Led by Klingberg (2002), the team was first to challenge a previous theory that claimed working memory is stable, stating that working memory could be modified. Researchers at Karolinska University showed a vacuum in visual working memory that may help distinguish children suffering from the ADHD from their normal peers. The studies showed that the distinction grows increasingly wider, dealing a hammer blow to mental concentration in ADHD patients (16).

Loccas (2008), a researcher at New York University found that children suffering from the ADHD show substantial improvement after receiving working memory training concerning the visual-spatial memory (17). Several researchers have studied the effects of methylphenidate and cognitive-behavioral therapies on children suffering from this disorder. Accordingly, medicines have proved effective in improving school performance, social interaction and behavioral symptoms. However, parents and physicians do not approve of drugs in light of their side effects and long term impact. On the other hand, administration of drugs has proved to be causing a range of initial problems (1). Furthermore, although methylphenidate may help improve daily performance in children suffering from the disorder, it is not that effective for the patients in the long run when applied in isolation from other therapeutic methods. The argument has thus led researchers to apply other therapeutic methods including cognitive-behavioral therapies and behavioral balancing methods (18).

The present study examines whether there is sufficient empirical evidence to argue that non-drug therapies such as working memory training may help rectify or remove numerous imminent problems in children with ADHD, particularly attention and behavioral problems. The study aims to contrast the outcome of therapy with methylphenidate plus working memory training with that of

methylphenidate in isolation in treating attention deficit hyperactivity disorder.

Material and Methods

In the present study, a pretest-posttest project was conducted and compared with the control group's results. The research examined the effect of methylphenidate and working memory training in rectifying ADHD in 6 to 12 year old children and compared the results with those of the control group who took methylphenidate only. Further, this study examined the pretest and posttest results and compared and contrasted the effects of the interventions.

The subjects were 6-12 year old children suffering from ADHD who were referred to Tehran's Children Psychotherapy Clinic in 2011 and qualified for research parameters.

For sampling, a list of all patients visiting the clinic was developed; and next, 48 individuals (having calculated the loss of subjects) were selected through a relative, stratified, randomized sampling using the Cochran formula. Having met the ratio of strata in the statistical universe, the selected samples were put into two groups: working memory training and methylphenidate group, and methylphenidate without any other intervention. The samples were involved in the research project after consent was obtained from their families. Inclusion criteria were: 1) age between 6-12; 2) diagnosis of ADHD based on the Diagnostic and Statistical Manual Disorders IV – Text Revised (DSM- IV-TR), confirmed by the clinic's psychiatrics as well as Conners' Parent Rating Scale (CPRS-48) which was applied by the researcher.

Exclusion criteria were: 1) simultaneity of pervasive developmental disorders; 2) mental retardation; 3) major physical disease; 4) records in drug abuse in subjects or parents, symptoms of psychosis in subjects or any need to be hospitalized.

Children who were written off based on the diagnostic interviews by psychiatrics were recorded in the samples' record.

Assessment

Conners' Parent Rating Scale (CPRS-48)

CPRS-48 revised questions out of a 93-item questionnaire (19). Four scales have been provided for every question rating from 'never' to 'very much,' graded from 0 to 3. The questionnaire must be filled up by one of the parents (of any subject involved in the project) once before and once after the interventions are carried out. Conners' 48-item scale has been designed to assist determining whether and how 3-17 year old children might suffer from ADHD (20). The test is sensitive to treatment effects (Pollard, Ward and Barkley). Having applied Pearson Correlation and Cronbach's Alpha methods, Khushabi et al. (2006) put the validity of the scale as well as level of correlation between every question and the whole scale at 98 percent after evaluating the empirical, standardized scale. They reported the scale's reliability in replications at 70 to 90 percent (21).

N-Back Neuropsychological Test:

As a complimentary study and to check the interventions, N-Back Neuropsychological Test was performed (besides Conners' Parent Rating Scale) to measure the subjects' working memory performance. The test was carried out by computer and through a gradual increase in mental assignments at three levels of 1-Back, 2-Back and 3-Back. The subjects were asked to look at monitors (where frames of images were displayed) and remember several moving and changing images. Once an image was re-displayed, they had to push a button.

The N-Back visual memory test has been designed to evaluate the cognitive sphere of working memory. The test series are all visually designed and free from any specific language. The test series are carried out by computer. Validity and reliability of the test for the Iranian population, it must be noted that the test designers recommended that the test be applied for any subjects in any different culture as the tool runs independent of any specific language or culture. On the other hand, the test does not serve as a diagnostic tool in the present study and subsequently no specific disorder is going to be determined within the test. It only serves to compare the raw marks gained by the target group in the pretest and posttest. For the same reason, the test has no need in aligned marks.

The test could be applied in the same manner as other neuropsychological tests before contrasting the results. However, the test can be used to determine any possible disorder in executive functions in the mind, including working memory disorder. Neuropsychological tests always prove successful in diagnosing and identifying disorders in executive functions in individuals suffering from ADHD. For data analysis, descriptive statistical methods and analytic statistical methods, including T-student test and Q-Q Plots diagram were applied.

Result

The target group and the control group have scored means of 58.13 and 60.28 in the pretest respectively while they have scored means of 49.73 and 58.40 in the posttest, as shown in (table 1). The means in the posttest are more than those of the pretest for both groups. The two groups have scored an equal median of 59 in the pretest while they have scored medians of 50 and 57 in the posttest respectively, indicating lesser median scores for both groups compared to pretest. As for variance in the pretest and posttest, the target group has scored 13\.39 and 17.11 respectively while the control group has scored 25.37 and 33.58 respectively, indicating a rise for both groups in the posttest, and put it another way In the other words, the two groups showed a wider data dispersion in the posttest compared to the pretest.

As Table demonstrated in table 2 indicates, the lowest mean in the pretest (58.13) has been was scored by the first group (working memory training) while the lowest and highest means in the posttest (58.4 and 49.37

respectively) have been were scored by the control group and target group respectively. Furthermore, the highest standard deviation in the pretest (5.03) belongs belonged to the control group while the lowest standard deviation belongs belonged to the first group. In the posttest, the lowest standard deviation (4.13) belongs belonged to the control group.

The table above shows demonstrates that the means are not equal with the level of significance in the T test being less than 0.001. The Table 3 for its part shows that the mean difference in the working memory training group in the CPRS pretest and posttest is 8.39, while the amount it is 1.88 for the control groups is 1.88, which indicating indicates a larger reduction in the working memory group than the control group, . or put it another way on the other words, levels of disorder in the children with ADHD who have received working memory training has grown lesser was less than those children who have failed to receive the training. The table above shows that the means are not equal with the level of significance in the T test being less than 0.001. It shows that the mean difference of the working memory training group as regards to the 1N-Back pretest and posttest is 34.52 while the figure for the control group is 1.48, indicating that the working memory training group has experienced a larger growth than the control group, or it can be said that the capacity of the working memory in children with ADHD increased after receiving the training. The available scientific evidence as well as the findings of the present study may suggest that working memory training would help alleviate ADHD symptoms in children.

Table 1: Mean, median and variance in pretest and posttest in experimental group and control group in children aged 6 to 12

Groups	Pre test				Post test			
	Frequency	Mean	Median	Variance	Frequency	Mean	Median	Variance
Group of Methylphenidate and Working Memory Training (WMT)	23	58.13	59	13.39	23	49.73	50	17.11
Control Group Methylphenidate in Isolation	25	60.28	59	25.37	25	59.40	57	33.58

Table 2: Summary of descriptive statistics for groups Methylphenidate plus working memory training and Methylphenidate in isolation

Groups	Methylphenidate Plus Working Memory Training (WAT)				Methylphenidate in Isolation			
	N	M	SD	M ± SD	N	M	SD	M ± SD
Pretest Conners' parent Rating scale (CPRS)	23	58.8	3.65	58.13 ± 3.65	25	60.28	5.28	60.28 ± 5.03
Posttest Conner's parent Rating scale (CPRS)	23	49.73	4.13	49.73 ± 9.13	25	58.4	5.79	58. ± 5.79

Table 3: Difference of means in the target and control groups in children aged 6 to 12 years old

Groups	Mean		Difference of mean
	Pretest CPRS ($M_{1)}$	posttest ($M_{2)}$	($M_1 - M_2$)
Methylphenidate and Working Memory Training (WMT)	58.1304	19.7391	8.3913
Control Group Methylphenidate in Isolation	60.28	58.4	1.88

Table 4: T test for the working memory training group and the control group in children aged 6 to 12 years old

Variables	Leven's test for equality of variances		T test for equality of variances				
	F	sig	T	df	Sig	Mean Different	std deviation
Difference of Pretest	0.033	0.856	-8.438	46	0	-6.5113	0.77165

Discussion

The means scored by given working memory and control groups in several other studies have been different (22, 23, 24), indicating that children with ADHD show substantial improvement in symptoms of ADHD after receiving working memory training. The results of comparison of mean difference of pretest and posttest scored by the target group and the control group meaningfully indicate that treating the target group with working memory training decreased ADHD symptoms in this group; thus, a cognitive intervention through working memory training may be effective in alleviating the severity of disorder measured in the pre-test.

The findings of this section comply with the findings of several other researches, namely Barkley (1997), Castellanos & Tannock (2002), Rapport et al. (2000), Westerberg et al. (2004), Klingberg (2002), Lucas (2008) and Holmes et al. (2009) (5, 6, 7, 8, 16, 17, 25). Holmes and his colleagues showed that cognitive trainings for children with working memory disorder would help enhance the skill and eventually improve their performance in mathematical tasks. They examined the children six months after the intervention and found that the training results were stably transferred to their school performance in a meaningful manner .

Klingberg and his colleagues tested a training project designed for ADHD. After five weeks of training, they witnessed positive effects on the visual-spatial working memory, verbal working memory, and complex reasoning as well as improvement in the children's attention deficit, hyperactivity and impulsive behavior reported earlier by their parents. The study proved once more that the effects of training would lead to emergence of non-trained skills and tangible positive behavior. The researchers examined the effects 3 months after the intervention and found them available and stable (26). Alloway and his colleagues (2010) compared the impact of training with that of stimulant drug on working memory disorders in children with ADHD (27). They applied the working memory model (3) as the platform of their evaluation and found that cognitive trainings would similarly improve all verbal, visual-spatial and executive aspects of working memory. The positive effects of the intervention were still stable six months later whereas stimulant drug had proved to have left unstable improvement on the visual-spatial working memory.

One more relevant study titled 'cocktail party effect' (an individual's ability to concentrate on a sound unlike a slew of noises in a given environment) has shown that the given ability is directly related to the capacity of the working memory (28). Recent studies have showed that low-capacity working memory is directly related to daydreaming and 'failure to perform assigned works' (29).

Limitations

This present study faces several limitations including low distribution at every given age, albeit caused by the limited age range of the subjects and training and application of behavioral management training method.

Conclusion

This study showed that working memory group had a greater reduction than the control group. In other words, the rate of ADHD in children who have received working memory training is further reduced than the children who have failed to receive the training. Also, it indicated that a cognitive intervention through working memory training would help alleviate ADHD symptoms in the children.

Acknowledgment

We thank children and their families for their participation, and we also extend our gratitude to the staff of Psychiatry and Psychology Research Center.

References

1. Sonuga-Barke EJS, Sergeant J, Nigg J, Willcutt E. Executive Dysfunction and Delay Aversion in Attention Deficit Hyperactivity Disorder: Nosological and Diagnostic Implications. Child and Adolescent Psychiatric Clinics of North America 2008; 17: 367-384.
2. Tannock R., Chaban P. (2007). http://www.aboutkidshealth.ca/IWK/ADHD/ADHD-and-Brain-Function.aspx?articleID=6897&categoryID=IWK_AD-nh1-04
3. Baddeley A. D. (2000). The episodic buffer: A new component of working memory? Trends in Cognitive Sciences 2000; 4: 417-423.
4. Conway AR, Cowan N, Bunting MF. The cocktail party phenomenon revisited: the importance of working memory capacity. Psychon Bull Rev 2001; 8: 331-335.
5. Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. Psychol Bull 1997; 121: 65-94.
6. Castellanos FX , Tannock R. Neuroscience of attention-deficit/hyperactivity disorder: the search for endophenotypes. Nat Rev Neurosci 2002; 3: 617-628.
7. Rapport MD, Chung KM, Shore G, Denney CB , Isaacs P. Upgrading the science and technology of assessment and diagnosis: laboratory and clinic-based assessment of children with ADHD. J Clin Child Psychol 2000; 29: 555-568.
8. Westerberg H, Hirvikoski T, Forssberg H , Klingberg T. Visuo-spatial working memory span: a sensitive measure of cognitive deficits in children with ADHD. Child Neuropsychol 2004; 10: 155-161.

9. Martinussen R, Hayden J, Hogg-Johnson S , Tannock R. A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2005; 44: 377-384.
10. Daneman M, Carpenter GPA. Individual differences in working memory and reading. Journal of Verbal Learning and Verbal Behavior 1980; 19: 450-466.
11. Conway A R A, Moore AB, Kane MJ. Recent trends in the cognitive neuroscience of working memory. Cortex 2009; 45: 262-268.
12. Korkman M, Kemp S, Kirk U. (1998). NEPSY A developmental neuropsychological assessment. San Antonio, TX: The Psychological Corporation; 1998.
13. Seidman LJ, Biederman J, Monuteaux MC, Doyle AE , Faraone SV. Learning disabilities and executive dysfunction in boys with attention-deficit/hyperactivity disorder. Neuropsychology 2001; 15: 544-556.
14. McNab F , Klingberg T. Prefrontal cortex and basal ganglia control access to working memory. Nat Neurosci 2008; 11: 103-107.
15. Klingberg T, Forssberg H , Westerberg H. Training of working memory in children with ADHD. J Clin Exp Neuropsychol 2002; 24: 781-791.
16. Klingberg T, Forssberg H , Westerberg H. Training of working memory in children with ADHD. J Clin Exp Neuropsychol 2002; 24: 781-791.
17. Lucas C, Abikoff H, Petkova E, Gan W, Sved S, Bruett L, Eldridge B. (2008). A randomized controlled of two forms of computerized working memory training in ADHD. New York University: Meeting of the American Psychiatric Association; 2008.
18. National Institute of Mental Health (NIMH), Multimodal Treatment Study of Children with Attention Deficit and Hyperactivity Disorder (MTA), First Received: November 2, 1999 Last Updated: March 26, 2008, ClinicalTrials.gov Identifier; 2008.
19. Conners CK, Epstein JN, March JS, Angold A, Wells KC, Klaric J, et al. Multimodal treatment of ADHD in the MTA: an alternative outcome analysis. J Am Acad Child Adolesc Psychiatry 2001; 40: 159-167.
20. Goyette CH, Conners CK , Ulrich RF. Normative data on revised Conners Parent and Teacher Rating Scales. J Abnorm Child Psychol 1978; 6: 221-236.
21. Khushabi K, Pour-Etemad H, Mohammadi MR, Mohammadkhani P. The prevalence of ADHD in primary school students in Tehran. Medical Journal of the Islamic Republic of Iran 2006; 20: 147-150.
22. 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: 106-113.
23. Klingberg T, McNab F. Working memory remediation and the D1 receptor. Am J Psychiatry 2009; 166: 515-516.
24. Mezzacappa E, Buckner John C. Working Memory Training for Children with Attention Problems or Hyperactivity: A School-Based Pilot Study. Journal of School Mental Health 2010; 2: 202-208.
25. Holmes J, Gathercole SE, Dunning D, (2009). Adaptive training leads to sustained enhancement of poor working memory in children. Developmental Science 2009; E-publ. DOI: 10.1111/j. 1467-7687.2009.00848.
26. 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: 177-186.
27. Alloway T, Elliott J , Holmes J. The prevalence of ADHD-like symptoms in a community sample. J Atten Disord 2010; 14: 52-56.
28. Conway AR, Cowan N , Bunting MF. The cocktail party phenomenon revisited: the importance of working memory capacity. Psychon Bull Rev 2001; 8: 331-335.
29. Kane MJ, Brown LH, McVay JC, Silvia PJ, Myin-Germeys I , Kwapil 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: 614-621.