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Effectiveness of Computer-Based Cognitive Training, Nutritional Supplementations Intervention and Both Combined on the Improvement of Attention, Working Memory, and Behavioral Symptoms of Attention-Deficit Hyperactivity Disorder

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ABSTRACT

Aims Attention-deficit hyperactivity disorder is a common neurodevelopmental disorder characterized by symptoms of hyperactivity, impulsivity, and inattention. This study aimed to compare the effectiveness of various interventions on the improvement of symptoms of attention-deficit hyperactivity disorder.
Materials & Methods Participants were 52 attention-deficit hyperactivity disorder children who were assigned to four experimental and control groups of 13. Data were gathered with strengths and difficulties questionnaire, n-back test, and continuous performance test.
Findings The findings showed that the effect of therapeutic interventions on behavioral symptoms, attention, and working memory was significant. The maximum useful size was observed to be 0.66 on reaction speed, 0.57 on the correct response, and then 0.52 on Omission error. The sustainability of interventions in the next stage was significant and different.
Conclusion The results indicate that most of the components of attention, working memory, and behavioral symptoms in children with attention-deficit hyperactivity disorder have been improved in all experimental groups.

Keywords Attention-Deficit/Hyperactivity Disorder; Cognitive Neuroscience; Dietary Supplementations; Executive Function

CITATION LINKS

[1] Diagnostic and statistical manual of mental ... [2] The worldwide prevalence of ADHD: A systematic ... [3] Prevalence estimations of attention-deficit/hyperactivity ... [4] Maternal report of attention deficit ... [5] Randomized, controlled trial of OROS methylphenidate once a day in ... [6] ADHD prevalence in four Brazilian plublic ... [7] Hyperactivity, attention and concentration deficit ... [8] Prevalence of attention deficit hyperactivity ... [9] Reproductive and environmental casualties: A ... [10] Epidemiology of attention deficit and disruptive behaviour ... [11] xecutive dysfunction in school-age children with ... [12] Executive ... [13] Effects of a computerized working memory ... [14] Working memory: theories ... [15] Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of ... [16] Cognitive deficits in multiple sclerosis: A systematic ... [17] Improving attention and managing attentional ... [18] Annual research review: Infant development, autism ... [19] Handbook of attention deficit hyperactivity ... [20] Preliminary data suggesting the efficacy of attention ... [21] The effect of executive function training ... [22] Effect of action video games on the spatial ... [23] The effect of cognitive computer games on working memory, attention and cognitive flexibility in students with attention deficit/hyperactivity ... [24] Computer-based attention training in the schools ... [25] Increased prefrontal and parietal activity ... [26] Computer-based attention training for treating ... [27] Computerized working memory training ... [28] Role of docosahexaenoic acid in maternal and ... [29] Nutrition and mental performance: A lifespan ... [30] Omega-3 fatty acid status in attention-deficit/hyperactivity ... [31] Dietary protein, carbohydrate, and fat enhance memory ... [32] The role of nutrition in children's neurocognitive development ... [33] The diet factor in attention-deficit/hyperactivity ... [34] Parent management training group fits Iranian ... [35] Captain's log cognitive ... [36] Therapist's guide to learning and attention ... [37] Effect of n-3 supplementation on hyperactivity, oxidative stress and inflammatory mediators in children with ... [38] Zinc sulfate as an adjunct to methylphenidate for the treatment ... [39] Zinc deficiency in attention-deficit hyperactivity ... [40] Relationships between serum free fatty acids and ... [41] Comparative effectiveness of monotherapies and combination therapies for ... [42] Relation between omega 3 fatty acid, Iron, Zinc and treatment of ...

Introduction

Attention-Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder characterized by symptoms of hyperactivity, impulsivity, and inattention and a range of cognitive dysfunctions [1]. There is clear evidence that the symptoms interfere by reducing the quality of social, academic, and/or occupational functioning. The symptoms do not occur exclusively during schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, substance intoxication, or withdrawal). ADHD is a worldwide phenomenon. However, interestingly, the prevalence estimates for ADHD in children vary widely from as low as 1% to as high as 20% [2]. Examples of the prevalence of ADHD in countries: in Colombia 16.4% (in boys 19% and in girls 12%) [3], in the United States 9.5-26% [4, 5], in Brazil 13% [6], and in some cities in Iran: in Tehran 11% [7], in Yazd 16.3% (in boys 19.5% and in girls 13%) [8]. Also, in a small number of studies, the prevalence of ADHD in girls is higher than that in boys or almost equal [9, 10].

A wide range of Executive Functions (EF) is affected in ADHD, and as yet, a specific ADHD cognitive profile has not been identified. The cognitive impairments are very heterogenic in severity and affected areas. Spatial working memory, impulse inhibition, selective and sustained attention are found to be the most impaired functions [11]. Core EF are inhibition [response inhibition (self- control and resisting acting impulsively) and interference control (selective attention and cognitive inhibition)], working memory, and cognitive flexibility [12]. Gray *et al*. showed that dysfunctional neural structures like the posterior and external prefrontal cortex are the cause of ADHD [13]. Working memory is involved in many cognitive tasks. Working memory involves the manipulation, updating, reordering, and processing of information held in short-term memory [14].

There are various treatments for ADHD, including behavior therapy, cognitive-behavior therapy, parental based interventions, nutritional therapy, cognitive rehabilitation training (CRT), group therapy, and self-esteem enhancement. CRT and nutritional therapy are relatively new to the treatment armamentarium and have relatively adequate empirical support [15]. Early diagnosis and proper treatment of ADHD is an essential part of ADHD management that compensates for disabilities and creates practical skills in children with ADHD. The review of ADHD research literature points to the focus on pharmacologic treatment and is primarily based on psychostimulant drugs. However, among experts, there remain issues regarding the scope, effectiveness, and side effects of psychostimulant drugs and the role of drugs in the treatment of children. Therefore, a study in the field of multimodal intervention and an alternative to pharmacologic treatment is essential regarding the impacts of CRT [13]. It is assumed that the interaction of neurons is the basis of behavior. If we accept this assumption, we also have to admit that if the behavior is harmed, this damage is due to a defect in the functioning and interaction of the neuronal system. The improvement of neuronal function is due to the improvement of neurobiological factors, neurochemistry, and neuropsychology [16]. In research on laboratory animals, the formation of dendritic nuclei has been observed after damages in different regions of the brain had occurred. It has been determined that neurons that cannot receive incoming messages due to these damages can create new dendritic nuclei, and this Synaptic Plasticity can also be seen in the improvement and normal learning process as a result of experience, i.e., learning and recovery do not occur without sensory stimulation of the nervous system [17]. In explaining the plasticity of the neurons, Hebe assumed that the transfer of sensory stimuli to adjacent neurons has synaptic properties, and the activation of the neurons leads to simultaneous activation in the damaged neurons [18]. The ability of the human brain to be flexible and self-healing has provided robust evidence that it can be improved with the help of CRT [19]. CRT programs include exercises focused on the visual response, attention, processing speed, memory, and problem-solving. These exercises not only provide flexibility and compatibility in the treatment area but shorten the duration of treatment [20]. In a research on the effect of CRT and psycho stimulant drugs on the ability of planning in children with ADHD, it was shown that CRT leads to improved planning [21]. CRT has the same effects as psychostimulant drugs to improve attention in children with ADHD, and its benefits are sustainable and cause no complications [22]. Studies show that this therapeutic approach leads to the promotion of cognitive skills such as attention, mental flexibility, memory, and other skills, by challenging individual cognitive skills and sequential successes in these challenges and less active brain [23]. It is worth mentioning, in a meta-analytic review, Rapport *et al*. reported that benefits associated with cognitive training programs are unsupported in ADHD. CRT also increases the self-esteem and positive motivation of patients [24]. The recognition of the importance of cognitive skills, the development of computer technology, and the pervasiveness of educational programs and the accuracy and ease of use, have led to the development of diverse CRT programs in a variety of educational areas. These programs were designed to enhance and reinstate past behavioral patterns, as well as stabilization of new behavioral patterns or to compensate for damaged nervous system functions [25, 26]. For example, in a study, it has been shown the impact of using different CRT software on memory improvement [27].

The nutritional ADHD evidence suggests that the mammalian brain is rich in unsaturated Fatty Acids that are not produced in the mammalian body and should be fed through dietary; the role of Fatty Acids is due to the fluidity cortex and function of vectors [28]. Among other effective nutritional supplements, Zinc is also involved in the production of Fatty Acids and Serotonin and is a dopamine inhibitor (Sinn, 2008). Several research evidence suggests that adding Omega-3, Vitamin B, and Iron to children's nutrition will improve cognitive functions and reduce ADHD's behavioral symptoms). Over the past two decades, special attention has been paid to dietary effects on ADHD, and many studies have shown that imbalance of minerals, lack of essential Fatty Acids, deficiency of Amino Acids, and inadequate vitamin B have adverse effects on behavior and food quality is adequate on neuropsychology functions from embryonic to childhood course [29]. Laboratory studies indicate low levels of essential fatty acids in red blood cell membrane phospholipids and low levels of Zinc in the plasma of these ADHD children [30]. Essential fatty acids are components of the Myelin construct in the nerve cell membrane. In the context of the relationship between Omega-3 deficiency and the severity of ADHD symptoms, many studies have been conducted with varying degrees of omega-3 consumption showing contradictory results.

On the one hand, the natural levels of micronutrients in cerebrospinal fluid (CSF) are not necessarily guaranteed for proper central nervous system (CNS) function, and the amount of micronutrients always changes in plasma and is dependent on the daily diet. Therefore, many controlled studies must be undertaken to obtain the desired Micronutrient Indicators that bring about the evolution and normal functioning of the nervous system [31]. On the other hand, research has been conducted to support the effectiveness of Zinc, Iron, and Vitamin B supplements in improving the behavioral symptoms of ADHD patients [32]. Due to the lower cost of these supplements and the absence of side effects of chemical drugs, and when pharmacologic treatment fails or is not preferred by parents and patients, nutritional supplementation can be an optimal alternative [33].

Although CRT has been performed on ADHD patients earlier, in most previous studies, the ADHD patient groups under study were not matched to the severity of their ADHD symptoms, and their therapies were not combined (or compared) with nutritional supplementation therapies. Besides, due to the beginning stage of CRT studies and the treatment regimen, the results were controversial. Such inconclusive outcomes necessitate further research and exploration of the therapeutic areas. Also, the purpose of the combined intervention in which CRT was performed immediately after two months of the nutritional intervention was to determine if the potential positive effects of using food supplements (improving attention and memory and reducing hyperactivity) can facilitate the process of implementing CRT and ultimately make CRT more effective. Furthermore, despite identifying various therapeutic approaches and the multidimensional nature of the problems in people with ADHD, some studies have suggested a combination of therapeutic approaches [34].

n the present study, in addition to reviewing CRT and nutritional supplementation therapies, the effectiveness of the combination of these two classes of treatments on the improvement of behavioral symptoms, attention, and work memory in children with ADHD, without causing any complications, is investigated.

Materials and Methods

The experimental design of the study on a control group was used with three pretests, posttests, and follow-up time measurements (SDQ, CPT, n-back). Raven Test scores and severity disturbances (SNAP-IV scores) were drawn in a coordinate axis. Students who had similar scores of intelligence and severity of ADHD were selected as quadruple blocks and randomly divided into four groups of 13 (three interventional groups and one control group). Age variables were homogeneous in four groups so that the mean age of the four groups did not show a significant difference ($p>0.05$). This study was conducted single-blind.

The statistical population consisted of all primary school girls in Tehran, from among four schools were selected randomly. Few studies have been conducted on the impact of interventions on girls with ADHD disorder. SNAP-IV was completed by the parents of all students from first to sixth-grade elementary school in each of the four schools (150-168 students per school), and children with higher scores were selected. The SNAP-IV teachers' form was also completed and evaluated by the teachers of a positive diagnosis. In cases where ADHD was confirmed at home and school, the children were screened for diagnosis and final approval by a psychiatrist. Students identified with ADHD were included in the selective list for experimental and control groups. In each of the four schools, 15-16 students were identified. The average age of students (all girls) in the selected sample was 8.02 years (SD= 0.98), ranging from 7 to 11. To match groups in terms of their cognitive ability and assess the participants in terms of not having a cognitive disability, the Raven test was conducted. The results of the analysis of variance showed that there was no significant difference in cognitive ability scores between the four groups ($F= 0.009$; $p>0.05$). In the next stage (CSI-4), the parent's form was completed to determine the absence of severe comorbidity disorders in students. The criteria for entry into the study included ADHD recognition, the age range of 7-11 years, cognitive ability of over 85, parental satisfaction, and collaboration. Output criteria for research included mental retardation or having a type of motor or cognitive impairment that interferes with computer work, having severe abnormalities such as Oppositional defiant disorder, Autism, Asperger syndrome, and Depression, and being in the pharmacologic treatment process.

Captains Log Software

Cognitive education software is based on a range of cognitive research that can help people with brain injury, ADHD, learning disabilities, and congenital cognitive disabilities. This program is for people aged 5-90 years and beyond the cultural difference framework. One of the prominent people in the creation of the Captains Log cognitive development system was Sandford [35], who has been working with his colleagues during various researches until 2001 to upgrade the software. Captain Log consists of 50 programs at multiple levels, with many benefits including the existence of various cognitive exercises tailored to the needs of the subjects, easy to difficult hierarchical training, and rapid and effective feedback [36]. The version used in the present study is the English version (produced by the American company Brain Train, version 2014), and before the start of the session, exercises explained for the subjects by the executor. This system contains five modules and 33 separate cognitive-exercises to develop attention, concentration, processing speed, memory, and problem-solving skills. These exercises are directed towards the visual, auditory, and combined visual-auditory stimulus. Captains Log software is implemented in research by Saha *et al.* [26], leading to improved attention, working memory, and processing speed.

After performing pretests in Group 1 (CRT), 22 sessions of 45-minutes cognitive rehabilitation were performed individually using Captain Log software at five-day intervals for four months, which focused on the improvement of attention, concentration, processing speed, working memory, and impulsivity skills. The second group (food supplements intervention), after pretest, Zinc (1mg/kg/day), B6 vitamin (0.6mg/kg/day), and Omega-3 (250mg/day) were prescribed for four months (the administration of supplements was determined in consultation with the pediatrician and the pharmacist). In the third Combined Group, the first phase of the administration of Zinc, B6, and Omega-3 supplements (with the same amount but for two months) was performed, after which the supplements were discontinued, and the CRT sessions started for 45 minutes, twice a week over two months. A total of 15 CRT sessions were held for the 3rd group. Group 4 (the Control Group), after performing pretests (SDQ, CPT, n-back), administration of sucrose tablets, and irrelevant tasks, one day in between was performed as a placebo for four months. In all four groups, at the end of four months and six months, posttest and follow-up time measurements (SDQ, CPT, n-back) were completed for all participants (experimental and control groups).

The statistical analysis conducted in this study is based on a mixed analysis of variance. In this study, four groups were measured in three periods. Hence, there is a between-group variable with four levels, a within-group variable with three levels as independent variables and three-times of measurements. The dependent variables included behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed scores. In doing so, an analysis of variance with repeated measures was used to analyze the data.

Findings

The mean scores and standard deviations of dependent variables are presented in Table 1. For three experimental groups, mean scores of the variables have improved from the pretest to the posttest.

An analysis of variance of repeated measurements was used to check that the changes in the mean scores of dependent variables were not due to an accident. Before the statistical analysis, its assumptions were examined.

Shapiro-Wilk Test was used to examine normal distribution. Distribution of behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed were average in groups ($p>0.05$)

Box Test was used to examine the homogeneity of the variance-covariance matrix. The findings showed that homogeneity assumption is true for behavioral symptoms ($p= 0.2$) and attention subscales including commission ($p= 0.1$), omission ($p= 0.76$), correct response ($p= 0.2$), reaction time ($p= 0.09$), working memory subscales including accuracy ($p= 0.07$) and reaction speed ($p= 0.06$).

Leven Test was used to examine the homogeneity of between groups variance. The results showed that the assumption of homogeneity between groups variance is true for behavioral symptoms ($p= 0.14$), commission ($p= 0.05$), omission ($p= 0.17$), correct response ($p= 0.12$), reaction time ($p= 0.06$), accuracy ($p= 0.06$) and reaction speed ($p= 0.11$).

Mauchly's sphericity test was used for homogeneity analysis of within-group variance. The results showed that homogeneity of within-group variance is not true for behavioral symptoms ($p= 0.001$), commission ($p= 0.001$), omission ($p= 0.003$), correct response ($p= 0.02$), accuracy ($p= 0.02$) and reaction speed ($p= 0.001$). However, it is true for reaction time ($p= 0.2$). The Greenhouse-Geisser correction statistics were used.

The findings of this study showed that the effect of CRT therapeutic interventions, nutritional supplementation, and combined interventions on behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed in children with ADHD was significant in comparison with the control group. The findings showed that the primary and interactive effects were significant.

The main effect of the group or the effect of therapeutic interventions was significant on the variables of behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed, compared to the control group (Wilks's Lambda= 0.28; $F_{21,121.15}$= 14.27; p= 0.0001; Partial Eta Squared= 0.69). Also, the main effect of time (pretest, posttest, and follow-up) was significant on the variables of behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed (Wilks's Lambda= 0.02; $F_{13.36}$= 140.31; p= 0.0001; Partial Eta Squared=0.98). The results showed that the interaction of the group × test time on behavioral symptoms, commission, omission, correct answer, reaction time, accuracy and reaction speed was significant (Wilks's Lambda= 0.02; $F_{39,107.35}$= 7.80; p= 0.0001; Partial Eta Squared= 0.73). Since the interaction effect indicates that the difference in groups is significant at any time (pretest, posttest, and follow-up), one-variable tests were used.

The results of univariate tests of the effect of therapeutic interventions × test time on each of the dependent variables are presented in Table 2. The findings show that the effect of interaction is significant on behavioral symptoms, commission, omission, correct response, reaction time, accuracy, and reaction speed. The maximum effect size is shown in reaction speed (0.66), correct response (0.57), and then in omission (0.52). Bonferroni correction tests were applied after the experiment to monitor the difference in the mean of treatment interventions compared to the control group.

The results of the paired comparison of the mean of the intervention groups with the mean of the control group are presented in Table 3. The findings show no significant difference between the mean of the intervention groups and the control group in the behavioral symptoms' variable in the pre-intervention stage. In post-interventional conditions, behavioral symptoms have improved in the nutritional supplementation intervention and also combined intervention compared to the control group, and sustainability was observed in the follow-up. In CRT intervention, there was no significant change in behavioral symptoms improvement compared to the control group (Table 3; Diagram 1).

In the commission variable, the findings indicate no significant difference between the mean of the intervention groups with the control group before the intervention. However, in the post-intervention period, the commission rate has improved in all three groups of CRT, nutritional supplementation, and combined compared to the control group. Sustainability was observed in commission reduction in the CRT group and combined group in the following. In the nutritional supplementation group, stability was not observed in following the condition than the control group (Table 3; Diagram 2).

In the omission variable, the findings indicate no significant difference between the mean of the CRT group and the combined group with the control group in the pre-intervention stage. Nevertheless, there was a significant difference between the mean of Nutritional Supplementation interventions and the control group. In the post-intervention period, Omission levels in all three therapy groups (CRT, nutritional supplementation, and combined) improved compared to the control group. Sustainability was observed in omission rates in all groups in follow-up (Table 3; Diagram 3).

In the correct response variable, the findings show no significant difference between the mean of three groups than the control group in the pre-interventional conditions. Nevertheless, in the post-intervention period, the correct response in all three CRT, nutritional supplementation, and combined groups has improved compared to that of the control group. Sustainability was observed in the number of correct responses in all groups in follow-up (Table 3; Diagram 4).

In the reaction time variable, the results showed no significant difference between the mean of groups compared to the control group before the intervention. Post-intervention, the reaction time in all three CRT, nutritional supplementation, and combined groups has improved compared to the control group. Sustainability in the reaction time improvement was observed only in the nutritional supplement group. In the CRT group and combined group, no significant sustainability was observed compared to the control group (Table 3; Diagram 5).

In the accuracy variable, the findings indicate no significant difference between the mean of groups compared to the control group before the intervention. However, in the post-intervention phase, the accuracy in the CRT group and the combined group has improved compared to the control group. Stability inaccuracy in the CRT group and the combined group was observed in the following. In the nutritional supplementation group, despite no significant difference in post-interventional conditions, there was a significant difference in the following in comparison with the control group (Table 3; Diagram 6).

In the reaction speed variable, the findings show no significant difference between the mean of the nutritional supplementation group and the combined group compared to the control group in the pre-intervention stage. However, there was a significant difference between the mean of the CRT group compared to the control group. In post-intervention conditions, reaction speed in the nutritional supplementation group improved compared to the control group. Stability was observed in the reaction speed in nutritional supplementation, and combined group in the follow up. There was a significant difference in the CRT group in the follow up compared to the control group, despite no significant difference in the post-interventional conditions (Table 3; Diagram 7).

Table 1) Mean and standard deviations of dependent variables (each group= 13)

Variables	BY	CO	OM	CR	RT	PR	PROP
Cognitive training							
Pre	26.76±5.47	11.23±5.65	23.23±2.24	115.53±6.88	792.92±104.1	69.46±12.25	707.76±143.64
Post	19.23±4.08	1.69±1.49	7.69±3.88	140.6±3.81	585.53±47.07	91.61±6.87	659.70±107.97
Follow	19.46±3.12	1.76±1.53	6.92±2.53	141.3±2.89	546.23±30.67	90.61±9.57	660.38±151.95
Nutritional supplementations							
Pre	25.38±5.5	6.69±6.71	18.84±8.40	124.46±2.17	689.53±4.75	55.53±7.25	547.69±77.41
Post	17.53±3.8	3.69±2.79	7.50±4.46	138.61±4.46	597.92±45.96	67.23±7.81	456.23±32.28
Follow	17.46±3.66	3.76±1.87	7.46±2.22	138.76±3.16	509.53±44.57	78.61±9.81	476.00±10.25
Combined							
Pre	25.07±5.73	4.84±3.86	20.53±2.81	124.61±4.61	727.46±106.05	57.15±6.84	564.3±68.84
Post	17.84±4.16	2.07±2.06	6.23±2.48	141.69±3.4	625.53±40.22	73.15±6.68	468.69±54.51
Follow	17.53±3.47	2.3±1.6	6.76±1.92	140.92±2.28	561.07±50.43	82.84±4.45	438.69±36.44
Control							
Pre	25.84±5.66	9.15±5.74	22.00±2.70	118.00±7.30	744.38±69.05	60.38±9.96	572.3±64.39
Post	23.15±5.42	16.7±7.11	20.15±3.18	113.76±7.49	743.07±161.9	60.46±10.58	586.00±80.53
Follow	22.76±4.71	5.00±1.35	17.3±2.01	127.69±2.52	567.92±36.13	59.23±4.32	1013.38±243.59

Note: BY= Behavioral Symptoms; CO= Commission; OM= Omission; CR= Correct response; RT= Reaction time; PR= Precision; PROP= Promptitude

Table 2) Effect of group interaction×test time on dependent variables

Variables	ss	df*	ms	F	p	Partial Eta Square
Behavioral Symptoms	145.17	3.67	39.67	7.16	0.001	0.31
Commission	1139.52	4.54	245.31	11.34	0.001	0.41
Omission	850.60	4.92	172.86	17.49	0.001	0.52
Correct response	3404.15	5.19	655.93	21.07	0.001	0.57
Reaction time	15798.70	5.63	28060.17	4.31	0.001	0.21
Precision	3723.33	5.15	722.58	12.01	0.001	0.43
promptitude	1735609.49	4.11	422365.59	31.07	0.001	0.66

* Green House Geisser correction has been used.

Table 3) Comparison of paired groups in terms of pre- and posttest and following conditions independent variables

Variables		i	j	Mean Differences[a]		
				Pre	Post	Follow
Behavioral Symptoms		Control	Cognitive Training	-.92	3.92	3.31
			Combined	.77	5.31*	5.23*
			Nutritional Supplementations	.46	5.61*	5.31*
Attention	**Commission**	Control	Cognitive Training	-2.08	14.38*	3.23*
			Combined	4.31	14.00*	2.69*
			Nutritional Supplementations	2.46	12.38*	1.23
	Omission	Control	Cognitive Training	-1.23	12.46*	10.38*
			Combined	1.46	13.92*	10.54*
			Nutritional Supplementations	3.15*	12.61*	9.85*
	Correct response	Control	Cognitive Training	3.31	-26.85*	-13.61*
			Combined	-5.77	-27.92*	-13.23*
			Nutritional Supplementations	-5.61	-24.85*	-11.08*
	Reaction time	Control	Cognitive Training	-48.53	159.23*	21.69
			Combined	16.92	119.23*	6.85
			Nutritional Supplementations	54.85	146.85*	58.38*
Working memory	**Precision**	Control	Cognitive Training	-9.08	-31.23*	-31.38*
			Combined	3.23	-12.69*	-23.61*
			Nutritional Supplementations	4.85	-6.77	-19.38*
	promptitude	Control	Cognitive Training	-180.46*	-73.08	353.00*
			Combined	-37.00	117.31*	574.69*
			Nutritional Supplementations	-20.38	129.77*	537.38*

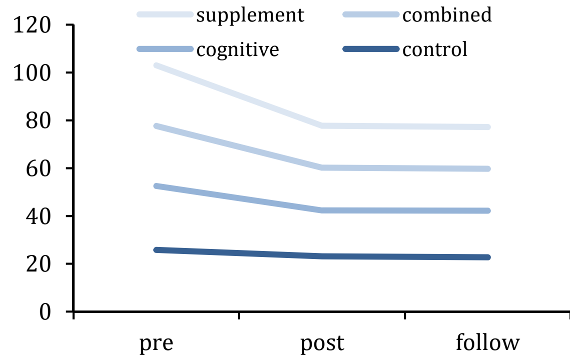

Diagram 1) Interaction effect of group×time on behavioral symptoms

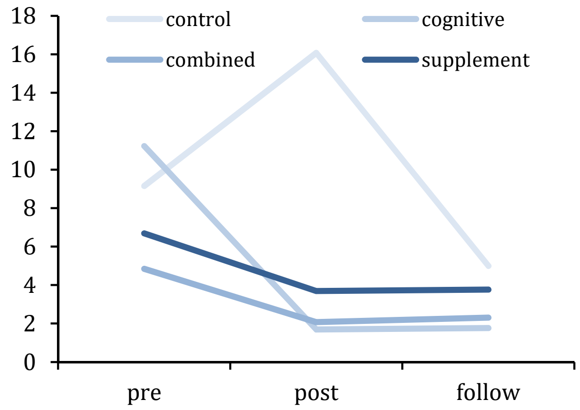

Diagram 2) Interaction effect of group×time on Commission

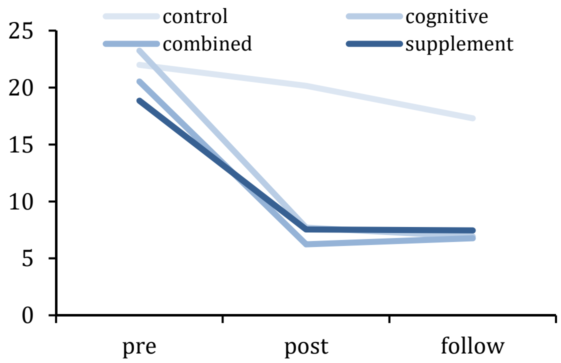

Diagram 3) Interaction effect of group×time on Omission

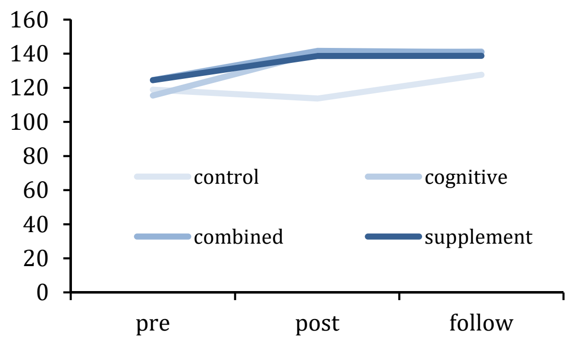

Diagram 4) Interaction effect of group×time on Correct Response

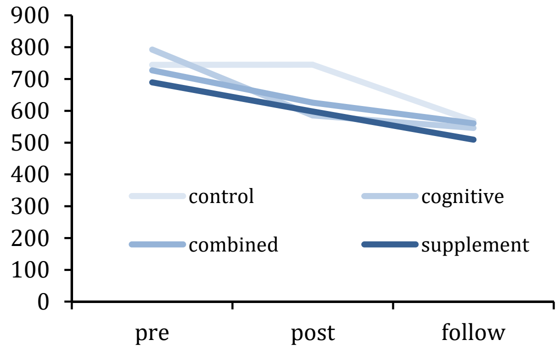

Diagram 5) Interaction effect of group×time on Reaction Time

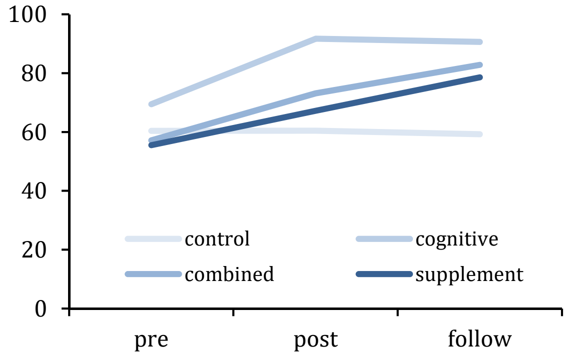

Diagram 6) Interaction effect of group×time on Precision

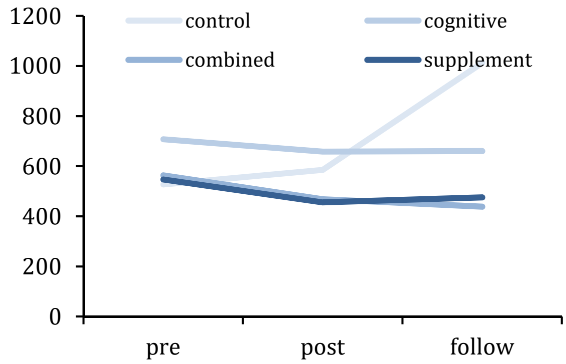

Diagram 7) Interaction effect of group×time on Promptitude

Discussion

The purpose of this study was to investigate the effect of CRT, nutritional supplementation, and a combination of the two interventions on behavioral symptoms, attention, and working memory in students with ADHD. The results indicate that all or most of the components of attention, working memory, and behavioral symptoms in children with ADHD have been improved in all experimental groups compared to the control group. In the Cognitive Rehabilitation Training (CRT) approach, the goal is to reinforce and rehabilitate cognitive components that, by employing exercises and cognitive tasks designed for specific functions, increase the individual's ability to process and interpret information and improve performance in all aspects of social and family life [17]. Repeated activation and stimulation of attention systems make it easier to change cognitive capacity and enhance brain functions. It seems that the exercises provided in cognitive rehabilitation software can improve response inhibition, attention, and work memory in children because they learn orientation skills, response inhibition, multistage commands, and auditory and visual memory. These exercises provide quick stimuli, fast feedback, sequencing, and locative calling, lead to learning new subjects, which improve cognitive abilities and self-control to achieve academic and cognitive success. Further, evidence of the efficacy of CRT in enhancing EF, are all indicative of the significant effect of CRT on EF enhancement [20, 22-26].

Also, consistent with the effectiveness of nutritional supplementation in the present study, the positive effects of Omega-3 in previous studies have been confirmed [31, 32, 37]. Many studies have shown positive effects of Vitamins and Minerals such as Iron and Zinc on the growth and performance of neuropsychology [29, 30, 38]. In explaining the effectiveness of nutritional supplementation, it can be argued that Omega-3, vitamin B6 and Zinc play a role in nerve growth and cognitive functions [39]. For example, Zinc is a vital cofactor for more than one hundred enzymes involved in the metabolism of carbohydrates, proteins, fatty acids, and Nucleic Acids. Also, Zinc has been involved in the production and transformation of melatonin, which effectively sets the sleep cycle in children with ADHD. Melatonin is useful in dopamine regulation, which is an agent involved in ADHD. Zinc is a cofactor for Delta 6 Desaturase production, an enzyme involved in converting fatty acids [40].

Combined intervention (CRT and nutritional supplementation) had a significant effect on improving behavioral symptoms, working memory, and attention, but did not have more efficacy than the other two experimental groups. Of course, the possible explanation is that time of CRT and nutritional supplementation intervention in the combined group (2 months) was half the duration of each intervention (4 months), and a short period can lead to reduced effectiveness of the combined intervention. However, some studies have confirmed the effectiveness of a combination of therapeutic approaches [34, 41].

One of the limitations of this study is that Zinc, vitamin B6, and Omega-3 in the blood of subjects in nutritional and combined groups were not measured before the start of the intervention to determine whether there was a shortage below their normal levels. Second, there was a limitation related to the sample size. Therefore, the strength of the analysis is low in the case of the small samples. According to the findings of this study, it is recommended that CRT and nutritional supplementations be used along with pharmacologic treatment. It is easy to perform CRT for children, it is fun, even with the help of family members at home, and it can lead to improved attention and working memory. Besides improving attention and behavior, nutritional supplementation also has other positive benefits, such as strengthening the immune system, leading to health improvement, and it is relatively less costly than other treatments [42]. You can also perform both interventions according to the benefits mentioned in the absence of any side effects, co-administration, and prolonged periods for children with ADHD. Finally, it is recommended that, in future studies, nutritional interventions should be performed by measuring serum levels of these supplements before and after consumption.

Conclusion

Cognitive rehabilitation training (CRT) as well as dietary supplements can affect cognitive function. Although the combination of the two interventions was effective, it was not as severe as either intervention. In general, these interventions can be used as complementary interventions. Because these interventions are introduced as play or supplementation, they can be more accepted by families than medication.

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Ethical Permissions: Written consent was obtained from the parents of participants. All information about the participants and their families were kept confidential. The Ethics Committee Board of XXX University of Medical Sciences has approved this study (the ethics code: IR.SEMUMS.RC.1397.008). All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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References

1- American psychiatric association. Diagnostic and statistical manual of mental disorders (DSM-5®). Philadelphia: American Psychiatric Association; 2013.

2- Polanczyk G, De Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: A systematic review and metaregression analysis. Am J Psychiatr. 2007;164(6):942-8.

3- Pineda DA, Lopera F, Palacio JD, Ramirez D, Henao GC. Prevalence estimations of attention-deficit/hyperactivity disorder: differential diagnoses and comorbidities in a Colombian sample. Int J Neurosci. 2003;113(1):49-71.
4- Gimpel G, Kuhn BR. Maternal report of attention deficit hyperactivity disorder symptoms in preschool children. Child Care Health Dev. 2000;26(3):163-76.
5- Wolraich ML, Greenhill LL, Pelham W, Swanson J, Wilens T, Palumbo D, et al. Randomized, controlled trial of OROS methylphenidate once a day in children with attention-deficit/hyperactivity disorder. Pediatrics. 2001;108(4):883-92.
6- Fontana RDS, Vasconcelos M, Werner J, Goes F, Liberal EF. ADHD prevalence in four Brazilian plublic schools. Arq Neuropsiquiatr. 2007;65(1):134-7.
7- Ardalan G, Farhoud D, Shah Mohammadi D. Hyperactivity, attention and concentration deficit in preschool children. Iran J Pediatr. 2002;12(4):53-7. [Persian]
8- Akhavan Karbasi S, Golestan M, Fallah R, Sadr Bafghi M. Prevalence of attention deficit hyperactivity disorder in 6 year olds of Yazd city. J SSU. 2008;15(4):29-34. [Persian]
9- Werner E, Bierman JM, French FE, Simonian K, Connor A, Smith RS, et al. Reproductive and environmental casualties: A report on the 10-year follow-up of the children of the Kauai pregnancy study. Pediatrics. 1968;42(1):112-27.
10- Tavakkolizadeh J, Bolhari J, Mehryar AH, Dezhkam M. Epidemiology of attention deficit and disruptive behaviour disorders in elementary school children of Gonabad town, north east Iran (1996-1997). Iran J Psychiatr Clin Psychol. 1997;3(1-2):40-52. [Persian]
11- Lambek R, Tannock R, Dalsgaard S, Trillingsgaard A, Damm D, Thomsen PH. Executive dysfunction in school-age children with ADHD. J Atten Disord. 2011;15(8):646-55.
12- Diamond A. Executive functions. Annu Rev Psychol. 2013;64:135-68.
13- Gray SA, Chaban P, Martinussen R, Goldberg R, Gotlieb H, Kronitz R, et al. Effects of a computerized working memory training program on working memory, attention, and academics in adolescents with severe LD and comorbid ADHD: A randomized controlled trial. J Child Psychol Psychiatr. 2012;53(12):1277-84.
14- Baddeley A. Working memory: theories, models, and controversies. Annu Rev Psychol. 2012;63:1-29.
15- Sonuga-Barke EJS, Brandeis D, Cortese S, Daley D, Ferrin M, Holtmann M, et al. Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. Am J Psychiatr. 2013;170(3):275-89.
16- Ferreira MLB. Cognitive deficits in multiple sclerosis: A systematic review. Arq Neuropsiquiatr. 2010;68(4):632-41.
17- Sohlberg MM, Mateer CA. Improving attention and managing attentional problems. Ann N Y Acad Sci. 2001;931(1):359-75.
18- Johnson MH, Gliga T, Jones E, Charman T. Annual research review: Infant development, autism, and ADHD–early pathways to emerging disorders. J Child Psychol Psychiatr. 2015;56(3):228-47.
19- Fitzgerald M, Bellgrove M, Gill M. Handbook of attention deficit hyperactivity disorder. Hoboken: John Wiley & Sons; 2007.
20- Tamm L, Epstein JN, Peugh JL, Nakonezny PA, Hughes CW. Preliminary data suggesting the efficacy of attention training for school-aged children with ADHD. Dev Cogn Neurosci. 2013;4:16-28.
21- Rostaman H, Talepasand S, Nazifi M. The effect of executive function training on executive performance and behavioral symptoms of children with attention deficit hyperactivity disorder. J Clin Psychol 2013;5(1):93-106. [Persian]
22- Green CS, Bavelier D. Effect of action video games on the spatial distribution of visuospatial attention. J Exp Psychol Hum Percept Perform. 2006;32(6):1465-78.
23- Abdi A, Arabani DA, Hatami J, Parand A. The effect of cognitive computer games on working memory, attention and cognitive flexibility in students with attention deficit/hyperactivity disorder. J Except Child. 2014;14(1):19-33. [Persian]
24- Steiner NJ, Sheldrick RC, Gotthelf D, Perrin EC. Computer-based attention training in the schools for children with attention deficit/hyperactivity disorder: A preliminary trial. Clin Pediatr. 2011;50(7):615-22.
25- Olesen PJ, Westerberg H, Klingberg T. Increased prefrontal and parietal activity after training of working memory. Nat Neurosci. 2004;7(1):75-9.
26- Saha P, Chakraborty P, Mukhopadhyay P, Bandhopadhyay D, Ghosh S. Computer-based attention training for treating a child with attention deficit/hyperactivity disorder: An adjunct to pharmacotherapy-a case report. J Pharm Res. 2015;9(11):612-7.
27- Alloway TP, Bibile V, Lau G. Computerized working memory training: Can it lead to gains in cognitive skills in students?. Comput Hum Behav. 2013;29(3):632-8.
28- Ramakrishnan U, Imhoff-Kunsch B, DiGirolamo AM. Role of docosahexaenoic acid in maternal and child mental health. Am J Clin Nutr. 2009;89(3):958-62.
29- Riby L, Smith M, Foster J. Nutrition and mental performance: A lifespan perspective. London: Red Globe Press; 2012.
30- Antalis CJ, Stevens LJ, Campbell M, Pazdro R, Ericson K, Burgess JR. Omega-3 fatty acid status in attention-deficit/hyperactivity disorder. Prostaglandins, Leukot Essent Fat Acids. 2006;75(4-5):299-308.
31- Kaplan RJ, Greenwood CE, Winocur G, Wolever TMS. Dietary protein, carbohydrate, and fat enhance memory performance in the healthy elderly. Am J Clin Nutr. 2001;74(5):687-93.
32- Nyaradi A, Li J, Hickling S, Foster J, Oddy WH. The role of nutrition in children's neurocognitive development, from pregnancy through childhood. Front Hum Neurosci. 2013;7:97.
33- Millichap JG, Yee MM. The diet factor in attention-deficit/hyperactivity disorder. Pediatrics. 2012;129(2):330-7.
34- Khushabi K, Ghadiri F, Jazayeri A. Parent management training group fits Iranian culture in reducingssymptoms of attention deficit disorder/hyperactivity comparison with pharmaco therapy. Fam Res. 2006;2(7):269-83. [Persian]
35- Sandford J, Browne R. Captain's log cognitive system. Richmond: Brain Train. 1988.
36- Fine AH, Kotkin RA. Therapist's guide to learning and attention disorders. Cambridge: Academic Press; 2003.
37- Hariri M, Djazayery A, Djalali M, Saedisomeolia A, Rahimi A, Abdolahian E. Effect of n-3 supplementation on

hyperactivity, oxidative stress and inflammatory mediators in children with attention-deficit-hyperactivity disorder. Malays J Nutr. 2012;18(3):329-35.
38- Akhondzadeh S, Mohammadi MR, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: A double blind and randomized trial [ISRCTN64132371]. BMC Psychiatr. 2004;4(1):9.
39- Toren P, Eldar S, Sela BA, Wolmer L, Weitz R, Inbar D, et al. Zinc deficiency in attention-deficit hyperactivity disorder. Biol Psychiatr. 1996;40(12):1308-10.
40- Bekaroglu M, Aslan Y, Gedik Y, Deger O, Mocan H, Erduran E, et al. Relationships between serum free fatty acids and Zinc, and attention deficit hyperactivity disorder: A research note. J Child Psychol Psychiatr. 1996;37(2):225-7.
41- Hutton B, Tetzlaff J, Yazdi F, Thielman J, Kanji S, Fergusson D, et al. Comparative effectiveness of monotherapies and combination therapies for patients with hypertension: Protocol for a systematic review with network meta-analyses. Syst Rev. 2013;2:44.
42- Farhud D, Shalileh M. Relation between omega 3 fatty acid, Iron, Zinc and treatment of ADHD. Zahedan J Res Med Sci. 2014;16(8):1-5. [Persian]