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The pros about Ritalin

ORIGINAL ARTICLE

The efficacy of Ritalin in ADHD children under neurofeedback training

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Abstract

Current research has shown that neurofeedback (NF) is a viable treatment for attention deficit hyperactivity disorder (ADHD), however having pharmacological approach alongside such stimulants is still inevitable. Therefore, the purpose of this study is the comparison of neurofeedback with Ritalin and without Ritalin in treating children with ADHD. This study was causal-comparative in design. Participants were children aged 5–10 years with ADHD; seven participants were in neurofeedback group with Ritalin and seven in neurofeedback without Ritalin group according to random split and parent's conformation. Clinical Q, Conner's continuous performance test (CPT), and WISC-R were used before and after treatment. For analyzing data, we used descriptive statistical and Mann Whitney *U* tests. Results showed that even if the two groups were modified in all components, modifications of commission and reaction time of the CPT and F4 theta/alpha of the clinical Q were more accurate in NF with Ritalin treatment rather than the other group. These findings suggest that neurofeedback is efficient in improving some of the behavioral concomitants of ADHD in children whose parents favored non-pharmacological treatment, but Ritalin and neurofeedback combination is more efficient. So, multimodal approach is strongly recommended for ADHD treatment.

Keywords ADHD · Ritalin · Neurofeedback · Clinical Q

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by symptoms of inattention, hyperactivity, and impulsivity and emerges before age of 7 in children. Estimated worldwide prevalence of ADHD is up to 5% in school-aged children [1]. The etiology of ADHD is complicated and multiplex in nature, with research implicating interplay between genetic and environmental agents and their neurological consequences as main causal factors [2–5]. According to neurophysiological studies, behavioral symptoms in ADHD are mostly related to impairments in executive functions such as inhibitory control, problem solving, task performance planning, and working memory [6]. These impairments lead to problems in various domains, including poor academic performance, lower occupational success, poor social relationships, and higher risk-taking behavior [7]. Due to these significant impacts of ADHD on individuals' functioning, considerable effort has been directed at developing effective treatments.

Pharmacological treatment is most successful, efficacious, and widely used in reduction of core ADHD symptoms and improving social behavior. In fact, stimulants such as methylphenidate and various formulations of amphetamine have been demonstrated to improve a wide range of abnormal behaviors of ADHD in a multitude of well-controlled studies with large samples and across long periods [8–10]. Indeed, in most cases, the application of pharmacological interventions is still unavoidable to prevent high impulsive aggressive behavior in ADHD patients [11].

Alongside this usefulness, pharmacology therapeutics have several side effects. A number of children treated with

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stimulants either fail to show long-term improvement in ADHD symptoms or suffer from negative effects on sleep, appetite, and growth [12–15]. Some parents, patients, and clinicians prefer no pharmacologic treatments; in fact, these limitations highlight the need for therapeutic innovation in ADHD to develop effective non-pharmacologic interventions that can improve short-term and long-term outcomes [16].

A range of non-pharmacologic interventions is available to treat ADHD, e.g., psychological interventions, dietary elimination strategies, nutritional supplements, and herbal and homeopathic treatments [17, 18]. Among non-pharmacologic treatment approaches, neurofeedback (NF) has emerged as a promising non-invasive treatment for children with ADHD [19]. Neurofeedback as a subdivision of biofeedback is a self-regulation method aiming to achieve control over brain activity patterns to normalize them and thereby reduce the symptoms of ADHD altering cognition, emotions, and behavior [20, 21].

Since the efficacy of both medication and neurofeedback has been studied separately in majority of well-organized and controlled studies, in the current study, we concentrated on investigating the differences between neurofeedback accompanied with Ritalin and without Ritalin to evaluate whether pharmacological intervention can be removed from ADHD treatment since nowadays most parents and patients prefer using non-pharmacological treatment.

Methods

Participants

The initial sample included 29 participants aged 5 to 10 years. All children belonged to Tehran, Iran, and were referred to psychiatrist from kindergarten and (pre-) school for the first time without history of drug use or any other interventions. Due to Wechsler intelligence scale, children in both groups had intelligence quotient (IQ) higher than 80 [22]. The child behavior checklist (CBCL) [23] and interview by psychiatrist and clinical psychologist were used as an evaluator. Participants with comorbid aberrations were excluded from the study.

From the initial sample, seven clients were excluded from the training process because parents did not agree on continuing treatment based on random classification of study. Two clients were excluded due to getting other interventions such as occupation therapy and play therapy in addition to neurotherapy and pharmacotherapy. One client was excluded because of having an IQ score less than 80. Two other clients were excluded from the study because of comorbid aberration autism spectrum disorder (ASD) and learning disorder (LD). Therefore, our study started with 17 participants: nine clients in NF group, eight clients in NF with Ritalin group. A client from NF with the Ritalin group was excluded from the study in the 21st session because of family issue and his absence in remaining sessions. Two clients from the NF group according to severity of symptoms and lack of enough cooperation were excluded from the study in sessions 5 and 8 (Fig. 1).

Design

Fourteen children aged 5–10 years with ADHD; seven were assigned to the NF with Ritalin group and seven to NF without Ritalin group based on study randomization and family consent. Psychiatrist, psychologist, and neurotherapist diagnosed all participants independently based on semi-structured interviews with their parents and children using DSM-V criteria for inattentive, hyperactive-impulsive, and combined subtype. About two thirds of participants had electroencephalogram test (EEG) as a powerful method of diagnosing brain dysfunctions. Neurofeedback with methylphenidate (Ritalin) group received typically three times 10 mg Ritalin while they were at school or kindergarten and one time 10 mg Ritalin while they stayed at home. Individual dosages were adjusted during the treatment based on psychiatrics' designed drug dosage (5 to 30 mg) because neurotherapy can change the threshold efficacy of medicines during intervention.

The present study is a semi-randomized controlled trial that compares the efficacy of two treatments: neurofeedback and neurofeedback with pharmacological intervention. Figure 2 shows the design of the study. Assessments were applied at two time phases: pre-treatment and post-treatment. The pre-assessment was conducted about a week before starting the treatment and post-assessment was carried out after 6 months from the start because neurofeedback treatment lasts 40 sessions (two sessions in each week).

Treatment phase

dopamine

Neurofeedback training

Neurofeedback training was conducted over a period of 6 months with two training sessions per week. Training was administered to all clients by the same therapist. The procedure followed the paradigm described by Lubar [24] and based on clients' clinical Q profile. Participants were seated in a comfortable armchair in a quiet room. EEG was recorded from two electrodes at position C3–C4 as bipolar montage, Fz and Cz with mono polar montage based on International 10–20 system [25], referenced to linked ear lobes (mastoid ground electrode, sampling rate 128 Hz). SMR training (11–15 Hz) in C3–C4 position was used in the children for the hyperactive–impulsive symptoms, Fz and Cz Beta training (15–18 Hz) were used for primarily inattentive symptoms.

The rationale behind this distinction was that SMR reflects inhibition of the thalamocortical loop and that hyperactivity

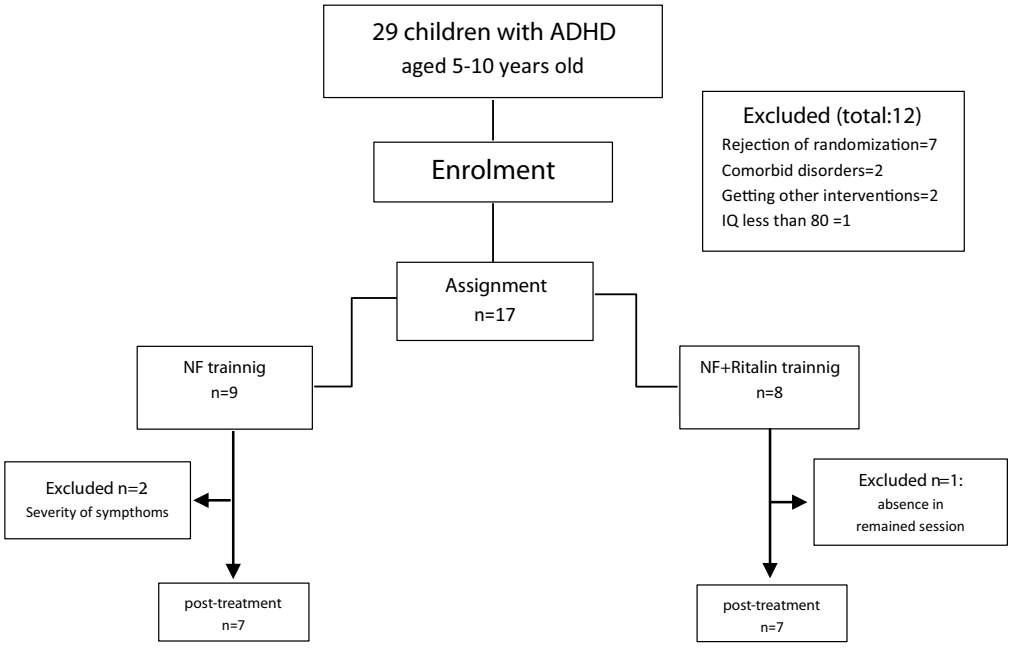

Fig. 1 Flow of participants through each phase

may be related to a right hemispheric overresponsiveness [26]. Attention deficits (decreases in vigilance) on the other hand may be reflected by predominantly left hemispheric slow theta activity and a relative absence of beta activity. The aim of neurofeedback training was to increase the power in the SMR or beta1 bands "reward bands" and simultaneously decrease the power in delta, theta, and beta2 bands "inhibit bands." The therapist throughout the sessions monitored information about the power in each of these frequency bands via a personal computer. Neurofeedback training consisted of 45–60 min of visual and auditory feedback per session, interrupted for short breaks if required by the participant. At the beginning of a training session, threshold levels were determined for each participant from 2-min baseline amplitude measures of activity in the four frequency bands. These levels ranged between 0.5 and 1 μV below or above the baseline values for inhibit or reward bands, respectively. Reward criteria were set, so reward thresholds had to be exceeded in 70% of sampled events in a 500-ms period, and spectral amplitudes had to range below inhibit thresholds in 30% of sampled events to receive a reward. When participants consistently achieved the defined goals (e.g., remained above the reward threshold for 70% of events for two consecutive trials), their thresholds were made more difficult. Visual feedback was provided by a variety of means that translate the EEG amplitude in the reward and inhibit bands into the brightness, size, and/or velocity of objects on a computer monitor. An example would be the Pac Man-type game (mazes) in which an icon moved through a maze eating dots as well as their own DVDS with cartoons. The power in the reward bands (12–15 Hz or 15–18 Hz) determined the speed and brightness of the icon: the higher the power, the faster and brighter the icon. When reward criterion was attained, scores were indicated by an audiovisual signal (a beeping noise and a counter increasing its value). Conversely, when the power in the inhibit bands (1–7 Hz or 22–30 Hz) exceeded its limit, the icon stopped moving and turned black. When the icon reached the end of the maze, a bar chart appeared showing the performance and there was a short break before the next maze started with games such as N-Back and Amazing Brain Train.

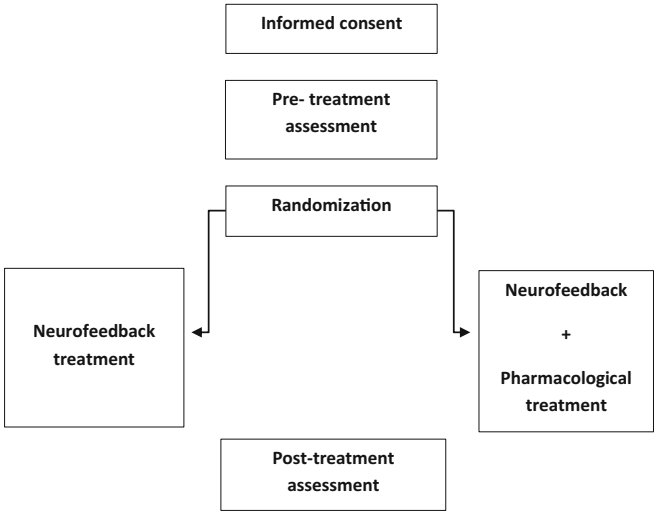

Fig. 2 Design of study

Test materials

Regarding recording treatment progression, the following tests were administered during treatment phase.

Conner's continuous performance task

Conner's continuous performance task (CPT) is a neuropsychological task that has been used frequently to distinguish ADHD patients from normal people in clinical practice [27]. CPT mainly measures sustained attention, distractibility and response inhibition through errors (omissions and commissions), reaction time (RT), and RT variability. In fact, CPT measures the ability to maintain focused attention over usually a 5–20-min period, while responding to target stimuli and inhibiting responses to non-target stimuli [28]. Studies have shown that the CPT paradigm consistently distinguishes control groups from those with ADHD [29]. A meta-analysis by Losier [30] investigated 26 studies on ADHD children. The studies have indicated that ADHD children made significantly more omission and commission errors than normal children. Its variables, including errors of commission, omission, mean hit reaction time (RT), mean hit RT standard error, d', and β, can assess different dimensions of ADHD, based upon clinical assumptions and the face validity of each measure [27].

EEG Z (clinical Q)

The clinical Q is a powerful and accurate assessment tool to evaluate patient's abnormal brainwave patterns, treatment protocols design, and neurofeedback training progress across sessions based on Dr. Swingle's research. The sensor placement for the clinical Q includes five critical regions for rapid and efficient determination of the client's symptoms and requires about 6 min of recording time [31] as shown in Fig. 3.

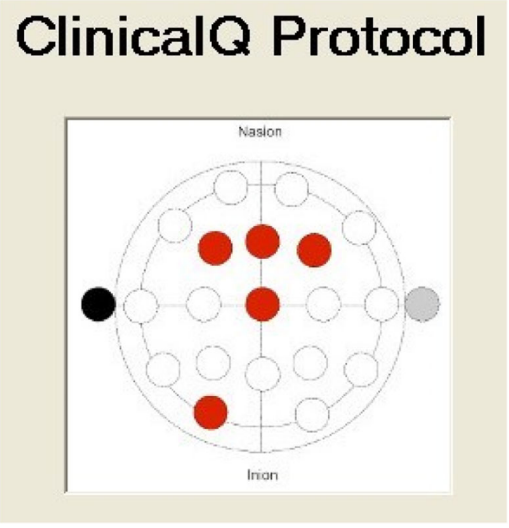

Fig. 3 Clinical Q protocol. The clinical Q requires three bands at any particular site. The 5-point clinical Q locations are Cz, O1, F3, F4, and Fz, using the International 10–20 system

Wechsler intelligence scale for children

In addition to the ADHD-related measures above, the Wechsler Intelligence Scale for Children (WISC)-Revised [22] was applied in order to measure participant's intelligence quotient (IQ) and its change in two treatment groups to assess whether treatment with neurofeedback and medication improves children performance in IQ tests. The WISC-IV contains 15 subtests, 10 of which form the core battery. The 10-core sub-tests are organized to provide four primary index scores (verbal comprehension, perceptual reasoning, working memory, and processing speed). It generates a full-scale IQ that represents a child's general intellectual ability [22]. In addition, WISC-IV was composed of separate verbal and performance scales, each with five or six separate subtests. In this study, we used performance and verbal subscales with reporting the general intelligence. Intelligence quotients ($M = 100$, SD = 15) are calculated based on age norms both for the complete test and for the performance and verbal subscales separately.

Data analysis

Statistical analyses were made using the Statistical Package for the Social Sciences (SPSS) version 19.0. We applied the Mann-Whitney U test for data analysis. The Mann-Whitney U test is a non-parametric test [32]. It means that the test does not assume any properties regarding the distribution of the underlying variables in the analysis [33]. This makes the Mann-Whitney U test the analysis to use when analyzing variables

Table 1 Demographic characteristics and ADHD subtype of participants in treatment groups

	Groups	
	Neurofeedback group ($n = 7$)	Neurofeedback + Ritalin ($n = 7$)
Age	7.29 (2.215)	7.86 (2.410)
Gender (girls/boys)	3/4	2/5
DSM-V subtypes		
Combined type	3	2
Hyperactivity-impulsivity	4	5
IQ (WISC-IV)	91.64 (27.57)	97.83 (12.39)

Table 2 Pre- and post-treatment mean percent rank scores and standard deviations for the subscales of the CPT for the neurofeedback with Ritalin ($N = 7$) and neurofeedback without Ritalin ($N = 7$) groups

Variables	Error	Pre-test Mean (SD)	Post-test Mean (SD)
Neurofeedback with Ritalin	Commission	11.14 (12.7)	0.57 (1.5)
	Omission	10.29 (10.4)	3.57 (4.1)
	Correct	128.57 (18.8)	145.86 (5.0)
	Reaction time	611.86 (85.8)	492.57 (30.6)
Neurofeedback without Ritalin	Commission	17.86 (7.5)	5.00 (5.0)
	Omission	6.43 (6.6)	1.86 (1.2)
	Correct	125.71 (12.3)	143.14 (5.3)
	Reaction time	663.86 (115.0)	543.71 (42.7)

of ordinal scale [34]. We refer to the Mann-Whitney *U* test as the non-parametric version of the parametric *t* test [35].

Results

We showed description of the groups, demographic characteristics, and ADHD subtypes in Table 1, means and standard deviations for the subscales of CPT test at pre and post for NF with Ritalin ($N = 7$), and NF without Ritalin groups ($N = 7$) are presented in Table 2. Moreover, pre- and post-treatment mean percent rank scores and standard deviations for the subscales of the clinical Q for the NF with Ritalin ($N = 7$) and NF without Ritalin ($N = 7$) groups are presented in Table 3.

Pre-post comparison

The changes achieved between the pre-test and post-test scores on the dependent measures provided information about the effectiveness of both methods of therapies in modifying the symptoms of ADHD of the participants. Integrally, subscales of both tests were modified after treatments; however, the rate of modification in NF with Ritalin shows more slightly positive adjustment. In CPT subscales, the most important points are the change of commission and reaction time in NF with Ritalin group in comparison with the other group, so that mean of commission in post-test is near 0 (0.57), and the mean of reaction time is so close to sufficient amount which is considered 500 ms as stimulus presentation time.

On the other side, in clinical Q test, most of the variables were placed in defined acceptable range. The changes of some variables test are so dramatic after treatment, while FZ delta > 9.0 shows probe for cognitive deficits such as problems in concentration and forgetfulness. The marked shift was observed after treatment, especially in NF with Ritalin group. Other subscales have adjusted in normal range too.

NF without Ritalin-NF with Ritalin comparison

As mentioned above, we used Mann-Whitney *U* test for comparison (Table 3) of two independent groups NF with Ritalin vs. NF without Ritalin. Non-parametric tests generally have less statistical power than their parametric counterparts. This means that there is an increased chance of a type II error (i.e., there is more chance of accepting that there is no difference between groups when, in reality, a difference exists).

Table 3 Pre- and post-treatment mean percent rank scores and standard deviations for the subscales of the clinical Q for neurofeedback with Ritalin ($N = 7$) and neurofeedback without Ritalin ($N = 7$) groups

Groups	Variables	Pre-test Mean (SD)	Post-test Mean (SD)
Neurofeedback with Ritalin	FZ delta	20.85 (8.8)	10.13 (3.1)
	CZ theta/beta EO	3.46 (0.7)	2.19 (0.5)
	CZ theta/beta UT	3.46 (0.6)	1.96 (0.3)
	CZ theta/SMR EC	3.94 (0.9)	2.76 (0.5)
	F3 theta/alpha EC	1.41 (0.4)	1.36 (0.1)
	F4 theta/alpha EC	1.37 (0.4)	1.43 (0.2)
Neurofeedback without Ritalin	FZ delta	21.30 (11.2)	12.09 (4.7)
	CZ theta/beta EO	3.11 (0.6)	2.3 (0.6)
	CZ theta/beta UT	3.19 (0.7)	2.15 (0.5)
	CZ theta/SMR EC	4.17 (0.6)	3.36 (0.5)
	F3 theta/alpha EC	0.94 (0.4)	1.07 (0.3)
	F4 theta/alpha EC	1.04 (0.5)	1.04 (0.3)

Table 4 Mann-Whitney *U* test between neurofeedback with Ritalin and neurofeedback without Ritalin groups in CPT

Variables	Groups	Mean rank	Mann Whitney *U*	*Z*	*P*[1]
Commission	Neurofeedback with Ritalin	5.07	7.50	− 2.32	0.02
	Neurofeedback without Ritalin	9.93			
Omission	Neurofeedback with Ritalin	7.50	24.50	0.00	1.00
	Neurofeedback without Ritalin	7.50			
Correct	Neurofeedback with Ritalin	8.71	16.00	− 1.09	0.2
	Neurofeedback without Ritalin	6.29			
Reaction time	Neurofeedback with Ritalin	4.71	5.00	− 2.49	0.01
	Neurofeedback without Ritalin	10.29			

[1] *P* value <0.05 was considered significant for the t test

There were no specific anticipations about which treatment would have the most effect, so the analysis should be 2-tailed. This test relies on scores being ranked from lowest to highest; therefore, the group with the lowest mean rank is the group with the greatest number of lower scores in it. Similarly, the group with the highest mean rank should have a greater number of high scores within it. The important part of the table is the significance value of the test.

This finding indicates that NF with Ritalin is no more of omission and correct than NF group. Both groups report comparable levels of these two items. However, for the commission and reaction time measures, the results are highly significant ($p < 0.05$). The value of the mean rankings indicates that the NF+Ritalin group was significantly more treated in two variables, commission and reaction time, than the other group. The results received by Mann-Whitney *U* test show the better effect of NF with Ritalin treatment on ADHD patients in comparison with NF without Ritalin treatment in two variables of CPT, which are commission and reaction time ($Z < 0.00$ and p value<0.05).

The Mann-Whitney *U* test for clinical Q tool was carried out by SPSS software (Table 4). In this measurement, the results show that NF with Ritalin is no more of all subscales than standard group, except one element, which is F4 theta/alpha EC. In fact, in defined significant level (p value < 0.05), just the variable F4 theta/alpha EC was approved (Table 5).

Discussion

This study aimed to compare the efficacy of neurofeedback with Ritalin and neurofeedback without Ritalin on core symptoms of ADHD in children to evaluate whether medication-based multimodal treatment has any particular superiority relative to single intervention method with the currently popular neurofeedback training.

Former studies on the effect of neurofeedback on ADHD cure have shown that neurofeedback training has a large standardized mean difference (SMD) for inattention and medium SMD for hyperactivity/impulsivity on post- and follow-up treatment relative to baseline [36, 19, 16, 37], in particular neurofeedback can be considered as attention training intervention for children with ADHD [38]. Our results for NF training were in line with these previous studies in terms of NF efficiency on attention improvement. However, the most important output in the current study was the results of commission and reaction time when patients received NF with Ritalin relative to NF group. Indeed, these results demonstrated that when multimodal intervention was applied in addition

Table 5 Mann-Whitney *U* analysis between neurofeedback with Ritalin and neurofeedback without Ritalin groups in clinical Q

Variables	Groups	Mean Rank	Mann Whitney U	*Z*	*P*
FZ delta	Neurofeedback with Ritalin	8.36	16.50	− 1.02	0.30
	Neurofeedback without Ritalin	8.64			
CZ theta/beta EO	Neurofeedback with Ritalin	6.79	19.50	− 0.64	0.53
	Neurofeedback without Ritalin	8.21			
CZ theta/beta UT	Neurofeedback with Ritalin	6.64	18.50	− 0.76	0.45
	Neurofeedback without Ritalin	8.36			
CZ theta/SMR EC	Neurofeedback with Ritalin	5.57	11.00	− 1.73	0.08
	Neurofeedback without Ritalin	9.43			
F3 theta/alpha EC	Neurofeedback with Ritalin	9.57	10.00	− 1.85	0.06
	Neurofeedback without Ritalin	5.43			
F4 theta/alpha EC	Neurofeedback with Ritalin	10.00	7.00	− 2.23	0.02
	Neurofeedback without Ritalin	5.00			

to attention improvement, hyperactivity/impulsivity and reaction time in response to target stimulus have reduced significantly. In 2016, Janssen et al. argued that stimulant-based treatments showed particular improvements in brain function in the P3 region (International 10–20 system) related to response inhibition [39]. In the current study, a similar difference was demonstrated in NF with Ritalin group rather than NF group but in F4 region and on theta/alpha ratio which based on clinical Q report is described to probe for frontal alpha ADD, which makes problems with organization, sequencing, planning, and task completion in ADHD patients. Because clinical Q report is based on five places on the 10–20 system, there must be other differences that can appear in QEEG-based brain mapping which clinical Q failed to show.

Based on the reports, it is possible to infer that reducing hyperactivity and impulsivity can lead to the differences that is shown in clinical Q variables. Both tools approved that medication-based treatment alongside neurofeedback can improve more the hyperactivity/impulsivity symptoms compared to NF treatment. However, side effects of Ritalin threaten this combined method; the role of drugs in the first steps of treatment trend is inevitable especially in children with high hyperactivity. Therefore, it can be concluded that in some chronic conditions with particular patients, prescription of Ritalin is useful. Regarding this, optimization of Ritalin dosage must be carried out because of its side effects.

Conclusion

The significance of this study is being a semi-randomized controlled trial, which compares multimodal training effect (NF treatment with NF plus Ritalin treatment) on ADHD children. Previous studies mostly concentrated on the comparison of these two treating methods separately compared to the control group. In this study, we introduced pharmacological treatment, as a complement method alongside neurofeedback in cases where parents are reluctant to take pharmacological treatment as a first-line treatment, especially if it is essential for reducing high hyperactivity/impulsivity symptoms in combined type ADHD patients who do not even permit therapists to start the preparation process of neurofeedback training. Therefore, this combined method can be useful in these cases. Moreover, NF method is able to decrease the dosage of medication when implemented in conjunction with pharmacological intervention. Determination of optimum dosage of Ritalin combined with neurofeedback can be the goal of future studies as well.

The main limitation of this study is its small sample size. Because in this study, parents paid the cost of treatment, so tendency rate to participation in this study was low; consequently, the sample size of the study is just 14 participants. Investigation in larger sample groups for evaluating multimodal treatment is highly recommended.

The other limitation is that the research team could not investigate the effects of treatments on participants in follow-up periods that could have caused different results. Regarding this, follow-up studies, including 2 months and 6 months, are highly recommended by this study to indicate the long-term stability situation of different treatment methods applied in this study. Moreover, for these sorts of studies which involve brain functioning, having brain map such as QEEG can be very important to infer the outcomes more accurately.

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