

Neurofeedback Versus Pharmacological Intervention in the Treatment of Childhood Attention Deficit/Hyperactivity Disorder (ADHD): First Spanish Clinical Neuropsychological Study

Denise Medici^{1, 5, *}, Pau Giner Bayarri², Rosa Chilet Chilet², Juan Moliner Ibáñez², Maria Morales Suarez-Varela^{1, 3, 4, *}, Dayana Calvo⁶

¹Department of Preventive Medicine, University of Valencia, Valencia, Spain

²Department of Neurophysiology, Hospital Universitario Dr. Peset, Valencia, Spain

³Department of Biomedical Research Consortium for Epidemiology and Public Health (CIBERESP), Valencia, Spain

⁴Center for Public Health Research (CSISP), Valencia, Spain

⁵Department of Neuropsychology, Hospital Vithas Nisa 9 de Octubre, Valencia, Spain

⁶Department of Neuropsychology, James A. Haley Veteran's Hospital, Tampa, USA

Email address:

denise_medici@yahoo.es (D. Medici), maria.m.morales@uv.es (M. M. Suarez-Varela)

*Corresponding author

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Abstract: In this study, twenty children diagnosed with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria (DSM-IV) were randomly assigned to receive NFB training or MPH treatment. The participants were evaluated at the beginning of the study and four months later on measures of behavioral (CPRS/CPRT), executive functions (BRIEF, CPT), attention (TOVA), and electrical activity (qEEG, ERPs). Post-intervention results showed improvements in attention, hyperactivity, executive functioning and in continuous performance measurement (CPT). Improvements noted in the NFB group were greater than that of the MPH group. Results of this study suggest NFB training resulted in greater improvements in executive functioning, behavior, attention, and qEEG compared to MPH treatment. Results indicate that neurofeedback may treat cognitive and behavior functions before these functions worsen or decrease. This study suggests future research to compare the efficacy of each of these treatments in larger populations with a greater heterogeneity in gender is warranted.

Keywords: ADHD, Quantitative Electroencephalogram, Event-related Potentials, Continuous Performance Test, Neurofeedback, Methylphenidate

1. Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common behavioral problem encountered by pediatricians in primary care settings and has a worldwide-pooled prevalence was 5.29% [1] (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Several studies have found that ADHD subjects had more lifetime

psychopathology. Male gender increases risk for disruptive behavior disorders. Female gender and oppositional defiant disorder contributed to risk for depression and anxiety. They had more parent-reported problems in terms of emotional-behavioral role function, behavior, mental health, and self-esteem [2] (McGough, Smalley, & McCracken, 2005). The problems of children with ADHD show a significant impact on the parents' emotional health and parents' time to meet

their own needs, and they interfered with family activities and family cohesion [3] (Klassen, Miller, & Fine, 2004).

In the childhood ADHD population, disturbances can include: behavioral disorders (30-50%), oppositional defiance (15-75%), anxiety (25-50 %), mood alterations (15-75%), and co-morbid learning disorders (8-39%) [4] (Monastra, Lynn, Linden, Lubar, Gruzelier, & LaVaque, 2005). Co-morbid learning disorders can include mathematics (12-30 %), written expression (30-50 %) and spelling (12-27 %) [5] (Monastra, 2005).

ADHD in children is typically treated with stimulants medication. The Methylphenidate (MPH) is currently the first-line pharmacological treatment for children [6] (Myer, Boland & Faraone, 2017) has been show to improved spatial working memory (WM), attention-set shifting and visual-search task performance [7] (Metha, Goodyer, & Sahakian, 2004). However results from a recent meta-analysis highlight the importance of carefully weighing the potential benefits and adverse effects of stimulant medications when prescribing to children. Another important aspect is the sleep impairment because is related to many cognitive (e.g., inattention) and emotional/behavioral (i.e., defiant, anger) and sleep adverse effects could undermine the benefits of stimulant medications in some cases [8] (Kidwell, Van Dyk, Lundahl, & Nelson, 2015). Further, pharmacological treatment works only while it is present in the patient's cerebral system, so ADHD symptoms return after pharmacological management has ended [9] (Barkley, Fischer, Fletcher, & Smallish, 2004). Thus, alternative effective treatments for ADHD are desired.

Neurofeedback (NFB) training has been proposed as an non-invasive method for treatment of neurobehavioral symptoms in ADHD, and to date, there are no known negative side effects [5] (Monastra, 2005). NFB involves recording electrical activity in the brain and transforming it into a digital visual and/or auditory signal that is utilized as feedback to teach the patient to self-regulate the amplitude of specific frequency waves [10] (Hammond, 2011). A significant clinical improvement was reported in nearly 75% of the children treated with NFB [4] (Monastra, Lynn, Linden, Lubar, Gruzelier, & LaVaque, 2005). NFB training seems to have long-lasting effects because learning is internalized [11] (Lubar, 1997). Evidenced of NFB's effectiveness in improving attention and impulsive behavior [12-15] (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009; Magee, Clarke, Barry, McCarthy, & Selikowitz, 2005; Rossiter, 2004; Bluschke, Broschwitz, Kohl, Roessner, & Beste, 2016), and ADHD symptoms [16-21] (Beauregard, & Lévesque, 2006; Fuchs, Birbaumer, Lutzenberger, Gruzelier, & Kaiser, 2003; Kropotov, Grin-Yatsenko, Ponomarev, Chutko, Yakovenko, & Nikishena, 2005; Lubar, Swartwood, Swartwood, & O'Donnell, 1995; Nash, 2000; Thompson, & Thompson, 1998) has been documented. In these studies, the effects of NFB were very specific for situations requiring inhibitory control over responses [15] (Bluschke, Broschwitz, Kohl, Roessner, & Beste, 2016).

In a recent review, the American Psychiatric

Electrophysiological Association summarized the evidence found for clinical utility of quantitative electroencephalogram (qEEG) in dementia [22, 23] (Fahimi, Tabatabaei, Fahimi, & Rajebi, 2017; Garn, Coronel, Waser, Caravias, & Ransmayr, 2017), mood disorders [24, 25] (Haghighi, et al., 2017; Khaleghi, Sheikhan, Mohammadi, & Moti Nasrabadi, 2015), mild head injuries [26] (Thatcher, 2000), learning disabilities [27] (Arns, Peters, Breteler, & Verhoeven, 2007), attention disorders [28-35] (Clarke, Barry, McCarthy, & Selikowitz, 2001, 2001b, 2001c, 2001d; Clarke, Barry, McCarthy, Selikowitz, & Brown, 2002; Lazzaro, Gordon, & Whitmont, 2000; Hobbs, Clarke, Barry, McCarthy, & Selikowitz, 2007; Linden, Habib, & Radojevic, 1996) and psychosis [36] (Fuggetta, Bennett, Duke, & Young, 2014). QEEG allows the determination of EEG differences between children with and without ADHD. Electrophysiological studies have provided consistent evidence for several abnormal oscillations during the resting states in patients with ADHD and the frontal inhibitory system has been implicated in problems with inhibitory regulation. [37] (Barry, Johnstone, & Clarke, 2003). Children with ADHD generally demonstrated qEEG findings characterized by excess of slow theta and/or slow alpha peak performance in the fronto-parietal regions, which might lead to the finding of increased "theta" power [33, 38, 39] (Lazzaro, Gordon, & Whitmont, 2000; Vernon, Egner, Cooper, Compton, Neilands, Sheri, & Gruzelier, 2003; Mann, Lubar, Zimmerman, Millar, & Muenchen, 1992). Other studies have identified greater absolute delta and theta activity and an increased theta/beta ratio as compared to controls [15, 34, 40, 41] (Bluschke, Broschwitz, Kohl, Roessner, & Beste, 2016; Hobbs, Clarke, Barry, McCarthy, & Selikowitz, 2007; Zhang, et al., 2017; Loo, & Scott, 2012). Negative correlations between coherence anomalies in qEEG and ADHD symptoms suggest that several anomalies reflect compensatory brain function, and studies have reported reduced frontal coherence in delta, alpha and gamma waves in patients with ADHD [42] (Barry, Clarke, Hajos, Dupuy, McCarthy, & Selikowitz, 2011). Moreover, coherence differences in ADHD had been may reflect anomalous frontal right-hemisphere linkages that help compensate functional brain anomalies in the left frontal regions. The slighter left-lateralized coherences correlated negatively with the DSM-IV Inattentive and DSM-IV Total scores, and a slighter frontal inter-hemispheric coherence in alpha correlated negatively with the DSM Hyperactive/Impulsive Score [42] (Barry, Clarke, Hajos, Dupuy, McCarthy, & Selikowitz, 2011). One recent work related resting-state EEG anomalies in individuals with ADHD, to their symptom profile and could indicate links between increased inattention scores and reduced resting EEG gamma power. With resting-state EEG coherence, reduced left lateralized coherences across several bands was correlated negatively with inattention scores, while reduced frontal interhemispheric coherence was correlated negatively with hyperactivity/impulsivity scores [43] (Barry, & Clarke, 2013). Finally, the event-related potential (ERP) is a measured brain response that is a direct

result of a specific cognitive event. ERPs have revealed important findings on the background pathologies of children with ADHD [37, 44] (Barry, Johnstone, & Clarke, 2003; Kröger, et al., 2014).

The current study sought to evaluate effects of physiological self-regulation (i.e., NFB) in behavior, cognition, and qEEG and ERP finding in children with ADHD as compared to treatment by stimulant medication (MPH).

2. Methods

2.1. Participants

All patients in the Pediatric Department of the Hospital Universitario Dr. Peset who had been diagnosed with ADHD invited to participate in the current study. ADHD was diagnosed by a pediatrician using a detailed physical examination and clinical interview. The study was supported by the Consellería de Sanitat i Salut Pública of Valencia (DOCV 6507, 26/04/2011) and was conducted in keeping with the Declaration of Helsinki (World Medical Association, 2013, October). Ethics Committee: 10/061 and 11/083.

In the first phase, 20 children (18 males and 2 females) with diagnosed ADHD (10 children per group) participated in the study. Participants had not received any therapeutic and/or pharmacological treatment. Patients were randomized to either NFB or MPH group. In the NFB group (8 males and 2 females), one patient discontinued. The MPH group also started with 10 children, however, two children discontinued due to medication side effects. The participants were required to meet the following inclusion criteria: age 8 to 14 years old; a primary formal diagnosis of ADHD based on a semi-structured interviews with their parents using DSM-IV in the Pediatric Department; no diagnosis of comorbid neurological disorders (epilepsy, traumatic brain injury, Tourette's syndrome); no serious medical conditions; no use of psychostimulants or atomoxetine medication treatment before the study; an intellectual quotient ≥ 80 ; normal EEG results; and a well-structured family, referring to families with the following characteristics: parents who do not obstruct child motivation, perfect attendance at the NFB sessions, and families with a sense of responsibility, because this condition could have an equally strong impact.

Children were excluded from participation if they failed to meet any of these requirements, or if they had serious medical conditions, EEG with abnormal results or brain injury, seizures or epileptic disorders.

2.2. Materials and Procedure

We had access to all records from the diagnoses made by the Pediatric Department and from academic reports. Neither group showed statistically significant differences as between social, educational, family conditions. referring to children from the same neighborhood and similar public schools, and the parents with similar income and studies between Junior and High School.

Prior to the study's initiation, parents of the subjects were informed about their rights and provided with a written informed consent. In the informed consent form, permission was requested to use the participant's neurophysiologic and neuropsychological data for the specified scientific research. The importance of parental support during the four months in both groups was emphasized as a vital consideration for participating. We made a previous stipulation about the importance of parents' support and the probability of perfect attendance for the next four months. This was a random assignment process.

No participant was allowed to leave the treatment during the study.

After considering the diagnostic usefulness of EEG, we obtained more measures using rigorous diagnostic procedures (i.e., structured diagnostic interviews, neuropsychological assessments) and for careful identification of co-morbid diagnoses (including specific learning disorders) and the impact of these disorders on EEG characteristics (see Table 1). The measures in both groups when we started and finished the study were the following: qEEG and ERPs assessment data collection, Parent and Teacher Conners' Rating Scale (CPRS & CTRS in Short Version, Behavior Rating Inventory of Executive Functions Parent and Teacher Form (BRIEF), and Test of Variables of Attention (TOVA).

Pre-treatment screening and baseline neuropsychological measurements

Both scales were rated by parents and teachers.

The Behavior Rating Inventory of Executive Function (BRIEF) parent and teachers rating form contains 86 items in eight non-overlapping clinical scales. These theoretically and statistically derived scales form two indexes: a) Behavioral Regulation (three scales) and b) Metacognition (five scales), as well as a Global Executive Composite score which takes into account all of the clinical scales and represents the child's overall executive function [45].

The Conners 3rd Edition-Parent and Teachers Short form (CPRs and CTRs) is an assessment tool used to obtain the parent's and teacher's observations about the youth's behavior. This short version provides evaluation of the key areas of inattention, hyperactivity/impulsivity, learning problems, executive functioning, aggression, and peer relations. Each of the items on the scale is rated using four categories: "not at all," just a little, "much," and "very much" [46] (Conners, 2007).

Finally, children meeting the clinical criteria for inclusion in the study were evaluated on pre and post both treatments with the TOVA. It is a computer administered/scored test of attention abilities and is considered one of the most widely used measures of attention and impulsivity. These Continuous Performance Tests (CPTs) provide an assessment of an individual's performance on a task that requires tracking of visual stimuli with differential response/nonresponse to target and nontarget stimuli. Scores obtained included errors of inattention (i.e., failure to respond to a target stimulus or absence of a response when one is required and it is called error of omission) and impulsivity

(i.e., response to a nontarget stimuli or when no response was required and it is called error of commission), response time rate and the consistency of response rate (variability). The duration of testing is 21.8 minutes long in each sensory modality (visual and auditory) [47] (Greenberg, Kindschi, & Corman, 2000).

The behavioral scale, the executive functions scale and the two CPT's modalities are reliable markers of executive brain functioning.

Participants were instructed to quietly while the qEEG was recorded on a Neuronic® Medicid using with 36 electrodes (according to the 10-20 electrode international system) for 5 minutes with eyes closed and 30 minutes with eyes open in resting-state conditions. Data were referenced to a common reference placed between Fpz and Fz and the ground electrode was placed on the forehead, according to the International 10-20 system. EEG data were filtered online with a bandwidth of 0.1-30 Hz and electrode impedance was kept constant at ≤ 5 k Ω . EEG estimates were calculated for four frequency bands: delta (1.5-3.5 Hz), theta (3.5-7.5 Hz), alpha (7.5-12.5 Hz) and beta (12.5-25 Hz), for relative power, and the total power of EEG (1.5-25 Hz). The most common form of EEG analysis in this study is the calculation of the absolute and relative power estimates.

ERPs were registered and were computed off-line during the performance of the visual and auditory GO/NOGO task. The epoch of analysis included 100 ms before the first stimulus and 900 ms after the second stimulus. Trials containing electro-oculogram artefacts (exceeding 100 μ V thresholds) were discarded in the analysis.

The time in the study was the same for both groups. In the MPH group, medication lasted the same time (4 months). In the NFB group, 40 sessions per child were run 4-month period.

MPH treatment Condition: Prior to achieving a consistent dose of 36 mg/day, participants began the trial with 18 mg/day for fifteen days, and then increased to 27 mg/day for the following two weeks. Children received one daily dose of 36 mg stimulant prolonged release tablets (Concerta®) for 3 months administered after breakfast.

NFB treatment Condition: Continuous data from NFB recordings were collected, and training carried out, using the Pro-Comb 2 by Thought Technology hardware and software. The protocol used a mono-polar montage with active electrode cup on the scalp (Cz), the reference cup in the right earlobe (A2) and the ground electrode in left earlobe (A1), according to the International 10-20 system.

The individual sessions was started when participants felt relaxed and were able to maintain normal diaphragmatic breathing, referring to breathing that is done by contracting the diaphragm and give more power to empty lungs. Participants were instructed about the rationale of the procedure and about the dependence of the biofeedback signal on brain activity and on attention.

Protocol and Frequency NFB training

The NFB protocol was dependent on the abnormalities (high theta band measures) observed in the qEEG. In the first

phase, children were trained to enhance the amplitude of "sensorimotor rhythm" (SMR, 12-15 Hz) and decrease the amplitude of slow-band theta activity (4-7 Hz). After session number 20, Beta/theta training was conducted during the second phase and children were instructed to decrease the amplitude of theta waves and increase the amplitude in Beta1 waves (15-18 Hz). This intervention is based on the well-known operant conditioning NFB training regimes SMR and "theta-beta" (TB). SMR training is known to reduce hyperactivity and impulsivity, while the beta-1 protocol was maintained to alleviate inattentiveness symptoms. The reward threshold levels were automatically adjusted and the child improved by about 70-80% with the following duration: 50 minutes and a digitally filtered real-time EEG signal every 30 seconds. The 40 to 45 sessions were held over a period of 15 weeks, three sessions of 60 minutes each per week.

2.3. Statistical Analysis

Repeated measures t-tests and ANOVAs were conducted to analyze how behavioral scales and neuropsychological test performance changed after both interventions. The TOVA test measures by ANOVA were corrected by the Bonferroni test.

3. Results

3.1. Effects of NFB Training Compared to the MPH Treatment Group

Pre and post Behavioral ratings: CPRs/CTRs and BRIEF Parent & Teachers Scales

A one sample t test showed statistically significant changes in CPRs/CTR and Brief scales as rated by parents and teachers in both conditions (see Table 1). Based on the findings, specific scales were then analyzed (CPRS Parents & CTRs Teachers: Inattention (In), Hyperactivity/Impulsivity (H/I), Learning Problems (LP), Executive Functioning (EF), Aggression (A), Peer Relations (PR); BRIEF Parents: Inhibit (I), Shift (S), Emotional Control (EC), Working Memory (WM), Plan/Organize (P/O), Organization of Materials (OM), Monitor (M), Global Executive Composite (GEC); BRIEF Teachers: the form evaluates the same functions except Monitor (M).

A one-sample t-tests showed statistically significant differences in many behavior items in both treatment groups (see Table 2): e.g., CPRs: In (NFB, $p = .001$; MPH, $p = .006$). In BRIEF Parents: I (NFB, $p = .024$; MPH, $p = .002$); S (NFB, $p = .001$; MPH, $p = .001$), EC (NFB, $p = .001$; MPH, $p = .001$), WM (NFB, $p = .001$; MPH, $p = .001$), P/O (NFB, $p = .003$; MPH, $p = .003$), OM (NFB, $p = .007$; MPH, $p = .001$), M (NFB, $p = .001$; MPH, $p = .001$) and GEC (NFB, $p = .011$; MPH, $p = .003$). And in the CTRs (In, NFB, $p = .001$; A, NFB, $p = .016$; PR, NFB, $p = .017$). In BRIEF Teachers: S (NFB, $p = .001$; MPH, $p = .001$), EC (NFB, $p = .001$; MPH, $p = .001$), WM (NFB, $p = .001$, MPH, $p = .001$), P/O (NFB, $p = .001$; MPH, $p = .003$), OM (NFB, $p = .001$; MPH, $p = .001$) and M (NFB, $p = .001$; MPH, $p = .001$).

= .001). Notably, the NFB group training group showed statistically significant improvements in some subscales, while the MPH group did not (e.g.: Learning Problems, Executive Functioning and Peer Relations). In contrast, the

MPH group showed statistically significant improvements in some subscales, while the NFB group did not (e.g.: Inhibit in Teacher BRIEF).

Table 1. Description of the groups.

Description of the groups	Neurofeedback (n = 9)	Medication (N = 8)
Male/Female	8/1	7/1
Age mean (SD)	10.1 (1.3)	9.7 (1.0)
Range (years)	8.9/12.11	8.1/12
Diagnosis (DSM IV)		
Inattentive (fr. %)*	22.22	25.00
Hyperactive-impulsivity (fr. %)	0	0
Combined (fr. %)	77.77	75.50
Disorders Associated		
Motor area: tics, anychophagia (fr. %)	11.11	12.50
Behavior: obsessive, aggressive, irritable (fr. %)	33.33	12.50
Social Relations Problem: with parents, sibling, friends (fr. %)		25.00
Emotional Control: anxiety, rigid, ritualistic (fr. %)	11.11	75.50
Psychosomatics: pain (fr. %)	11.11	12.50
Language: dyslalias, verbal comprehension deficit, reading and/or written problems (fr. %)	66.66	75.00
Medication (MPH, Concerta®)	no	36 mg/day

Note: *frequency percentage

Table 2. Comparison in Conners Comprehensive Behavior Rating Scales (CPRS/ CTRS) and in the Behavior Rating Inventory of Executive Function (BRIEF) from Parents and Teachers Pre- and Post-treatment standard scores (means + 1SD).

	Neurofeedback group (n=9)				MPH group (n=8)			
	Time 1 [#]	Time 2 [#]	t.	p value	Time 1 [#]	Time 2 [#]	t.	p value
Parents Ratings								
CPRS								
Inattention	79.56 (9.35)	56.56 (7.16)	5.879	0.001**	72.50 (9.59)	61.00 (12.70)	3.880	0.006*
Hyperactivity/Impulsivity	64.56 (19.34)	52.56 (8.36)	2.813	0.023*	68.00 (16.62)	60.50 (14.78)	1.651	0.143
Learning Problems	66.44 (11.89)	55.78 (6.66)	2.619	0.031*	70.75 (10.99)	63.00 (12.60)	1.802	0.115
Executive Functioning	69.00 (13.05)	55.56 (7.19)	4.182	0.003*	64.50 (11.31)	62.13 (11.49)	0.653	0.532
Aggression	52.78 (9.00)	51.22 (5.47)	0.639	0.540	57.63 (8.10)	53.63 (7.85)	1.375	0.212
Poor Relations	63.22 (9.71)	54.00 (6.30)	2.874	0.021*	71.63 (14.55)	64.38 (13.19)	0.960	0.369
BRIEF								
Inhibit	-1.10 (1.33)	0.55 (0.52)		0.353	0.00 (0.94)	0.62 (0.51)		0.016*
Shift	83.33 (21.68)	0.55 (0.52)		0.009*	76.62 (14.22)	0.62 (0.51)		0.006*
Emotional Control	10.00 (144.00)	0.44 (0.52)		0.001**	10.00 (75.28)	0.50 (0.53)		0.002*
Initiate	0.00 (1.35)	0.44 (0.52)		0.731	0.22 (0.82)	0.50 (0.53)		0.427
Working memory	93.33 (20.38)	0.33 (0.50)		0.006*	102.87 (12.31)	0.50 (0.53)		0.001**
Plan/Organize	2.28 (1.27)	0.44 (0.52)		0.072	2.48 (0.96)	1.00 (0.00)		0.075
Org. of Materials	0.00 (1.13)	0.44 (0.52)		0.157	0.00 (0.48)	1.00 (0.00)		0.072
Monitor	76.66 (17.08)	0.44 (0.52)		0.006*	73.75 (7.62)	1.00 (0.00)		0.001**
Global Executive Composite	6.78 (6.01)	0.55 (0.52)		0.116	10.51 (6.46)	0.55 (0.35)		0.075
Teachers Ratings								
CTRS								
Inattention	77.67 (8.07)	61.00 (5.00)		0.001**	69.13 (9.76)	63.13 (10.81)		0.259
Hyperactivity/Impulsivity	60.00 (15.74)	55.11 (10.71)		0.449	52.25 (11.59)	46.50 (7.05)		0.246
Learning/Executive Functioning	63.89 (9.77)	57.11 (2.61)		0.189	60.88 (10.62)	58.50 (5.52)		0.580
Aggression	65.33 (19.98)	56.78 (14.03)		0.351	54.13 (13.86)	51.00 (8.58)		0.596
Poor Relations	66.00 (10.42)	61.33 (7.10)		0.537	74.63 (16.64)	70.75 (15.67)		0.636
BRIEF								
Inhibit	0.00 (0.73)	0.00 (0.00)		0.332	0.00 (1.13)	0.35 (0.51)		0.117
Shift	93.66 (9.86)	0.00 (0.00)		0.001**	83.37 (16.98)	0.37 (0.51)		0.007*
Emotional Control	566.88 (107.45)	0.00 (0.00)		0.004*	622.25 (91.74)	0.12 (0.35)		0.003*
Initiate	0.33 (0.92)	0.00 (0.00)		0.330	0.00 (0.83)	0.12 (0.35)		0.674
Working memory	104.66 (13.72)	0.00 (0.00)		0.342	98.50 (12.81)	0.12 (0.35)		0.002*
Plan/Organize	3.84 (0.92)	0.00 (0.00)		0.007*	3.06 (1.76)	0.37 (0.51)		0.075
Org. of Materials	0.00 (0.49)	0.00 (0.00)		0.053	0.00 (1.36)	0.37 (0.51)		0.282
Monitor	87.00 (7.21)	0.00 (0.00)		0.001**	80.00 (16.10)	0.37 (0.51)		0.007*
Global Executive Composite	3.49 (2.80)	0.22 (0.44)		0.099	7.59 (5.26)	0.62 (0.51)		0.094

Anova Test. * p < .05. ** p < .01.

3.2. Pre and Post CPT Measurement in Both Groups

Repeated measures ANOVA showed differences between pre- and post-treatment in both groups in the performance of TOVA (see Table 3). Inattention from the Visual test in NFB group ($p = .001$) and in Impulsivity and Inattention in MPH group ($p = .006$, $p = .001$, respectively). Both groups showed statistically significant from pre to post test, in Inattention (In), Impulsivity (Im) and Response Time (RT) from the Auditory test (In $p = .001$ / $p = .001$ respectively; Im $p = .001$ / $p = .001$ respectively; RT $p = .003$ / $p = .008$ respectively).

Table 3. Comparison in Visual and Auditory Test of Variables of Attention (T.O.V.A.®) Pre- and Post-treatment standard scores (means +1SD).

Visual TOVA	Pre-treatment		Post-treatment		P	Auditory TOVA	Pre-treatment		Post-treatment		P
	M	SD	M	SD			M	SD	M	SD	
Impulsivity						Impulsivity					
NFB	76.33	45.59	0.33	0.50	0.055	NFB	88.37	10.29	0.55	0.52	0.001
MPH	87.14	17.17	0.62	0.51	0.006	MPH	72.12	49.73	0.37	0.51	0.001
Inattention						Inattention					
NFB	78.77	11.45	0.55	0.52	0.001	NFB	214.66	51.81	0.00	0.00	0.001
MPH	82.87	18.45	0.37	0.51	0.001	MPH	268.00	89.78	0.37	0.51	0.001
Variability						Variability					
NFB	-1.11	1.63	0.77	0.44	0.442	NFB	4.90	3.12	0.00	0.00	-
MPH	-1.41	1.87	0.62	0.51	0.282	MPH	6.44	4.45	0.12	0.35	0.0634
Response time						Response time					
NFB	-0.66	1.33	0.33	0.50	0.409	NFB	101.0	20.24	0.44	0.52	0.003
MPH	-0.94	1.72	0.37	0.51	0.505	MPH	88.50	24.40	0.37	0.51	0.008

Note: Neurofeedback (NFB), Methylphenidate (MPH), M Mean, SD Standard deviation. Anova Test. * $p < .05$. ** $p < .01$.

3.3. Pre and Post ERPs Measurement in Both Groups

In pre - NFB training group, out of 18 ERPs (nine visual and nine auditory, selective attention tasks), 15 (nine visual and six auditory) had abnormal results (delayed latency and reduced amplitude). In the pre - MPH treatment group, out of 16 ERPs (eight visual and eight auditory), 13 (six visual and seven auditory) showed similar abnormal results. In the post-NFB training time, four Visual ERPs were normalized (normal parameters for latency and amplitude). In the post NFB group, one auditory ERP was normalized and three obtained normal results in the MPH group (Auditory ERPs Normal MPH = 42.85% vs. NFB = 16.66%). In the contrast, in the post - intervention MPH group, four visual ERPs showed more delayed latency compared to the pre-test measures; not negative changes occurred in the NFB group (decline in ERP, MPH = 66.6% vs. NFB = 0.00%).

3.4. Pre and Post qEEG Measurement in Both Groups

In the NFB group, eight pre - qEEGs showed abnormal results, while five abnormal results found in the MPH group. In the post - intervention qEEGs of the NFB group, six showed normal results (normal parameters for each age and gender), while only one had normal results in the MPH group (NFB = 75.00% vs. MPH = 20.00%). In the both groups, abnormal qEEGs showed increased in slow band power activity (an increase in theta, an increased in delta around central and anterior regions and increased in the theta/beta band). No changes were seen in remaining qEEG in either group.

4. Discussion

Both conditions, NFB and MPH treatment, proved

successful in improving the ADHD symptoms. Both groups showed similar improvements in behavioral and executive functioning rating scales. The effect of NFB training on executive functioning (as rated by parents), and in attention (as rated de by teachers) was greater compared to the MPH group, which showed significant improvement only on the Inhibit subscale of the BRIEF (as rated by parents).

Additionally, we discovered potential variations and clinical differences in TOVAs post - treatments in both groups. In pre - treatment NFB group, eight of the Visual TOVA had abnormal results and only one was normal. At post-test, however, five showed normal results, one had a significant improvement and two did not change. Six of the Auditory TOVA pre - NFBs showed abnormal results. At post-test, four had normal results, one displayed an important and significant improvement and only one did not improve. In the pre- MPH treatment group, seven Visual TOVA and eight of the Auditory TOVA had abnormal results. In the post-MPH treatment, three Visual TOVA showed normal results and four remained abnormal, while three Auditory TOVA had normal results and the rest remained abnormal. We found significant statistically changes in both Auditory TOVA in both groups compared with Visual TOVA changes.

In order to assess whether NFB contributed to sustained improvement on a computerized test of attention and impulse control, participants in this study were retested with the TOVA, four months after their initial evaluation. The TOVA was administered again after both treatment (NFB and MPH) washout periods. As described previously, errors of inattention (i.e., failure to respond to a target stimulus) and impulsivity (i.e., response to a nontarget stimuli), as well as, response rate and the consistency of response rate (variability) were obtained in order to assess the sustained effects of NFB. Standard scores below 80 on any of the

TOVA subscales are considered to be significantly less than anticipated in individuals with average intelligence (such as our sample). In this study, NFB training of SMR and beta band components led to significant general attention-enhancing effect and an arousal-enhancing effect and allowed improve both TOVA modalities and faster reaction times in ERPs latency. For these reasons, in post-SMR and Beta training, measures showed improvements in the visual perceptual sensitivity, fewer Omission and Commission errors, and good performance in inattention and impulsivity. Findings are comparable to those of one study, who used the same NFB training protocol for designed to reduce Theta band activity and increase Beta band activity. And as in our research, one study assessed Attention and impulse control were assessed using one Continuous Performance Test called Integrated Visual Auditory CPT (IVA). His results indicated that the predominantly inattentive group showed significant differences on the Control Scale and the Attention Scale of the IVA/CPT; meanwhile the predominantly hyperactive group showed significant improvement on the Control Scale [48] (Duarte E, 2017). This could directly relate to a improve result in the Visual ERPs. The finding and effects from NFB training in the ERPs performance suggests that NFB promising improve attention in ADHD [17, 19, 49, 50] (Fuchs, Birbaumer, Lutzenberger, Gruzelier, & Kaiser, 2003; Lubar, 1995; Egner, & Gruzelier, 2001; 2004).

These results also reflect that electrophysiological training proved improved some concomitant symptoms, such as increased self-attention and positive behavior in children diagnosed with ADHD. Since 2009 several new studies, including 4 placebo-controlled studies, have been published. These latest studies had been review and discussed in more detail. The assessment of specificity of NFB treatment in ADHD was discussed and it concluded that standard protocols such as theta/beta, SMR and slow cortical potentials NFB are well investigated and have demonstrated specificity [51] (Arns, Heinrich, & Strehl, 2014). After both NFB and MPH treatment, qEEG measures revealed a decrease in delta and theta bands in the anterior and central regions. Two participants showed improved absolute and relative alpha power activity. The percentage of this improvement in cortical arousal was high in NFB group, referring and defining by the non-active presence of slow waves as. During these 4 months of treatment, children and their parents did not receive advice, guidance about developing and practicing active and learning strategies to be implemented in daily life situations. which would optimize the performance effects of this training. The families did not report adverse effects.

Today when we talk about ADHD, we refer to a mild or moderate brain dysfunction that may cause a child or a teen with a normal or greater IQ to display poor academic performance and undesirable behaviors. In other words, despite receiving a good education, having normal family support, support of the person who oversees education, they may not be capable of delivering what is expected of him/her. For these reasons, appropriate treatment is vital to

ensure adequate functioning.

Results from this study suggest additional examination of alternative treatment for ADHD is warranted. Future studies may wish employ strategies that not only have potential to improve symptoms in ADHD, but also offer a warm, encouraging and informative environment.

It is very important to personalized the treatment. Patients with ADHD and families must have the opportunity to be heard. Professionals are encouraged to be able to communicate with patients and their families, in both directions because they not only provide information, and but they should to be responsive to the family's emotions and concerns, and they be able to lead the family to an individualized choice, offer treatment options and avoid making judgments. Participants and their families in both group showed differences in many behavior characteristics, e.g.: in the NFB group, desire and/or motivation for change, enthusiasm to work, interest in learning new skills, were genuine and constant. In contrast, in the MPH group, participants did not show these characteristics; they did not receive support in understanding, confidence and honesty from the neuropsychologist.

Based on the knowledge of Roger deBeus and David Kaiser, it is clear that in the future, additional research with larger sample sizes is needed to aid in identifying differences between those who respond positively to NFB training and those who do not. Larger patients samples may better allow the detection of participants who do not respond well to NFB training and thus determine personalized modifications that may result in improved outcomes, for example, patients may benefit participating in additional NFB training sessions [52] (deBeus, & Kaiser, 2011).

5. Conclusions

NFB training showed greater improvements in specific outcome measures in both neurophysiological markers (qEEG and ERP) and in more behavior and executive functioning subscales (CPRS/CTRS and BRIEF) when compared to the pharmacology MPH group.

Future research should address results in larger samples of children with ADHD for greater generalization ability. Conclusions must await upcoming evidence from larger controlled studies and future meta-analyses contrasting NFB and different outcome measures.

Study Limitations

This study is not without limitations. First, our small sample size limits the generalizability of findings, and thus these results should be considered preliminary. Further, while the number and frequency of sessions in NFB group (i.e., 40 sessions total three times a week lasting 50 minutes each) were deemed appropriate and successful in improving electrical brain activity. Future studies should consider altering treatment duration and samples sizes, and should be mindful of the fact that ADHD is a heterogeneous disorder

with several patterns of pathology and different processes that could play a role in successful treatment for children with ADHD.

Competing Interests

The authors declare that they have no competing interests.

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