### Effectiveness of Neurofeedback on the Event-Related Potentials in Children with Attention Deficit/Hyperactivity Disorder

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#### <u>ABSTRACT</u>

**Objective**: The aim of this study was to investigate the effectiveness of neurofeedback therapy on event-related potential (EPR) at both behavioral and physiological level in children (7-12 years) with Attention Deficit/Hyperactivity Disorder (ADHD).

**Methods**: The current study is a quasi-experimental project whit pre-test and post-test control group. In this study, the subjects (12 patients in the experimental group and 12 patients in the control group) were selected after initial evaluation, according to DSM-IV criteria for attention deficit/hyperactivity disorder and the type of sampling is purposeful. Due to control of intelligence variable, the children with normal range of IQ were selected. Subjects were matched as much as possible with respect to age, IQ, and comorbidity with other disorders. Subjects performed visual continuous performance task VCPT at two time points by two months interval (at the start and end of the program). Analysis of variance with repeated measures ANOVA and ANCOVA methods were used respectively for the evolution of neurofeedback effects on EPR and behavioral characteristics (omission error, commission error, and reaction time). For statistical processing SPSS software version 21 was used.

#### **Keywords:**

Attention deficit/ hyperactivity disorder (ADHD), Neurofeedback, Event-related potentials (ERP) **Results**: No significant differences were observed between experimental and control groups in event-related potentials of both behavioral and physiological level.

**Conclusion**: Application of neurofeedback is a useful approach in improving performance of patients with ADHD through the normalization of patient's brain waves, especially in the prefrontal area.

#### **1. Introduction**



ttention Deficit/Hyperactivity Disorder (ADHD) with a worldwide prevalence in children of about 5%-10% (Biederman, 2005; Faraone et al., 2005; Danckaerts et al., 2010; Harpin, 2005) is one of the most

frequent chronic psychiatric disorders in childhood and adolescence with substantial lifelong implications on social and personally functioning, academic performance, and quality of life in general (Danckaerts et al., 2010; Harpin, 2005). Core deficits of ADHD are cross-situational impairments in attention (distractibility), impulse control (impulsivity), and activity (hyperactivity). Neuroimaging studies suggest anatomical abnormalities in individuals with ADHD, consisting of smaller than normal sizes of several brain regions: e.g. frontal cortex (Seidman, Valera, & Makris, 2005), cerebellum (Castellanos et al., 2002), and subcortical structures, like the anterior cingulate cortex (ACC) (Seidman et al., 2006), caudatenucleus, globus pallidus, and corpus callosum (Seidman et al., 2005). These subcortical structures are part of the neural circuits underlying motor control, executive functions, inhibition of behavior, and the modulation

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of reward (Biederman, 2005). Additionally, the volume reductions are related to measures of symptom severity in patients with ADHD (Casey et al., 1997; Castellanos et al., 2002). Furthermore, functional studies referred to a "lazy frontal lobe" i.e. the frontostriatal regions of patients with ADHD are hypoperfused, hypometabolic, and functionally disrupted in comparison to control subjects (Hale, Hariri, & McCracken, 2000). As regards, functional imaging studies of children with ADHD, using Single Photon Emission Computed Tomography (SPECT) indicate a reduced blood flow in the frontal lobe and the basal ganglia but an increased blood flow to the occipital lobe (Lou, Henriksen, & Bruhn, 1990).

Among the various methods to evaluate the activity and function of the brain, event-related potentials (ERPs) due to their high temporal resolution (in ms) are of special significance. ERPs refer to a class of neuroelectric activity that occurs in response to, or in preparation for, a stimulus or response (Coles, Gratton, & Fabiani, 1990). The P300, first reported by (Sutton, Braren, Zubin, & John, 1965) is perhaps the most studied ERP component. P300 (also known as P3 or P3b) is a large, broad, positive component in the ERP that typically peaks 300 ms or more after the onset of a rare, task-relevant stimulus. It has a centro-parietal scalp distribution, which is maximal over midline scalp sites (Squires, Squires, & Hillyard, 1975). P3 reflects multiple cognitive processes, especially attentional resource allocation (Donchin & Coles, 1988). Its amplitude is thought to be a reflection of effortfulness of the stimulus response and the intensity of processing, whereas its latency is taken as a reflection of the speed of information processing(Rodriguez & Baylis, 2007).

Assessment of P3 is important in children with ADHD for several reasons. First of all, it is known that most important aspects of executive functioning frequently affected in children with ADHD are engagement operation (Kropotov, 2010). This process from neurophysiological point of view is associated with the activation of cortical and subcortical structures that are involved in the execution of selected actions, which are disturbed in children with ADHD. From psychological-functional point of view, the engagement operation is associated with combining all brain resources for the action to be accomplished (Kropotov, 2010). This operation is manifested in the P3 components. Secondly, according to Desmedt and Debecker's hypothesis, the occurrence of P3 corresponds to the termination of the decision making process, which is taking place during the categorization of the target stimulus (Desmedt & Debecker, 1979).

Studies of P300 in childhood disorders such as ADHD have suggested that children with this problem may have small P300 amplitudes inboth auditory and visual stimuli. This may be seen in a variety of paradigms. In contrast, the latency of P300 in the oddball task is generally not altered to ADHD (Barry & Rushby, 2006). P300 has been used to track medication effects in children with ADHD as well. For example, Lawrence et al. (2004) recorded that P300 was elicited by target stimuli in a visual CPT. A frontal shift in P300 observed in children with ADHD was found to normalize following administration of methylphenidate. In children with ADHD, a decrement in P300 at posterior electrode sites has been reported in conjunction with an augmentation at frontal sites (Johnstone & Clarke, 2009).

Several treatment options are available for children with ADHD with pharmacotherapy being the treatment of choice (Venter, 2006). Other treatment options include psychotherapy such as behavior management therapy and cognitive control therapy. However, to improve the behavioral symptoms of children with ADHD, other methods like neurofeedback are used. Neurofeedback (NF) is essentially EEG biofeedback, and allows individuals to learn modifying brainwave activity in order toalter and improve states of cognitive processes such as alertness, attention, calmness, internal focus, or flexibility (Demos, 2005; Thompson & Thompson, 2003). This brainwave training and learning self-regulation of brain activity is called EEG biofeedback or neurofeedback. Children with ADHD have specific EEG phenotypes identified as having theta/beta ratios greater than 3:1 in frontocentral region associated with inattention and poor concentration, indicating the need to inhibit slow wave frequencies while increasing sensorimotor and beta 1 (Demos, 2005; Thompson & Thompson, 2003).

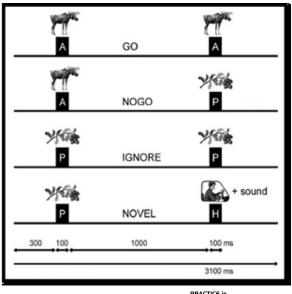
According to evidence-based practice in biofeedback and neurofeedback recommended by international society for mind-body research, health care, and education, the efficacy of NF in ADHD has satisfied the upper level of efficacy (level 4 efficacy) (Yucha & Montgomery, 2008). Such popularity of NF can be explained by the fact that stimulants frequently used for the treatment of ADHD can cause various side effects, including growth suppression. In addition, estimates indicate that as many as 30% of children with ADHD either do not respond to stimulant treatment or cannot tolerate the treatment secondary to side effects. This has lead to the consideration of treatment with both nonstimulant medications as well as alternative therapies, including diet, iron supplementation, and NF (Efron, Hazell, & Anderson, 2011). Only several papers are devoted to the impact of NF on ERP

measures (Kropotov, 2010; Wangler et al., 2011). According to Wangler et al. (2011, the decrease in P3 latency was observed after NF therapy but according to these authors this evidence is less valid, as 18 units for a single NF protocol might have been too small to obtain specific ERP effects. Besides this study was not consistent due to the lack of comparative analysis as it did not include untreated ADHD children as a control group. Thus, assessment of ERP parameters before and after NF treatment is extremely important in children with ADHD.

Therefore, as for non-pharmacological intervention, little is known about the impact of EEG biofeedback (neurofeedback-NF) on P3 characteristics. However, NF has become evidence-based treatment option for ADHD in recent years, so this research was carried out with the objective of designating the effectiveness of neurofeedback therapy on the event-related potentials in children with ADHD.

#### 2. Methods

The current study is a quasi-experimental project with pretest, posttest, and a control group. Population is all primary school children (7-12 years) who have ADHD diagnosis and This research was conducted on 24 children with ADHD and the type of sampling was purposeful. The subjects randomly were divided in two groups. A total of 12 subjects (experimental group) received neurofeedback therapy and the other 12 (group control) did not. The subjects were matched with respect to age, sex, education, intelligence quotient (IQ), disorder intensity, and affliction of another comorbid mental disorder. Both groups were conducted the visual continuous performance task VCPT at the beginning. Then, children in the experimental group received 24 sessions of neurofeedback therapy (3 sessions per week, for 8 weeks). At the end, experimental and control groups performed VCPT task. Before the research, necessary explanations about the procedure and research goals were given to the children's parents. Parents could withdraw their children out of the research anytime. If parents requested, in the form of an individual counseling session, the results would be



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presented to them. The following devices were used to collect data in the present research.

VCPT task: VCPT is a modification of the visual twostimulus GO/NOGO paradigm. Three categories of visual stimuli were selected: 20 pictures of animals, 20 pictures of plants, and 20 pictures of humans (presented together with an artificial "novel" sound). The trials consisted of presentations of pairs of stimuli (see Figure 1): animal-animal (GO trials), animal-plant (NOGO trials), plant-plant (IGNORE trials), and plant-human (NOVEL trials). The trials were grouped into four blocks. In each block, a unique set of 5 animal stimuli, 5 plant stimuli, and 5 human stimuli were selected. Each block consisted of a pseudo-random presentation of 100 stimuli pairs with equal probability for each trial category. The task was to press a button as fast as possible in response to all GO trials.

Neurofeedback Training: In the research, neurofeedback instruction was carried out on the subjects of the experimental group that included a training course modeled as 2 months, 3 times a week and totally 24 sessions. The experimental group received a feedback during the

Table 1. Univariate analysis of covariance of omission errors, commission errors, and reaction time.

	F	Sig.	Partial eta square
Omission error	0.798	0.382	0.037
Commission error	0.102	0.752	0.005
Reaction time	0.05	0.947	0.000
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**Figure 1.** Schematic representation of the two stimulus go/ no-go task.

Effect	F	Sig.	Partial Eta squared
Between-subject	1.762	0.198	0.074
Within-subject	0.004	0.950	0.000
Pillai's trance	1.329	0.251	0.059

Table 2. Test of ANOVA with repeated measure for P300 amplitude at GO stimulus in Fz.

session of the neurofeedback training that was based on their performances. The time allowed for each session was 1 hour. At the beginning of every session, the primary assessment was taken (for 2 min) and then the training was given in the experimental group with the protocol of increase SMR (12-15 Hz)/theta repression (4-7 Hz).

Analysis of variance with repeated measures ANOVA and ANCOVA methods were used respectively for the evolution of neurofeedback effects on EPR and behavioral characteristics (omission error, commission error, and reaction time). For statistical processing SPSS software version 21 was used.

#### 3. Results

## Effectiveness of neurofeedback treatment on behavioral features

In order to study the hypothesis of whether neurofeedback training affects the behavior features in children with ADHD, their omission error, commission error, and reaction time grades were compared in the stages of pretest and posttest in both control and experimental groups. Because of normal distribution grades of omission error, commission error, and reaction time in both groups (according to the results of the Kolmogorov-Smirnov test), univariate analysis of covariance was individually used to examine differences between groups in any of the omission errors, commission errors, reaction time. In addition, Levene's test of equality of error variances was set to default.

As it is shown in Table 1, the difference between the grades of omission error of two experimental and control groups was not significant (F=0.798, P>0.05). The

difference between the grades of commission error of two experimental and control groups was not significant (F=0.102, P>0.05). The difference between the grades of reaction time of two experimental and control groups was not significant (F=0.05, P>0.05) too.

# Effectiveness of neurofeedback treatment on the amplitude of P300 component in $F_z$ , $F_3$ , and $F_4$ scalp locations in the GO and NOGO stimulus

Repeated measure ANOVA was used (Table 2) to assess any difference between the experimental and control groups with respect to P300 amplitudes of  $F_z$ ,  $F_3$ , and  $F_4$  locations at GO and NOGO stimulus before and after neurofeedback treatment.

Table 2 shows that the difference between two experimental and control groups at GO stimulus in  $F_z$  was not significant (F=1.762, P>0.05), but with regard to the effect size column, it can be concluded that although there was no significant difference between the two groups in terms of statistics,the impact of neurofeedback treatment was average (=0.074).

The results of Table 3 shows that the difference between two experimental and control groups at NOGO stimulus in  $F_{\tau}$  was not significant (F=0.003, P>0.05).

Table 4 shows that the difference between two experimental and control groups at GO stimulus in  $F_3$  was not significant (F=0.785, P>0.05), but with regard to the effect size column, it can be concluded that although there was no significant difference between the two groups in terms of statistics, the impact of neurofeedback treatment was average (=0.084).

Table 3. Test of ANOVA with repeated measure for P300 amplitude at NOGO stimulus in F<sub>2</sub>.

Effect	F	sig.	Partial Eta Squared
Between-subject	0.003	0.958	0.000
Within-subject	0.034	0.855	0.02
Pillai's trance	1.386	0.252	0.059
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Effect	F	Sig.	Partial Eta Squared
Between-subject	0.785	0.385	0.034
Within-subject	0.200	0.659	0.009
Pillai's trance	2.016	0.170	0.084
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Table 4. Test of ANOVA with repeated measure for P300 amplitude at GO stimulus in F<sub>2</sub>.

Table 5 shows that the difference between two experimental and control groups at NOGO stimulus in  $F_3$  was not significant (F=0.023, P>0.05).

Table 6 shows that the difference between two experimental and control groups at GO stimulus in  $F_4$  was not significant (F=1.644, P>0.05), but with regard to the effect size column, it can be concluded that despite no significant difference between the two groups in terms of statistics, the impact of neurofeedback treatment was average (=0.070).

Table 7 shows that the difference between two experimental and control groups at NOGO stimulus in  $F_4$  was not significant (F=0.288, P>0.05).

#### 4. Discussion

Based on the present research, the neurofeedback treatment does not have significant effect on omission error, commission error, and reaction time of VCPT task in children with ADHD. Therefore, the first hypothesis of this research about the effectiveness of the neurofeedback treatment on behavioral characteristics in children with ADHD is rejected. These results are consistent with the results obtained from the researches of Faraone et al. (2005) and Nigg, Willcutt, Doyle, and Sonuga-Barke (2005). However, previous research did not investigate the effectiveness of neurofeedback therapy on improving the behavioral function in children with ADHD at VCPT task. ADHD children have failure in response inhibition, interference control, and sustained attention. Commission error measures sustained attention and compulsion control. It signifies first the weakness in the dominant response inhibition and second it is an indicator of weakness in interference inhibition. But omission error and the number of correct answers only measure sustained attention (Pfefferbaum, Ford, White, & Mathalon, 1991). The results of research have shown that the failure of the child in providing answers on NOGO trails depends on the strength of response readiness not on the inhibition response failure (Smith, Johnstone, & Barry, 2004). In addition, the GO/NOGO task entails the use of selective attention and decisions making (Johnstone & Clarke, 2009). So it is likely that a couple of executive functions have simultaneous interference in GO/NOGO task.

On the other hand, a higher reaction time based on the Barkley theory shows that children with ADHD have deficit in conflict inhibition or exclusion of irrelevant stimulus in order to keep paying attention to the current task; a problem that caused an increase in time required to problem solving or decision making. However, these findings may represent a lack of information processing speed in children with ADHD in general and this point of view confirms Barkley's theory that success in other executive functions depends on the individual ability of inhibition. According to the findings of present study, one of the reasons for increasing reaction time can be fatigue of subjects due to long VCPT task. Based on the research findings obtained in the field of neurofeedback training, increasing SMR activity is significantly correlated with reducing impulsivity/hyperactivity and increasing attention processing (Lubar & Shouse, 1976; Sterman, 1996). Thus, the SMR training will result in the decrease of omission error and a decrease in reaction time variation. On the other hand, the activity of the beta 1 are negatively correlated with reduction of commission error (Egner & Gruzelier, 2001). So the beta 1 training reflects the

Table 5. Test of ANOVA with repeated measure for P300 amplitude at NOGO stimulus in F<sub>3</sub>.

Effect	F	Sig.	Partial Eta Squared
Between-subject	0.023	0.880	0.001
Within-subject	0.154	0.699	0.007
Pillai's Trance	0.274	0.606	0.012

Effect	F	Sig.	Partial Eta Squared
Between-subject	1.644	0.213	0.070
Within-subject	0.644	0.431	0.028
Pillai's Trance	0.709	0.409	0.031

Table 6. Test of ANOVA with repeated measure for P300 amplitude at GO stimulus in F<sub>4</sub>.

tendency to the proper quick but not necessary answers because of the increased arousal in general. Therefore, with the improvement of behavioral efficiency in the implementation of assignments in children with ADHD, they gain more sustained attention and their performance on behavioral assignments will improve. However, the results of this study showed that neurofeedback training did not have impact on improving behavioral efficiency in children with ADHD. Perhaps the cause was the low number of neurofeedback sessions and increase in the number of neurofeedback sessions through increasing sustained attention can lead to a reduction of the omission errors, commission errors, and reaction time.

The results of various studies have shown defect in amplitude of P300 component in children with ADHD (Barry & Rushby, 2006; Brown et al., 2005; Johnstone & Clarke, 2009; Senderecka, Grabowska, Gerc, Szewczyk, & Chmylak, 2012; Smith et al., 2004). According to the results of this study, children with ADHD in experimental and control groups, after receiving neurofeedback training did not show a significant difference at P300 amplitude at  $F_z$ ,  $F_3$ , and  $F_4$  sides on the GO and NOGO stimuli. However, the neurofeedback treatment in the experimental group has the modest effect size in increasing the amplitude of P300 component at  $F_z$ ,  $F_3$ , and  $F_4$  at GO stimulus. In fact,one of the causes of the lack of significant results can be the low number of neurofeedback training sessions and the fatigue of subjects.

The lack of a significant effect of neurofeedback is based on (Wangler et al., 2011) the research that examined the impact of two distinct NF protocols (theta/beta and slow cortical potential SCP training) on the ERP components P3 and contingent negative variation CNV (elicited in the Attention Network Test). As a main result, an increase in CNV was observed after NF training. Children with a higher baseline CNV improved more in their parental ratings of ADHD symptomatology after SCP training and the complete NF treatment. Thus, the baseline CNV emerged as a relevant predictor variable for the treatment outcome. In addition, with respect to training related to the rate of changes in beta and theta waves, this research is expected to see the corresponding increase in the rate of P300 amplitude of children. In both groups, an improved test performance and a reduced target-P3 component were found after training, probably mainly reflecting adaptation to the attention test. However, according to the results of the present study, neurofeedback trainings have a modest effect size in increasing P300 component in children with ADHD.

Besides, according to (Desmedt & Debecker, 1979) theory, the occurrence of P300 corresponds with the ending of decision making process happened at the classification of target stimulus. On the other hand, children with ADHD have decreased P300 component to the target stimulus. The reduced amplitude of target P300, and its distinctive distribution in children with ADHD reflect deficit in the high level executive functions such as the allocation of attention and stimulus evaluation that accompanied whit the overall aspects of processing with defects in the right hemisphere (Senderecka et al., 2012). Children with ADHD have abnormalities in the basal ganglia and frontal cortex. These abnormalities included the low metabolic activity, small size, and the widespread transmission of dopamine in the basal ganglia.

In addition, the reduction of metabolic activity of frontal cortex in the children with ADHD is correlated with thalamocortical rhythm disorder that leads to increased theta activity and reduction in beta activity. The SMR

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Table 7. Test of ANOVA with repeated measure for P300 amplitude at NOGO stimulus in F<sub>4</sub>.

Effect	F	Sig.	Partial Eta Squared
Between-subject	0.288	0.597	0.013
Within-subject	0.366	0.552	0.016
Pillai's trance	0.054	0.819	0.002
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training in Cz simultaneously affect sensory-motor cortex, motor cortex, and cingulate cortex (Vernon et al., 2003). The sensory-motor cortex is the boundary of frontal and parietallobes and has a role in coding physical and cognitive assignments. The SMR and beta 1 training are correlated with frontal cortex arousal and increase in the activity of the anterior cingulate cortex.

In addition, both beta 1 and SMR training are positively correlated with increased amplitude of target P300. Also, the difference in the ERP waves resulting from training neurofeedback, can be distributed in the frontal lobes (Egner & Gruzelier, 2001). As a result, the presence of the delay ERP component (such as P300) in response to GO and NOGO stimuli is dependent on the arousal associated with the frontal lobe training and this arousal represents the normal functioning of the executive system. Late ERP components, including P300 are correlated with executive functions and employment and non-employment operations in controlling of behavior. Therefore, as the neurofeedback training leads to relative increases (mean effect size) of P300 amplitude in children with ADHD, this technique can be fitted as an appropriate health care method, in order to improve the event-related potential (ERP), through increased P300 amplitude, in children with ADHD. From practical point of view, neurofeedback treatment through normalizing brain waves of patients, especially in prefrontal cortex, can lead to successful reduction of symptoms of inattention and hyperactivity and improve academic performance in children with ADHD.

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