Macedonian Journal of Medical Sciences. 2010 Dec 15; 3(4):368-377.
doi:10.3889/MJMS.1857-5773.2010.0124
Basic Science

Quantitative EEG Characteristics of Attention Deficit Hyperactivity Disorder in Adults

Silvana Markovska-Simoska[1], Nada Pop-Jordanova[2]

[1]Division of Neuroinformatics, Research Center for Energy, Informatics and Materials, Macedonian Academy of Sciences and Arts, Skopje, Republic of Macedonia; [2]Department of Psychophysiology, University Pediatric Clinic, Faculty of Medicine, University "Ss Cyril and Methodius", Skopje, Republic of Macedonia

Citation: Markovska-Simoska S, Pop-Jordanova N. Quantitative EEG Characteristics of Attention Deficit Hyperactivity Disorder in Adults. Maced J Med Sci. 2010 Dec 15; 3(4):368-377. doi.10.3889/MJMS.1957-5773.2010.0124.

Key words: Attention deficit hyperactivity disorder; Adults; Brain waves; QEEG; Subtypes.

Correspondence: Dr. Silvana Markovska-Simoska. Division of Neuroinformatics, Research Center for Energy, Informatics and Materials, Macedonian Academy of Sciences and Arts. Bul. Krste Misirkov br. 2, P.O.Box 428, Skopje 1000, Macedonia. Phone: +389 2 3235 425; Fax: +389 2 3235 423. E-Mail: silvana@manu.edu.mk

Received: 01-Jun-2010; Revised: 14-Jul-2010; Accepted: 22-Jul-2010; Online first: 09-Nov-2010

Competing Interests: The author have declared that no competing interests exist.

Abstract

Background. Attention Deficit Hyperactivity Disorder (ADHD) in adults is fairly common, though it often goes unrecognized. The few published studies concerning the EEG assessment in the ADHD adults have demonstrated divergent EEG activity.

Aim. Our aim was to identify whether the dividing the ADHD adults into the four QEEG subtypes (according to the Kropotov's classification by comparing the each individual spectra to the Human Brain Institute (HBI) reference database) corresponds to our findings of electrophysiological measures - spectra absolute power (μV^2) for each frequency band (delta, theta, alpha, beta).

Material and Methods. In this study we examined the absolute spectra power of the brain waves through quantitative EEG (QEEG) in two resting conditions (eyes closed and eyes opened) and two neuropsychological tasks (visual and emotional continuous performance tests) from 67 adults diagnosed with ADHD.

Results. Four distinct QEEG subtypes of adults with ADHD were selected according to the Kropotov's classification and then were attested using statistical analysis. These were characterized by (a) increased delta-theta wave activity, (b) increased frontal midline theta, (c) beta excess and (d) alpha excess groups.

Conclusion. We can conclude that the QEEG spectrum power relatively clearly differentiates the ADHD adults into four subtypes. Namely, the obtained results confirmed that the absolute power of all frequency bands depends on the group qualification. These results indicate that adults with ADHD diagnosis constitute a heterogeneous group either with different underlying electrophysiological abnormalities or in clinical expression. These valid subtypes may also have significantly different causes underlying their behaviour, and may respond differentially to medication and neurotherapy, possibilities which merit further investigation.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is the most frequently diagnosed neurobehavioral disorder in childhood. Although ADHD usually first presents in childhood, many persons with the disorder continue to experience symptoms throughout life. ADHD in adults is fairly common, though it often goes unrecognized. According to the American Academy of Pediatrics the prevalence in childhood is estimated at between 6 and 9% [1]. Dennis Cantwell concluded "studies now suggest that as many as 60–70% of the children with this syndrome have continuing symptomatology in adulthood" (in Wender) [2, p.ix]. This would mean that almost 5% of the adults are affected. According to Barkley [3, p.9], clinically, ADHD in adults is viewed as involving two major symptom dimensions: (a) Inattention and (b) Hyperactive–Impulsive behaviour. This disorder may be co-morbid with some psychiatric disorders, especially with alcohol and drug abuse.

Diagnosis of the disorder in the adult population remains dependent on the skills and knowledge of the doctor. At present, no reliable objective measures of ADHD exist. In the last decade many studies have tried to define the neural correlates of ADHD, particularly changes in quantitative EEG (QEEG). Most of the studies concern the ADHD children and summarise that they have a reduced power in alpha and beta bands and an increased power in the delta and theta bands in comparison with the healthy control groups [4-7]. Furthermore, the theta/beta ratio has been introduced by Lubar et al. and Monastra et al. as a diagnostic marker in ADHD children [8, 9] and Clarke et al. and Pop-Jordanova et al. are several authors who have demonstrated that the children with ADHD have a higher theta/beta ratio than normal children [5, 6, 10, 11].

Findings concerning the adolescent population with ADHD showed similar results. Namely, Hobbs et al. [12] investigated EEG abnormalities in male adolescents with ADHD during an eyes-closed resting condition and found absolute dominance of delta and theta activity and a higher theta/beta ratio compared to the control subjects. Similar results (with increased theta activity, along with decreased beta power) but in eyes-open resting condition in adolescents with ADHD has been described by Lazzaro et al [13].

Opposite to the studies with children and adolescents, until now only a few EEG studies with adult ADHD patients have been carried out with different results. Thus, Clarke et al. [14] found global increase in the relative theta, with a decrease in the absolute delta activity, and midline reductions in the beta activity. While Koehler et al. [15] confirmed increased alpha and slow wave (theta) power in eyes-closed, along with no differences in the beta and delta power between ADHD adults and normal subjects. In the other two studies of Bresnahan et al. [16, 17] adult ADHD patients were investigated in an eyes-open condition and an increased power in the slow frequency bands (delta and theta power) as well as an elevated theta/beta ratio compared to the normal control subjects was described.

In contrast to the clear results of the slow frequency bands, the changes in the alpha and beta bands have not been consistent. As it was stated previously, no differences in the alpha and beta bands were found in the ADHD adults in the study of Hobbs et al. [12], but on the other hand, an increased alpha and decreased beta power in adolescents with ADHD was described in the study of Lazzaro et al. [13]. Finally, it has been shown in the paper of Bresnahan et al. [16] that adult ADHD patients had increased alpha and beta activity compared to the normal controls, but in another study of the same author [17] no differences in alpha (absolute and relative) and absolute beta activity in adult ADHD patients were confirmed.

Small number of studies included the EEG subtyping within their clinical samples of ADHD children. Clarke et al. reported that between 15 and 20% of the children with a diagnosis of ADHD combined type had significantly elevated levels of beta activity in their EEG [5, 6, 18]. A cluster analyses reported in the paper of Clarke et al. [19] gave three clusters in ADHD children – cluster 1 with predominance of high amplitude theta activity; cluster 2 with an increased slow wave activity in both the delta and theta bands and reduced fast wave activity; and cluster 3 characterized by high power beta activity, with deficiencies in the delta and alpha activity. The existence of distinct subsets of children with ADHD, separately characterized by excess theta, alpha and beta activity was also reported in the nineties years by Chabot et al. [20, 21]. These studies suggest that children with ADHD diagnosis may constitute a heterogeneous group with different underlying electrophysiological abnormalities.

In line with this, recently a QEEG spectrum classification of the ADHD population by Kropotov [22, p.409] was introduced with four subtypes of ADHD: 1) Abnormal increase of slow activity (in delta-theta frequency range) centrally or centrally-frontally; 2) Abnormal increase of frontal midline theta rhythm generated with maximum at Fz within the frequency range of 5.5-8 Hz in long (more than 1s) bursts and increased with task load; 3) Abnormal increase of beta activity within 13-30 Hz frontally; 4) Excess of alpha activities at posterior, central, or frontal leads.

In this study we examined the absolute spectra power of the brain waves through QEEG in two resting conditions (eyes closed and eyes opened) and during two neuropsychological tasks (visual and emotional continuous performance tests) from 67 adults diagnosed as ADHD. Our aim was to identify whether the dividing the ADHD adults into the four QEEG subtypes (according to the Kropotov's classification by comparing the each individual spectra to the Human Brain Institute (HBI) reference database) corresponds to our findings of electrophysiological measures - spectra absolute power (μV^2) for each frequency band (delta, theta, alpha, beta). We proposed that the classification of the ADHD subtypes according to the electrophysiological spectrum measures might explain the non consistent results for the EEG spectra found in the previous papers. Namely, because of the multifactorial origin of ADHD, with the QEEG subtyping we could try to identify its neurophysiological reasons and this will help in our understanding of the brain dysfunction in this disorder.

Material and Methods

Subjects

67 adults (between 18 and 50 years of age) diagnosed as ADHD participated in the study. The group consisted of almost equal number of females and males (33 females and 34 males), as the gender imbalance noted in children has not been established in adults with ADHD. The mean age of the group was 33.4 ± 8.39 years. 45 subjects were referred by their psychiatrist (with the previous diagnosis of ADHD) and 22 adults were new patients presented to a Private Psychiatric Practice in Chur, Switzerland or to the Division of Neuroinformatics at the Macedonian Academy of Sciences and Arts in the period from 2007 to 2009. The diagnosis was confirmed or made by a psychiatrist and a psychologist (and both had to agree on the diagnosis for the subject to be included in the study) according to the DSM-IV criteria [23] with at least 4 symptoms of inattention or at least 4 symptoms of hyperactivity/impulsivity, frequently present during the past 6 months, affected in at least 2 areas of life, with no history of epilepsy and with no history of head injury. It can be noted that 4 symptoms of inattention and/or hyperactivity/impulsivity is less than DSM-IV requires for ADHD diagnosis, but according to Barkley [24, p.87] this is acceptable for adults. All subjects met the criteria of the Barkley's Semi-structured Interview for adults with ADHD. In order to ensure diagnostic validity, additional information was collected from parents, partners, relatives and friends. According to the DSM-IV criteria, the assessment resulted in 26 ADHD subjects being diagnosed with the inattentive type, 4 with hyperactive/impulsive type and 37 with combined type. All subjects had normal or corrected to normal vision. Since, each ADHD individual was compared to an age and sex matched normal controls from the HBI reference database, the control group was not included in this study.

Procedure

All participants were individually assessed with neurophysiological testing in an environment free from distractions. Testing was carried out in a quiet, air-conditioned room with the experimenter and recording equipment present. The subjects were tested in a single session that lasted approximately 1.5h (altogether - the procedure with the placing of the Electrocap (30 minutes) and the recording in all four conditions mentioned above (50-60 minutes)). Electrodes were fitted while subjects were familiarised with the testing equipment and the procedure. All participants gave informed consent. Subjects were not allowed to take any medication in the 48-hour-period prior to testing (because 18 subjects of the previously diagnosed group were taking methylphenidate) and were asked not to use caffeine or tobacco in the morning of their testing. This "wash-out" period was chosen as the half-life of methylphenidate is only 2-7 hours (documented in adults by e.g. Faraj et al. [25]). All subjects were seated in a comfortable chair with a backrest and were instructed not to move their eyes and to avoid excessive blinking during the recording. Recording was suspended for a short period if the subject was found to be experiencing drowsiness or becoming restless. EEG was recorded at various times during office hours (from 08:00 to 15:00 h).

The EEG was recorded using a Mitsar 19-channel QEEG system in the following conditions:

1. 5 minutes eyes closed (EC) resting condition;
2. 5 minutes eyes open (EO) resting condition (sufficient for 2 minutes artefact-free data EC and EO);
3. Visual continuous performance test – VCPT from Psytask (two-stimulus Go/NoGo paradigm) with 20 minutes duration;
4. Emotional continuous performance test - ECPT from Psytask (two-stimulus Go/NoGo paradigm) with 20 minutes duration.

EEG electrode placement was in accordance with the international 10/20 system using an electrocap produced by Electrocap international. Activity in 19 derivations was recorded from Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1 and O2, referenced to linked ears. The ground electrode was placed between Fpz and Fz. In order to control the eye movement artifacts, the electrooculogram (EOG) was recorded, using two 9 mm tin electrodes, above and under the right eye, referenced to Fpz and Oz. The EOG rejection was set at 50 μV. The bandwidth of the amplifiers was set at 0.53 Hz for low frequency filter, 50 Hz for high frequency filter and 45-55 Hz for notch filter. The EEG digitization frequency was 256 Hz. The impedance levels for all electrodes were set to 5 kΩ. The EEG was continuously recorded on the hard disc for off-line analysis. The VCPT and ECPT were administered using the standard protocol. The 19 electrode positions were allocated to three sagittal regions: frontal (Fp1, Fp2, F3, Fz, F4, F8, F7), central (T3, T4, C3, Cz, C4), and posterior (T5, T6, P3, Pz, P4, O1, O2), and three lateral regions: left (Fp1, F3, F7, T3, C3, T5, P3, O1), midline (Fz, Cz, Pz) and right (Fp2, F4, F8, T4, C4, T6, P4, O2) by averaging the power within each region. The authors also visually appraised every epoch and decided to accept or reject it, based on the absence or presence of artefact. The EEG data was processed with the WinEEG software version 2.82.32 (St. Petersburg, Russia). Spectral analysis using fast Fourier transform was carried out for four frequency bands: Delta (0.5–4 Hz), Theta (4–8 Hz), Alpha (8–12 Hz) and Beta (12-30 Hz), for absolute power (μV^2). The transformed data were compared using the HBI database and analyzed separately for each subject, frequency band and measurement condition.

The Human Brain Institute (HBI) reference database [22, p.159-160] was developed to help researchers to perform both conventional and quantitative EEG and quantitative ERPs (Event Related Potentials) studies. It is a software for comparing the EEG spectra, coherence and ERP components computed for a given patient. Inclusion/exclusion criteria presume an uneventful perinatal period, with no head injury with cerebral symptoms, with no history of neurological or psychiatric diseases, with no convulsions, normal mental and physical development, average or better grades in school. The HBI database includes the results of processing more than 3000 EEG recordings collected from more than 1000 healthy subjects at the age from 7 to 89 years old. The EEGs were recorded at 7 different conditions. By comparing the data by means of parametric statistical procedures the differences between the patients and their appropriate age-matched reference group can be calculated. This computer analysis then serves as a valuable tool in the aid of diagnosis and treatment planning.

VCPT and ECPT tasks

We used the two-stimulus CPT tasks (GO/NOGO tasks) developed specifically for the Psytask software of Mitsar system. We applied them for the purpose of gathering the Event Related Potentials (ERPs), and that is the aim of our next paper. Here, in this study we used these tasks to assess the power spectra during a mental task, compared to the resting states in EC and EO conditions.

The task consisted of 400 trials. The duration of the stimuli is equal to 100 ms. The trials consisted of presentation of a pair of stimuli with inter stimulus interval of 1.1 sec. The interval between the trials is equal to 3100 ms and the response interval from 100 to 1000ms. Subjects were instructed to press a button with index finger of their right hand as fast as possible every time when animal or angry face was followed by an animal or angry face (Go-condition), respectively, and to withhold the suppressing on the other three trials (No-Go condition). Pictures were presented in a pseudo randomised order in the centre of a computer monitor placed 100 cm from the subjects' eyes. Before each session, the test was explained to the subject in details and 10–20 training tasks were performed. Accuracy and speed were encouraged.

More detailed explanation of the VCPT and ECPT tasks can be found in the study of Markovska-Simoska & Pop-Jordanova [26].

Comparison of the performance during visual and emotional CPT in meaning of omission, commission errors, reaction time and variation of the reaction time are not the subject of this paper and they will be considered in another one.

Data analysis

A series of factorial analysis of variance (ANOVA/MANOVA) were performed using the factors: sagittal and lateral topography (frontal, central, posterior and left, midline, right), measurement condition/task (EC, EO, VCPT, ECPT), and group (ADHD I, II, III, IV subtype) for each frequency band (delta, theta, alpha, beta) absolute power (μV^2). Then, the post hoc Bonferroni test was performed to explain significant interactions. Statistical analysis was performed using the Statistica 7.0 software. Due to space reasons only significant effects and interactions between groups are reported here.

Results

All individual spectra of the ADHD subjects were analyzed and compared with the HBI database. As a result of applying the Kropotov's classification, the ADHD subjects were divided in four subtypes: QEEG subtype

Table 1: Behavioral and QEEG subtypes of examined ADHD subjects.

QEEG ADHD subtypes	Behavioral ADHD types
I	4 inattentive + 9 combined
II	6 inattentive + 8 combined
III	8 inattentive + 8 combined
IV	8 inattentive + 4 hyperactive + 12 combined

I - 13 patients (19.4%), QEEG subtype II - 14 patients (20.9%), QEEG subtype III - 16 patients (23.9 %) and QEEG subtype IV - 24 patients (35.8%).

No correlation between the QEEG ADHD subtypes and the behavioral symptoms (Table 1) was found, illustrating the multifactorial character of ADHD.

Table 2: Summary of significant post hoc Bonferroni p values between subtypes, conditions and regions.

brain waves	region	Subtype effects						Condition effects					
		ADHD I vs.ADHD II	ADHD I vs.ADHD III	ADHD I vs.ADHD IV	ADHD II vs.ADHD III	ADHD II vs.ADHD IV	ADHD III vs.ADHD IV	EC vs. EO	EC vs. VCPT	EC vs. ECPT	EO vs. VCPT	EO vs. ECPT	VCPT vs. ECPT
DELTA	F		0,003	0,008					0,000	0,000	0,000	0,000	
	C		0,000	0,002					0,000	0,011	0,000	0,006	
	P		0,000	0,011					0,015	0,001	0,015	0,001	
	L		0,000	0,013					0,000	0,000	0,000	0,000	
	M	0,002	0,000	0,000					0,006	0,007	0,006	0,007	
	R		0,000	0,029					0,000	0,000	0,000	0,000	
THETA	F				0,000		0,014				0,016	0,005	
	C				0,001		0,043						
	P				0,047		0,005						
	L				0,006		0,006					0,027	
	M		0,039		0,000		0,027						
	R				0,004		0,004					0,019	
ALPHA	F			0,000			0,000	0,000	0,000	0,000			
	C			0,006	0,015		0,000	0,000	0,000	0,000			
	P			0,011			0,000	0,000	0,000	0,000			
	L			0,008			0,000	0,000	0,000	0,000			
	M			0,001		0,000		0,000	0,000	0,000			
	R			0,005		0,000		0,000	0,000	0,000			
BETA	F				0,002					0,017		0,015	
	C												
	P												
	L										0,035		
	M												
	R												

F-frontal; C-central; P-parietal; L-left; M-midline; R-right; EC-eyes closed; EO-eyes opened; VCPT-visual contionous performance test; ECPT-emotional contionous performance test.

A post-hoc Bonferroni test was performed in order to determine which bands were contributing the most to the multivariate effect in function of the QEEG subtype and condition. A summary of the significant difference is shown in Table 2 for each of the power spectra bands by the QEEG subtypes and conditions.

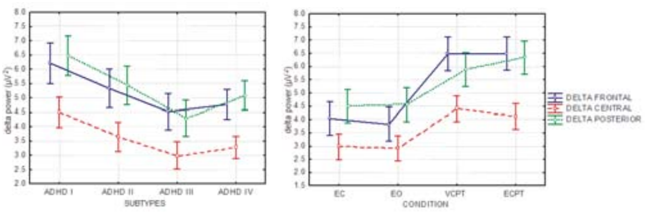

Figure 1: Absolute delta power for subtypes (left panel) and conditions (right panel).

Delta (0.5-4 Hz)

The factorial ANOVA/MANOVA results have shown that the total power of delta depends on the group qualification F(9, 609) = 2.91, p =.002 (the highest value of delta is found in ADHD I and the lowest in the ADHD III subtype - Fig. 1, left panel) and from condition F(9, 609) = 7.51, p =.000 (Fig. 1, right panel), with significantly higher delta power in the VCPT and ECPT tasks than the EC and EO conditions for all subtypes.

The analysis of the sagittal topography of delta shows greater power of delta in frontal and posterior, than in central regions F(2,504) = 156.13, p =.000 (Fig.2 left panel). Concerning the lateral topography, the lower value of delta (except for ADHD I subtype) is found in the middle region in relation to the left and right side F(2,504) = 8.01, p =.000 (Fig.2, right panel). There were no statistical differences in delta power for ADHD I and ADHD II for sagittal regions, while for lateral regions a significant increase of delta in the midline region was found in the ADHD I subtype compared to ADHD II. Also, significant differences in delta band between the ADHD I subtype and the ADHD III and IV subtypes have been detected for all regions (Table 2). For the condition periods we found that in the VCPT and ECPT tasks the absolute delta power is significantly higher than in the EC and EO condition for all subtypes (Table 2).

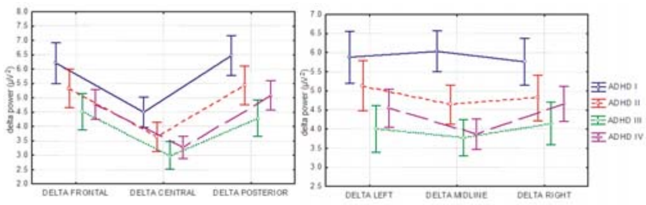

Figure 2: Absolute delta power for sagittal (left panel) and for lateral regions (right panel).

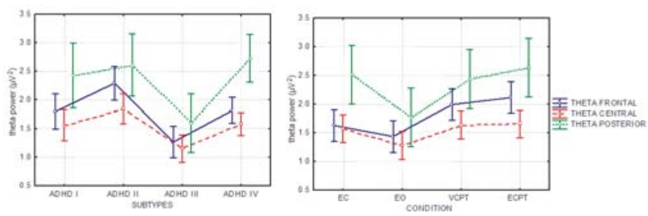

Figure 3: Absolute theta power for subtypes (left panel) and conditions (right panel).

Theta (4-8 Hz)

The amplitude of the total power of theta also

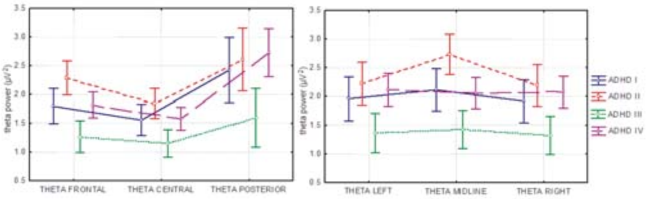

Figure 4: Absolute theta power for sagittal (left panel) and for lateral regions (right panel).

depends on the subtype qualification F(9, 609) = 4.62, p =.000 (Fig. 3, left panel) and from condition F(9, 609) = 4.08, p =.000 (Fig. 3, right panel). As it can be seen from the Figure 3 the amplitude values of theta are the highest in the ADHD II subtype. We also detected a significant difference of the sagittal topography of theta F(2, 504) = 65.52, p =.000, resulting in greater power for theta in posterior, than in frontal and central regions (Fig.4, left panel). While, concerning the lateral topography the highest value of theta was obtained at the middle region F(2, 504) = 18.69, p = 0.000 (Fig.4, right panel). A post-hoc Bonferroni test showed greater theta power for ADHD II compared to the ADHD III subtype and between ADHD IV compared to ADHD III for frontal, central and posterior theta distribution (Table 2). Concerning the difference in the lateral distribution a significant increase of theta has been found for ADHD II and the IV subtype compared to ADHD III (Table 2). For the condition periods we found that only for frontal and left/right regions there is higher amplitude of theta in VCPT and the ECPT tasks compared to the EO condition for all subtypes, while there is no statistical difference for the other sagittal and lateral regions (Table 2).

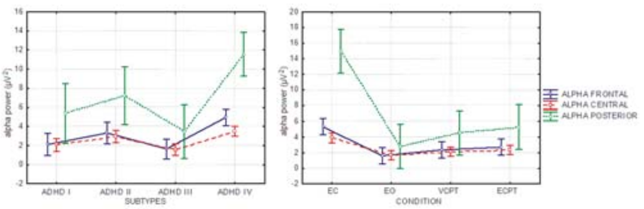

Figure 5: Absolute alpha power for subtypes (left panel) and conditions (right panel).

Alpha (8-12 Hz)

The obtained results for alpha total power show that the amplitude of alpha depends on both, subtype qualification F(9, 609) =4.86, p=.000 and condition F(9, 609)=7.26, p=.000 (Fig.5, left and right panel). As it can be seen from the figure the amplitude values of alpha are the highest in the ADHD IV subtype and the lowest in the ADHD III subtype.

The analysis of the sagittal topography of alpha shows greater power for alpha in the posterior regions,

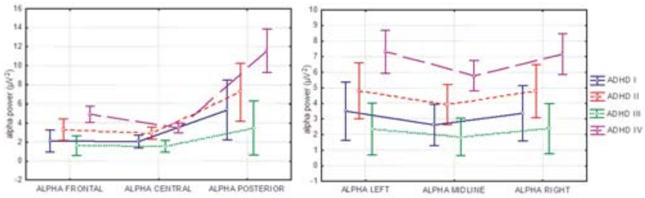

Figure 6: Absolute alpha power for sagittal (left panel) and for lateral regions (right panel).

which is expectable, than in the frontal and central ones F(2, 504) = 59.79, p=.000 (Fig.6, left panel). Concerning the lateral topography the highest value of alpha is at the sides and the lowest in the middle region, F(2, 504)=28.74, p=0.000 (Fig.6, right panel).

A post-hoc Bonferroni test showed greater alpha power for ADHD IV compared to the ADHD I and III subtypes (Table 2). For the condition periods we found

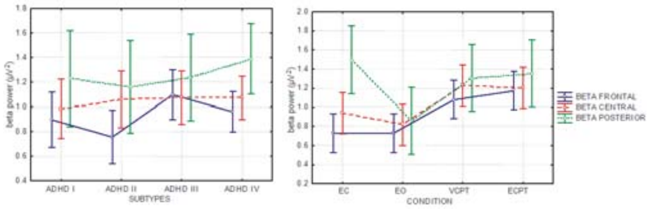

Figure 7: Absolute beta power for subtypes (left panel) and conditions (right panel).

higher amplitude of alpha in EC compared to EO, VCPT and the ECPT tasks (Table 2).

Beta (12-30 Hz)

The ANOVA results have shown that the total power of beta depends on the subtype qualification F(9, 609) = 2.06, p =.03 (the highest value of frontal beta is

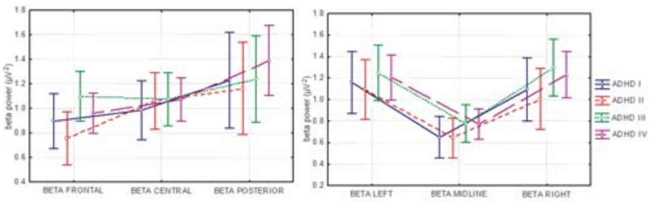

Figure 8: Absolute beta power for sagittal (left panel) and for lateral regions (right panel).

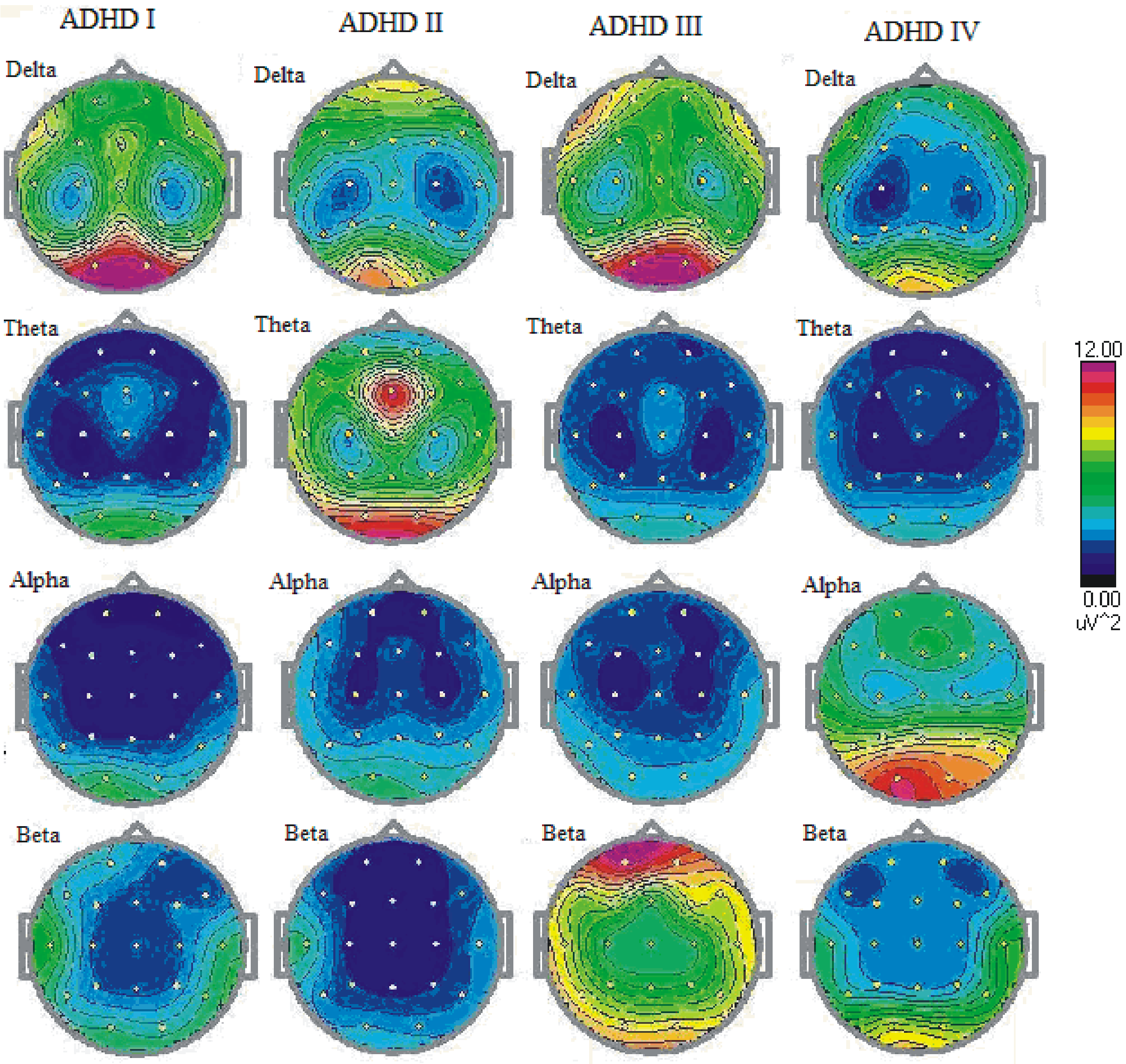

Figure 9: Topographic subtype differences in absolute power.

found in the ADHD III subtype - Fig. 7, left panel) and from condition F(9, 609) = 6.41, p =.000 (Fig. 7, right panel), with significantly higher beta power in VCPT and the ECPT tasks than the EC and EO conditions for all subtypes.

The sagittal topography results showed that there is no statistical difference for beta in sagittal (Fig.8 left panel) and lateral topography (Fig. 8, right panel). The post hoc statistical difference regarding the group effects was found only between the ADHD III and ADHD II subtypes, and concerning the condition effect between EO and ECPT and the VCPT conditions, particularly in frontal and left beta power (Table 2).

On Fig. 9 the topographic differences in absolute power of each band in all subtypes are presented for better image of the obtained results.

Discussion

The purpose of the present study was to determine the QEEG defined subtypes according to the Kropotov's classification in the sample of the ADHD adults and compare them with the DSM-IV classification.

While the EEG of the ADHD children has been extensively examined, comparatively little research has been conducted into the EEG of adults with the same disorder. The few published studies examining the use of EEG assessment in ADHD adults have demonstrated divergent EEG activity.

The obtained results between subtypes have shown elevated absolute delta power (0.5-4 Hz) in the ADHD I and II subtypes, while the ADHD III and IV subtypes had reduced delta power. These results for delta activity are in accordance with the findings in the studies of Hobbs et al., Bresnahan & Barry and Bresnahan et al. [12,16,17] where absolute and relative delta power has been found to be elevated in adolescent and adult ADHD patients similar to the results obtained for children. On the other hand, there are studies of Lazzaro et al. and Koehler at al. [13,15] in which no difference between adult or adolescent ADHD patients and control subjects has been shown for absolute and relative delta power. In our sample we have combination of these findings. We consider that this kind of divergence is a result of the qualification to the QEEG subtypes which was not considered in the previous studies.

Regarding the sagittal topography, the absolute delta power was greater in the posterior and frontal regions, then in the central and this is compatible with the previous findings of Koehler et al. [15]. For the lateral topography the distribution of the absolute delta power at the midline was higher then at the two hemispheres for ADHD I, but the opposite was found for the ADHD II, III and IV subtypes.

Concerning the theta activity, by definition, the highest values of absolute theta power (4-8 Hz) were found in the ADHD II subtype. The increased absolute and relative theta power, along with the decreased beta power has previously been described during an eyes-open resting condition in adolescents and adults with ADHD [12,13,15-17]. Regarding the lateral topography it was interesting to find and confirm the elevated midline absolute theta power only in the ADHD II subtype. This is in accordance with the results of Gasser et al. [27] where more low frequency activity was recognized at the midline, than at the two hemispheres. For the condition periods we found that only for frontal and left/right regions there is higher amplitude of the absolute theta power in the VCPT and ECPT tasks compared to the EO condition for all subtypes.

Regarding the absolute alpha power (8-12 Hz), the ADHD IV subtype had by definition the highest amplitude values. This is similar to the EEG studies of the ADHD adults by Clarke et al. and Koehler et al. [14, 15] where increased absolute and relative alpha power was found. In the study of Bresnahan et al. [16] it was shown that the adult ADHD patients had increased alpha and beta activity compared to normal controls, but in another study of the same author [17] no differences in alpha (absolute and relative) and absolute beta activity in adult ADHD patients were confirmed. So, the divergent findings (as was with the case of delta power) again can be explained as a result of viewing an ADHD as a whole group, not taking in consideration the probability of the existence of specified QEEG subtypes. In our study, the subtype IV is represented by the greatest number of the ADHD adults. As it was expected, for conditions there was statistically difference with highest values of absolute alpha power in EC regarding to EO, VCPT and ECPT. Between the last mentioned conditions there was no statistical difference in alpha, which in our opinion confirms the meaning of alpha as an idling rhythm of the brain.

Following this research, a group of adults named as the ADHD III subtype have been found to have excess of absolute beta power (12-30 Hz) as the dominant EEG abnormality. From the obtained results of the studies with children by Clarke et al. and Chabot et al. [4, 21], it can be seen that also a small group of ADHD children have excess beta activity. It is reported by Chabot et al. and Clarke et al. [20, 21, 28] that nearly one-third of the sample of the ADHD children had excess alpha activity. Our results are in accordance with these findings and we obtained the ADHD III subtype with the highest values of frontal beta activity. Following Lubar's theory of hypoarousal, it was hypothesized that, if reduced beta and increased theta represents underarousal, children with increased beta activity might be hyperaroused [8]. Increased beta power in eyes closed, compared to the eyes opened condition, is referred as "inner-arousal", already noted in previous studies of Pop-Jordanov & Pop-Jordanova, and Cooper et al. [29, 30].

The present results have important implications for the use of EEG in the diagnosis of ADHD adults. This study investigates the presence of the QEEG subtypes of adults clinically presented as inattentive, hyperactive and combined type of ADHD. The results indicated the presence of four distinct QEEG-defined subtypes of adults according to the Kropotov's classification characterized by: increased delta-theta activity, increased frontal midline theta, increased frontal beta and alpha excess. The identification of these subtypes by the HBI database is very simple and easy and has important implications for the studies of the utility of QEEG in the diagnosis of ADHD adults. Efforts aimed at developing QEEG into a tool to identify individual ADHD adults must recognize the variability within the ADHD population and this implies the importance of such tool to be reliable in clinical practice, especially when neurofeedback therapy is applied. These valid subtypes may also have significantly different causes underlying their behaviour, and may respond differentially to medication and neurotherapy, possibilities which merit further investigation.

One limitation of this study is the medication effects, because 18 subjects (less than 1/3 of the subjects) were taking methylphenidate 48 hours before the testing. We think that the 48 hours wearing off period is acceptable, but still the prolonged influence of the stimulant medications on the EEG pattern should be considered.

We can conclude that the QEEG power spectrum relatively clearly differentiates the ADHD adults into four subtypes. Namely, the obtained results confirmed that the absolute power of all frequency bands depends on the group qualification with the highest values of: a) slow waves (delta-theta) in the first; b) theta (frontal midline) in the second; c) frontal beta in the third and d) alpha in the fourth subtype. All this subtypes are characterized by different types of CNS dysfunction, and consequently, to the different responses to treatment regimes.

Additional to the clinical diagnosis, the present study confirms the need of QEEG recording and subtypization in patients diagnosed as ADHD. It was shown that their QEEG characteristics are specific and did not correspond to behavioural subtypes. It means that different brain activity can be presented clinically very similarly. With QEEG we can make more detailed discrimination of the type of inattentiveness and the reasons for that (e.g.; somebody can be inattentive because of pronounced delta-theta activity in the EEG and consecutive drowsiness, someone due to high alpha activity and corresponding super relaxation and the other due to strong beta and the related high arousal state). So, the inattentiveness is very complex with a lot of reasons and the power spectrum of each band can be related to it. The etiology of ADHD is multifactorial and can correspond to delta-theta, alpha and beta excess and because of that the existence of the QEEG subtypes is expected.

On the other hand, hyperactivity is something that requires more investigation (including psychological profiles) in order to reveal the reasons for hyperactive symptoms. One possible explanation, why in our study hyperactivity is related to high alpha as well, could be the fact that deep idling condition of brain corresponds to the lack of inhibition, resulting in impulsivity and hyperactivity, along with innatentiveness.

We can conclude that ADHD is heterogeneous disorder either in clinical expression or in the electrophysiological basis and more research is needed in that direction. In the future research we will analyse the QEEG spectrum weighted frequency (brain rate) characteristics (introduced by Pop-Jordanov & Pop-Jordanova [31]), through which we will try to explain the source of the disorder and at the same time to trace the way for the treatment.

Aknowledgement

We wish to thank to Dr. Andreas Müller and Mr. Gian Cadrian from GTSG, Switzerland, for sharing the data and for hospitality during two COST B27 STSMs stays of the first author in Chur, Switzerland. Also, we are thankful to Dr. Valery Ponomarev from Human Brain Institute in St. Petersburg, for his help with statistical analysis.

References

1. Clinical practice guideline: diagnosis and evaluation of the child with attention-deficit/hyperactivity disorder. American Academy of Pediatrics. Pediatrics. 2000;105:1158-1170.

2. Wender P. Attention-Deficit Hyperactivity Disorder in Adults. New York: Oxford University Press, 1995.

3. Barkley R.A. ADHD and the Nature of Self-Control Guilford Press, New York, 1997.

4. Clarke AR, Barry RJ, McCarthy R, Selikowitz M. EEG analysis in attention-deficityhyperactivity disorder: a comparative study of two subtypes. Psychiatry Research. 1998;81:19–29.

5. Clarke AR, Barry RJ, McCarthy R, Selikowitz M. Age and sex effects in the EEG: differences in two subtypes of attention-deficityhyperactivity disorder. Clinical Neurophysiology. 2001;112:815–826.

6. Clarke AR, Barry RJ, McCarthy R, Selikowitz M.

Electrophysiological differences in two subtypes of attention-deficityhyperactivity disorder. Psychophysiology. 2001;38:212–221.

7. Barry R, Clarke A, Johnstone S. A review of electrophysiology in attention deficit/hyperactivity disorder: I. Qualitative and quantitative electroencephalography. Clin Neurophysiol. 2003;114:171–183.

8. Lubar JF. Discourse on the development of EEG diagnostics and biofeedback for attention-deficit/hyperactivity disorders. Biofeedback Self Regulation. 1991;16:201–225.

9. Monastra V, Lubar J, Linden M, VanDeusen P, Green G, Wing W, Phillips A, Fenger T. Assessing attention deficit hyperactivity disorder via quantitative electroencephalography: an initial validation study. Neuropsychology. 1999;13:424–433.

10. Clarke A, Barry R, McCarthy R, Selikowitz M. EEG analysis of children with attention-deficit/hyperactivity disorder and comorbid reading disabilities. J Learn Disabil. 2002;35:276–285.

11. Pop-Jordanova N, Markovska-Simoska S, Zorcec T. Neurofeedback treatment of children with attention deficit hyperactivity disorder. Prilozi. 2005;26(1):71-80.

12. Hobbs MJ, Clarke AR, Barry RJ, McCarthy R, Selikowitz M. EEG abnormalities in adolescent males with AD/HD. Clin Neurophysiol. 2007;118:363–371.

13. Lazzaro I, Gordon E, Li W, Lim CL, Plahn M, Whitmont S, Clarke S, Barry RJ, Dosen A, Meares R. Simultaneous EEG and EDA measures in adolescent attention deficit hyperactivity disorder. Int J Psychophysiol. 1999;34:123–134.

14. Clarke AR, Barry RJ, Heaven P, McCarthy R, Selikowitz M, Byrne MK. EEG in adults with Attention-Deficit/Hyperactivity Disorder. Int J Psychophysiol. 2008;70:176–183.

15. Koehler S, Lauer P, Schreppel T, Jacob C, Heine M, Boreatti-Huemmer A, Fallgatter AJ, Herrmann MJ. Increased EEG power density in alpha and theta bands in adult ADHD patients. J Neural Transm. 2009;116:97–104.

16. Bresnahan S, Barry R. Specificity of quantitative EEG analysis in adults with attention deficit hyperactivity disorder. Psychiatry Res. 2002;112:133–144.

17. Bresnahan S, Barry R, Clarke A, Johnstone S. Quantitative EEG analysis in dexamphetamine-responsive adults with attention-deficit/hyperactivity disorder. Psychiatry Res. 2006;141:151–159.

18. Clarke AR, Barry RJ, McCarthy R, Selikowitz M. EEG analysis in attention-deficit/hyperactivity disorder: a comparative study of two subtypes. Psychiatry Res. 1998;81:19–29.

19. Clarke A, Barry R, McCarthy R, Selikowitz M. EEG-defined subtypes of children with attention-deficit/hyperactivity disorder. Clin Neurophysiol. 2001;112:2098–2105.

20. Chabot R, Serfontein G. Quantitative electroencephalographic profiles of children with attention deficit disorder. Biol Psychiatry. 1996;40:951–963.

21. Chabot R, Orgill A, Crawford G, Harris M, Serfontein G. Behavioural and electrophysiological predictors of treatment response to stimulants in children with attention disorders. J Child Neurol. 1999;14:343–351.

22. Kropotov JD. Quantitative EEG, event-related potentials and neurotherapy, Elsevier Inc., 2009.

23. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, 4th edition. American Psychiatric Association, Washington DC, 1994: pp. 78-85.

24. Barkley RA, Murphy KR, Fischer M. ADHD in adults: what the science says, The Guilford press, 2008.

25. Faraj BA, Israili ZH, Perel JM, Jerkins ML, Holtzman SC, Cucinel SA, Dayton PG. Metabolism and disposition of methylphenidate-Cl4: studies in man and animals. J Pharmacol Exp Ter. 1974;191:535-547.

26. Markovska-Simoska S, Pop-Jordanova N. Comparison of visual and emotional continuous performance tests performances related to sequence of presentation, gender and age. Prilozi. 2009;30(1):167-178.

27. Gasser T, Verleger R, Bacher P, Sroka L. Development of the EEG of school age children and adolescents. II. Topography. Electroenceph clin Neurophysiol. 1988;69:91-99.

28. Clarke AR, Barry RJ, McCarthy R, Selikowitz M. Excess beta activity in children with attention-deficit/hyperactivity disorder: an atypical electrophysiological group. Psychiatry Res. 2001;103:205–218.

29. Pop-Jordanov J, Pop-Jordanova N. Neurophysical substrates of arousal and attention, Cognitive Processing. 2009;10(Suppl 1):S71–S79.

30. Cooper NR, Croft RJ, Dominey SJ, Burgess AP, Gruzelier JH. Paradox lost? Exploring the role of alpha oscillations during externally vs. internally directed attention and the implications for idling and inhibition hypotheses. International J Psychophysiol. 2003;47(1):65-74.

31. Pop-Jordanova N, Pop-Jordanov J. Spectrum-weighted EEG frequency ("brain-rate") as a quantitative indicator of mental arousal. Prilozi. 2005;26(2):35-42.