We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

BOOK CITATION INDEX
CLARIVATE ANALYTICS
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

QEEG Characteristics and Biofeedback Modalities in Children with ADHD

Nada Pop-Jordanova
Department for Psychophysiology, University Pediatric Clinic, Skopje,
R. Macedonia

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequent neuropsychiatric diagnoses during childhood, varying between 2 and 10% depending on country or cultural area. In our country (R. Macedonia), the incidence of ADHD is about 2%. The other labels of the disorder introduced in the past are hyperactivity, hyperkinesis, hyperkinetic syndrome, minimal brain dysfunction and minimal brain damage. According to DSM – IV (American Psychiatric Association, 1994) there are three main clinical forms of this disorder: inattentive, hyperactive/impulsive and combined. European diagnostic criteria for hyperkinetic disorder as defined by the ICD-10 (International Classification of Diseases, 10th revision, 1993) include children displaying developmentally inappropriate levels of attention, hyperactivity and impulsivity that begin in childhood and cause impairment to school performance, intellectual functioning, social skills, driving and occupational functioning. Generally, ICD-10 criteria are more restrictive than DSM-IV diagnosis because they need a greater degree of symptom expression.

The overlapping of all three forms with learning disabilities is very high (up to 70%), as well as with conduct problems. The inattentive (ADD) form mainly overlaps with anxiety disorders and learning disability, while hyperactive form (ADHD) mostly overlaps with conduct disorder. Some children with ADHD have movement disorders or tics and occasionally they may have seizure disorders (Barkley, 1990). Strong genetic component related to defect in chromosome 11 is showed in some studies (Anokhin et all. 2006). Concerning the involvement of specific neurotransmitter systems in the pathophysiology of ADHD some authors suggest that the catecholaminergic dysregulations are centrally involved.

This chapter is mainly devoted to the QEEG characteristics of ADHD in children, connected to endophenotypes, event related potentials, brain rate and biofeedback treatment. Firstly, it will be explained why QEEG recording is important for the exact diagnostics and the therapy planning for ADHD children. Based on QEEG differentiation, the endophenotypes clustering enables more precise diagnostics. In addition, it will be shown that event related potentials (ERP's) are related to the possible dysfunction of executive system, as a part of the brain the most involved in this disorder. The applied calculation of brain rate is our original proposal for the evaluation of general mental activation level, considering under or over-arousal states, so that the planning of the treatment protocols becomes more easy.

Finally, biofeedback will be offer as the non-pharmaceutical treatment for ADHD, with long-term effects.

2. QEEG recording

The EEG recording is a noninvasive, painless, and safe measurement using digital technology of electrical patterns at the surface of the scalp which primarily reflect cortical electrical activity or brainwaves. The Quantitative EEG procedure uses multi-electrode EEG recording where the data are processed with various algorithms and than statistically analyzed comparing values with normative database reference values. The processed EEG could be also converted into color maps of brain functioning called brain maps.

The placement of electrodes from the first recording (introduced in 1924) was strongly precise and the system was called the10-20 International System of Electrode Placement. This system of recording is used until now. The "10" and "20" refer to the fact that the actual distances between adjacent electrodes are either 10% or 20% of the total front-back or right-left distance of the skull (Fig.1).
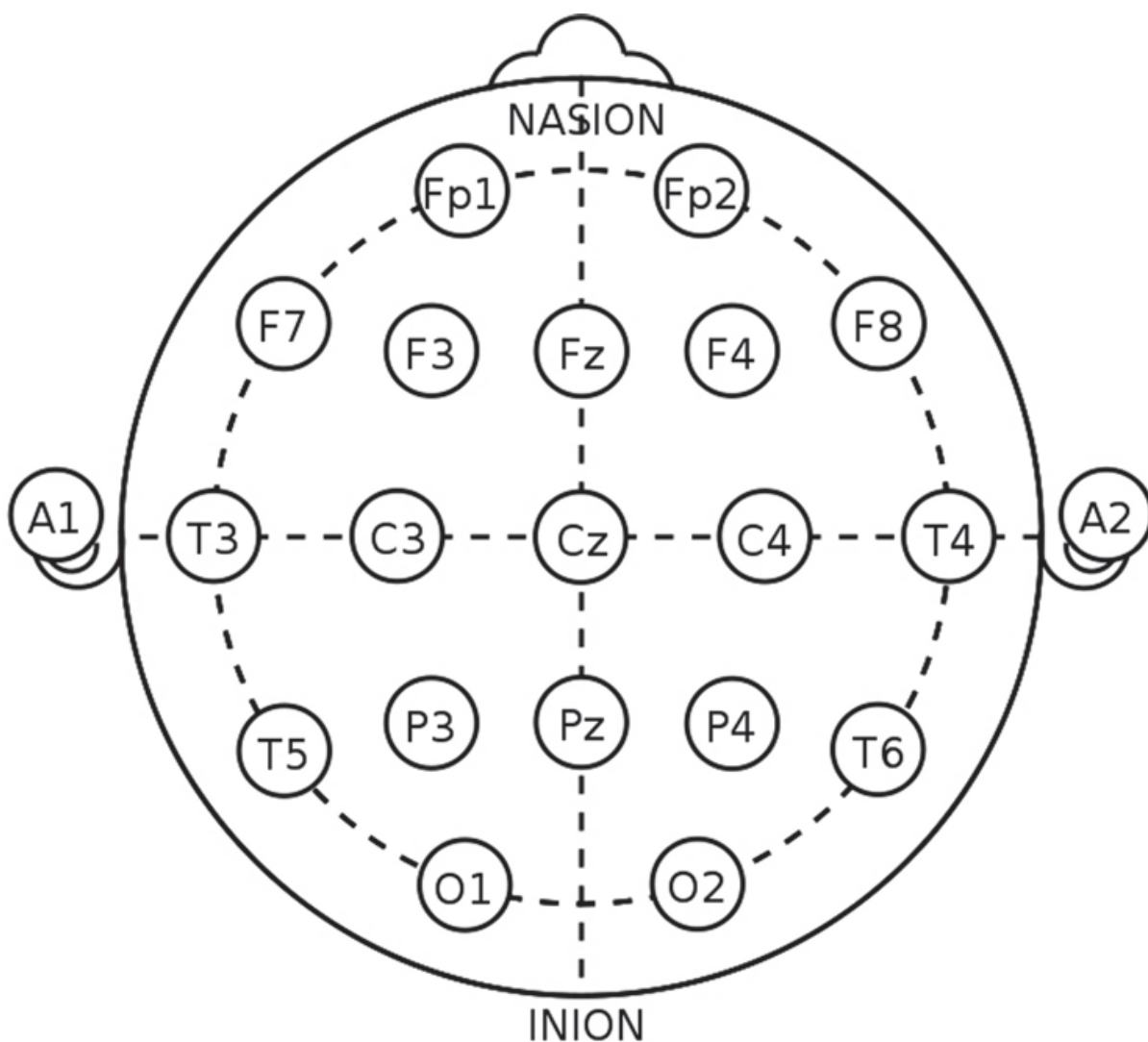

Fig. 1. The 10-20 International System

Each site has a letter to identify the lobe and a number to identify the hemisphere location. The letters F, T, C, P and O stand for Frontal, Temporal, Central, Parietal, and Occipital, respectively. Note that in fact there exists no central lobe, the "C" letter is only used for identification purposes only. The letter "z" (zero) refers to an electrode placed on the midline. Even numbers (2, 4, 6, 8) refer to electrode positions on the right hemisphere, whereas odd numbers (1, 3, 5, 7) refer to those on the left hemisphere.

One important element of the EEG signal is its rhythmicity. Rhythms differ in frequency, location, mechanism of generation and functional meaning. They evolve in time, so that a representative EEG recording usually takes three or more minutes (in our patients we use five minute recording). For compressing the information about rhythmicity over time, as a most powerful method, the Fourier analysis is used. The parameters of Fourier analysis can be adjusted to the goal of a specific task.

When EEG is recorded from many electrodes that cover the whole cortex, it is possible to compute a 2D representation of a measured EEG characteristic. The characteristics could be either potential or power taken at a particular frequency.

Computerized analysis of EEG signals involve a number of factors: frequency distribution, voltage (as amplitude of the signal), locus of the phenomena, wave shape morphology, inter-hemispheric symmetries, character of waveform occurrence and reactivity (changes in an EEG parameter with changes in state).

The pattern of neuronal oscillations plays an important role in the evaluation and treatment of children (and adult as well) with ADHD. These patients are characterized with QEEG abnormalities in up to 80%. In this population, frontal regions are most likely to show deviations from normal development, with disturbed thalamo-cortical and septal-hippocampal pathways, altogether named as executive system.

The term "executive functions" refers to the coordination and control of motor and cognitive actions to attain specific goals. In neuropsychology, the term "executive functions" has long been used as a synonym for frontal lobe function. A modern view postulates several sub-components in the hypothetical executive mechanism. In a frequently cited classification, Smith and Jonides (1999) distinguished between mechanisms relating to (a) attention and inhibition, (b) task management, (c) planning, (d) monitoring and (e) coding. There is, however, no consensus on the number and the precise nature of functional subcomponents.

As we said previously, it is supposed that the main brain system impaired in ADHD is the executive system. The executive system is characterized by two parameters: general activation of the system (arousal = A) and the response associated with different operations such as working memory, action selection, action inhibition and action monitoring (focused activation = At).

It is well known that EEG recorded in eyes open (EO) and eyes closed (EC) resting state is good indicator of metabolic activity in the brain cortex. Low metabolic activity in the area that generates the corresponding EEG is characterized by increase of slow activities (delta and theta waves) and decrease of beta activities. It means that in this condition, the level of activation is low (low A), as well as the amplitude of responses we named focused activity (At) is also low.

The early studies of EEG abnormalities in children with minimal brain dysfunction are made in the period 1930-1950. Basically, EEG studies showed the increase of delta and theta bands in central and frontal regions during EEG recording. This finding was confirmed by quantitative EEG analysis in the 1970s and later. These studies are supported by recent PET (positron emission tomography) and SPECT (single photon emission computerized tomography) scan studies, which also indicate abnormalities in cerebral metabolism in these particular brain areas.

The most studies of QEEG in ADHD population confirm elevated levels of slow wave power in frontal region indicating frontal lobe deactivation, in comparison to normal children. These children experience decreased metabolism in prefrontal regions of the brain and have been good candidates for the use of stimulant medication or neurofeedback. Other children show deficits in limbic system activity and are characterized as having oppositional behavior, emotional outbursts, and impulsiveness. These children also show significant decreased metabolism in the prefrontal lobes and the anterior cingulated gyrus. They are good candidates for the use of tricyclic antidepressants. The third subgroup comprises individuals who have increased activity in the medial superior frontal gyrus. Although these children experience ADD they are often characterized as having an attention deficit with obsessive-compulsive disorder. They have a very short attention span and are often impulsive and oppositional. These patients sometimes respond to clomipramine. By far the most common group of children with ADD consists of those with excessive slow activity in frontal and central brain regions.

Having in mind that the absolute values of EEG spectra depend on some brain unrelated features, such as thickness of the skull, a relative parameter defined as the theta-beta ratio is introduced. Multi-centric studies in USA (Monastra et al. 2001; Lubar 1991, 1997; Mann et al 1992) used the theta-beta ratio as an index of inattention. This so called *inattention index* is defined as a ratio of theta EEG power (measured within the 4-8 Hz frequency band) and beta EEG power (measured within 13-21 Hz frequency band). Usually this index is calculated by EEG recording at a single place Cz in reference to linked ears. It was found that this index is three times higher in inattentive and combine types of ADHD children at the age of 6-10 years compared with normal group. Monastra et al. (2001) found that the sensitivity of this index was 86% and his specificity is 98%.

Opposite to these findings Russian scientists from the Human Brain Institute in St Petersburg (Kropotov, 2009) showed that this index is a good measure only for a part of ADHD population. Mapping this index in normal population showed that the location of the maximum of this index changes significantly with age. For example, the maximum of theta-beta index move from central-parietal location at 7-8 years old children to frontal-central location in adults. The conclusion was that for better results in discriminating the ADHD population from healthy subjects this index must be measured in different electrode position depending on age.

Generally, we can infer that QEEG recording is needed for more precise diagnostics of ADHD, in addition to the clinical criteria. The method is a non invasive, relatively easy for manipulation with standardized locations of the electrodes over the scalp. The recording is performed in different conditions: eyes open, eyes closed and during some cognitive tasks (Go/ NoGo paradigm, visual or auditive performance tasks, reading or math tasks). QEEG is useful if neurofeedback treatment is planned to be applied.

3. Endophenotypes

Endophenotypes are characteristics indicating biological markers of the brain disease. Endophenotype must obey some requirements: a) to be stable and reproducible in time intervals during which behavioral patterns associated with the state of the brain remain unchanged; b) endophenotype must reflect a function of a certain brain system that in a specific way determine the human behavior; and c) it must be inherited. EEG spectra, or amplitude of the background EEG in certain frequency bands, obey these requirements and consequently can be considered as endophenotypes.

We said in the previous text that EEG oscillations (expressed as e.g. alpha or theta rhythm) wane and wax in time. The degree of variability of the basic oscillation depends on the frequency band and the state (eyes open, eyes closed, task etc) of the subject. For example, alpha spindles in the posterior regions vary with periods of few seconds, and burst of the frontal midline theta appear with interburst periods of few deco-seconds. However, if averaged over significantly long time intervals the resulting spectra become quite stable characteristics of the brain. So, these characteristics of EEG spectra could be considered as a reliable and stable estimation of the brain functional state.

Different oscillations reflect different mechanisms: alpha rhythms reflect the state of thalamo-cortical pathways; frontal midline theta rhythms reflect functioning of the limbic system; beta rhythms are more local reflecting state of specific cortical areas. So, defining abnormal rhythmic activities in EEG and associating these abnormalities with distinct systems fit the second requirement for endophenotypes as the biological markers of disease. Finally, there is strong experimental evidence that spectral characteristics of EEG are inherited.

Generally, it can be said that endophenotype is becoming an important concept in the study of different mental disorders such as ADHD, schizophrenia etc. The term was coined in 1966 and applied in psychiatry by Gottesman and Shileds in 1972. It is gradually substituting some similar terms such as "biological markers", "vulnerability marker", "subclinical traits" or "intermediate phenotype". An endophenotype may be neurophysiological, biochemical, endocrinological, neuroanatomical, or neurophychological in nature. Endophenotype represents simpler clue to genetic mechanism than the behavioral symptoms.Thereby, endophenotypes can help to define subtypes of a particular disorder and can be used as a quantitative trait in genetic analyses of probands and families.

For example, some researchers suggest a biological rationale for lack of inhibition as an endophenotype for ADHD. Inhibitory tasks activate the prefrontal cortex and basal ganglia, regions in which the dopamine system is associated with executive functioning. Tests of inhibitory function, such as the stop signal task, often consists of two concurrent tasks (a "Go" task and "NoGo" task) in which the subject is signaled to produce a particular response. An individual with a poor inhibitory system will have a long reaction time. This deficit, being replicated several times, is concerned to be specific to ADHD. Imaging studies have shown that this inhibitory task activates the prefrontal cortex and basal ganglia. Inhibition also correlates with family history, so that 48.1% subjects with poor inhibition have a family history of ADHD compared with only 7.7% of normal controls. (Crosbie, Schachar, 2001).

Endophenotypes may also be useful in exploring different pathways leading up to the disorder. Patients having the same diagnosis may differ strongly in the number and severity of symptoms they portray, suggesting heterogeneity in the causal pathways. Creating more

homogeneous subgroups of patients based on their endophenotypic functioning, may facilitate unraveling these differential causal pathways.

Recently, a QEEG spectrum classification of ADHD population has been developed defining four main subtypes: I subtype (abnormal increase of delta-theta frequency range centrally or centrally-frontally), II subtype (abnormal increase of frontal midline theta rhythm), III subtype (abnormal increase of beta activity frontally), and IV subtype (excess of alpha activities at posterior, central, or frontal leads).

In the following, I will show (on Figs. 2-8) some our examples of QEEG spectra from different subtypes of ADHD children (Pop-Jordanova 2007, 2009; Zorcec 2007, 2008).

The first and second subtypes are characterized clinically with inattention, while in the third subtype mainly hyperactivity, impulsivity and social inadaptation are prevalent. The low attention span is also the main complain of children with alpha excess.

Among the investigated Macedonian ADHD children (over 250), very slow alpha excess (subtype 4) was showed in 25% of children, and high theta/beta ratio in frontal-central cortex (subtype 1) in other 25% of children. The majority of 48% belong to the combined 1 and 2 subtypes. Very rarely (under 2%) we found subtype III were overactive cortex is typical finding (Pop-Jordanova et al. 2007; Zorcec et al. 2007, 2008).
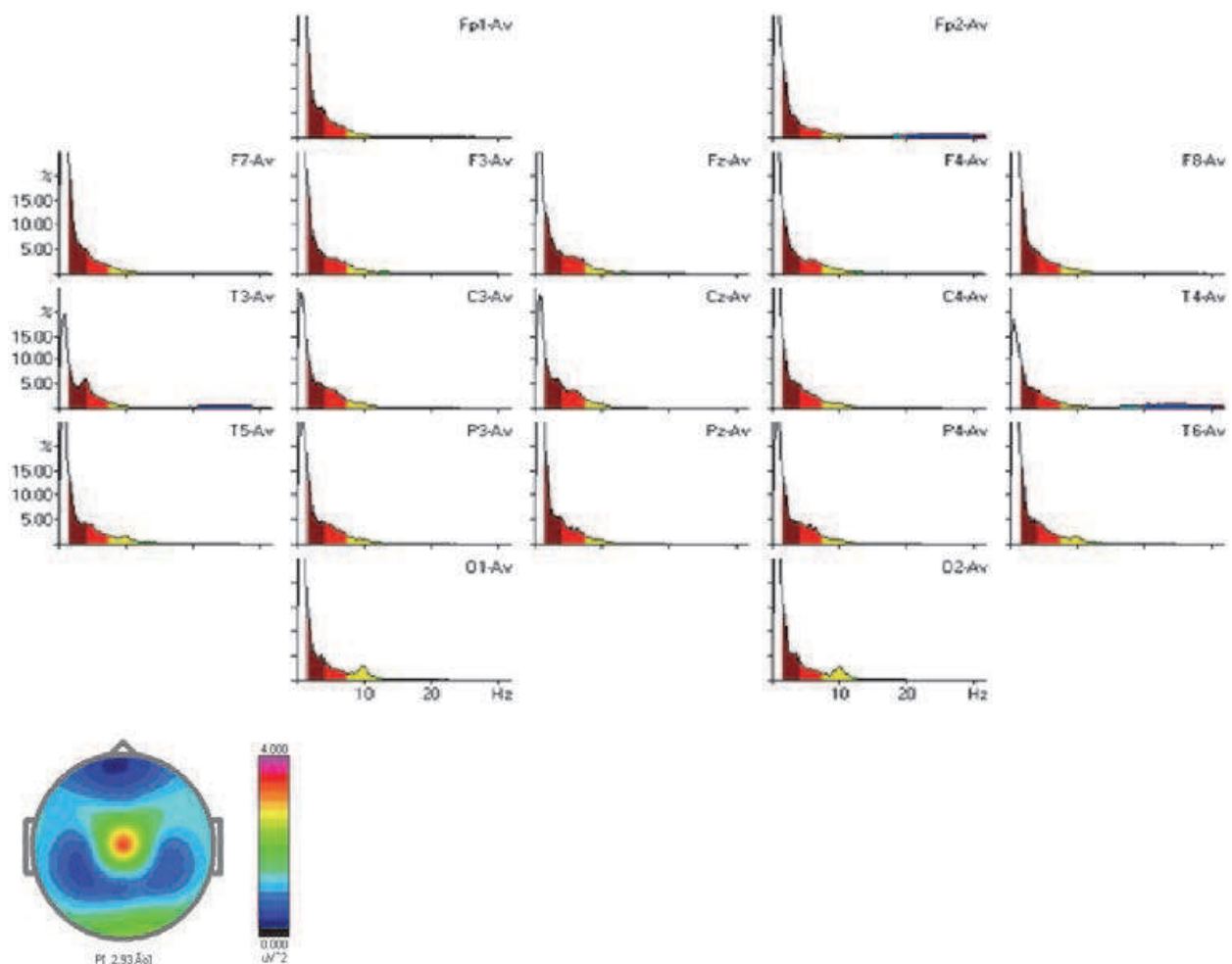

Fig. 2. Subtype I – High delta and theta amplitudes in frontal-central cortex

As can be seen on Fig. 1, in frontal and central region of brain cortex the dominant frequencies are in the range of delta and theta waves, while alpha and beta waves are practically absent.
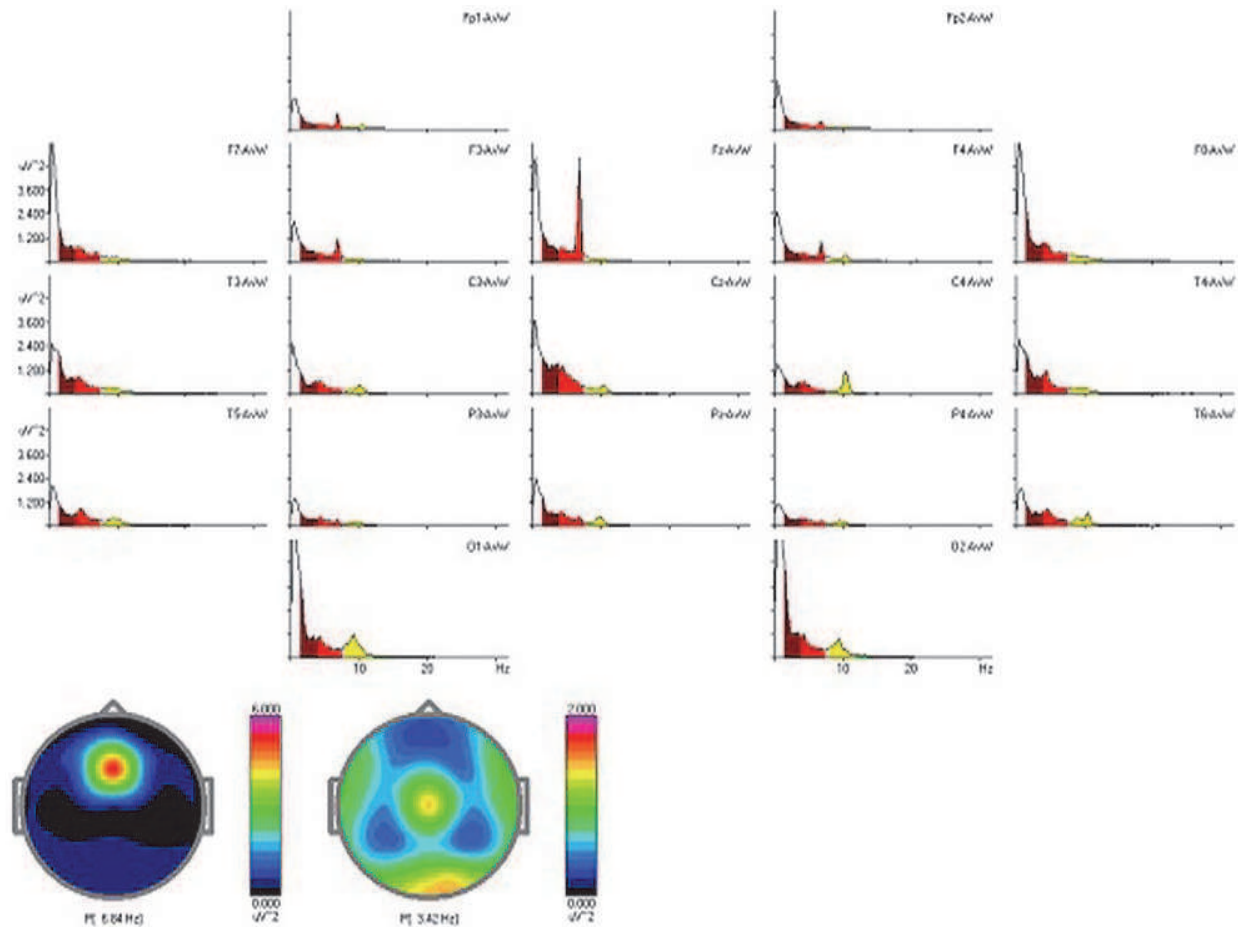

Fig. 3. Subtype II Excess of frontal-midline theta

On Fig.3 we can see a pick of theta activity (P 6.54 Hz) in frontal-midline area as the most important finding. It is also combined with generally slow activity (lack of alpha and beta activity). The same is visible on the row EEG record shown in Fig. 4.

Both Fig.5 and 6 show over activation of the cortex expressed by the pronounced beta brain waves.

In addition to the QEEG, SPECT (Amen, 1997, Amen et al. 1998) shows the corresponding specifics in ADHD children which can be summarized as:

- frontal lobe deactivation (presented clinically as ADD, which usually respond to therapy with Ritalin)
- temporal lobe dysfunction (very like temporal epilepsy, respond to therapy with anticonvulsant)
- homogenous cortical suppression (respond to combination antidepressives + Ritalin)
- increased activity in the anterior medial aspects of the frontal lobes - gyros rectus (responds to alpha adrenergic blockers like clonidine)
- hypofrontality at rest, but normal frontal activity in intellectual stress (respond to Ritalin)
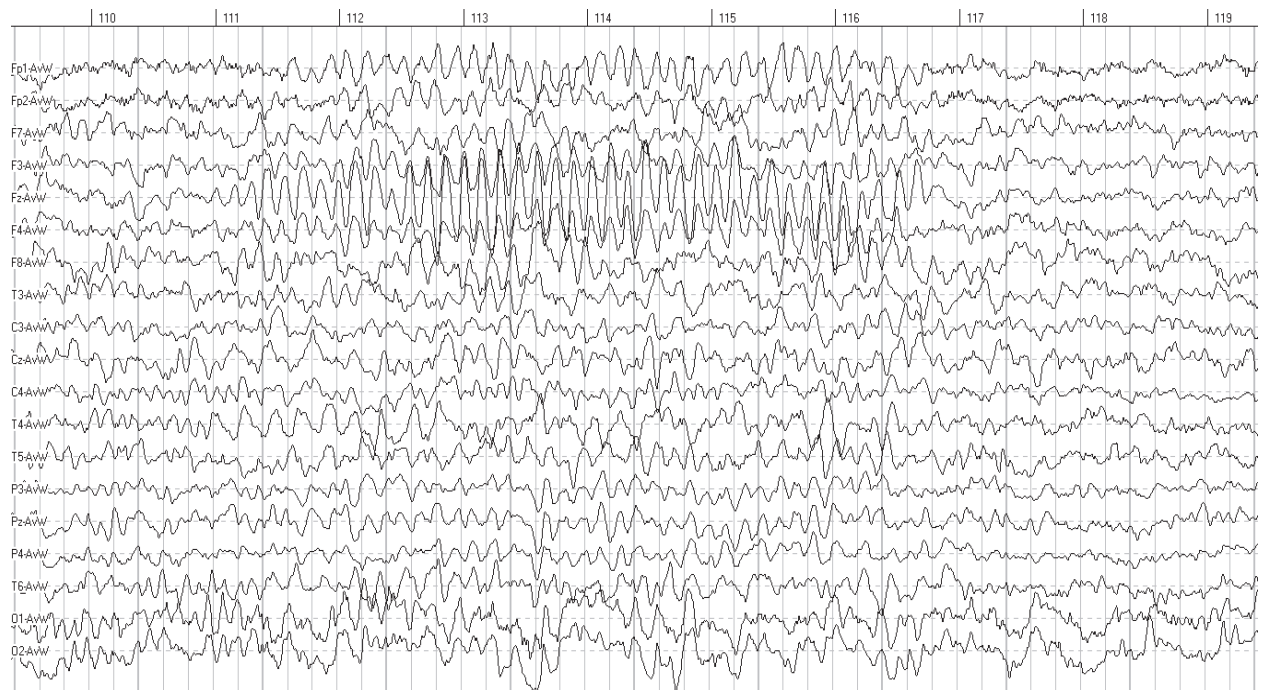
(Note slow delta/theta waves in frontal and central area)
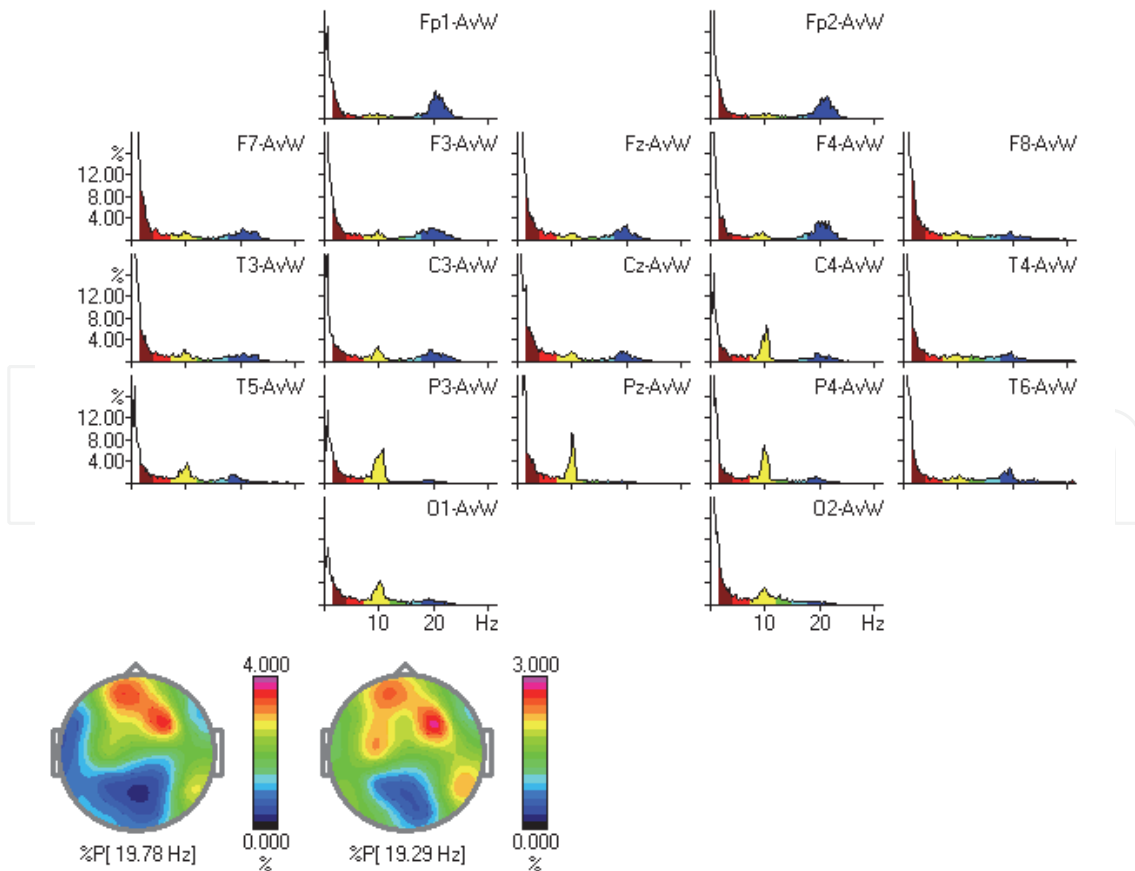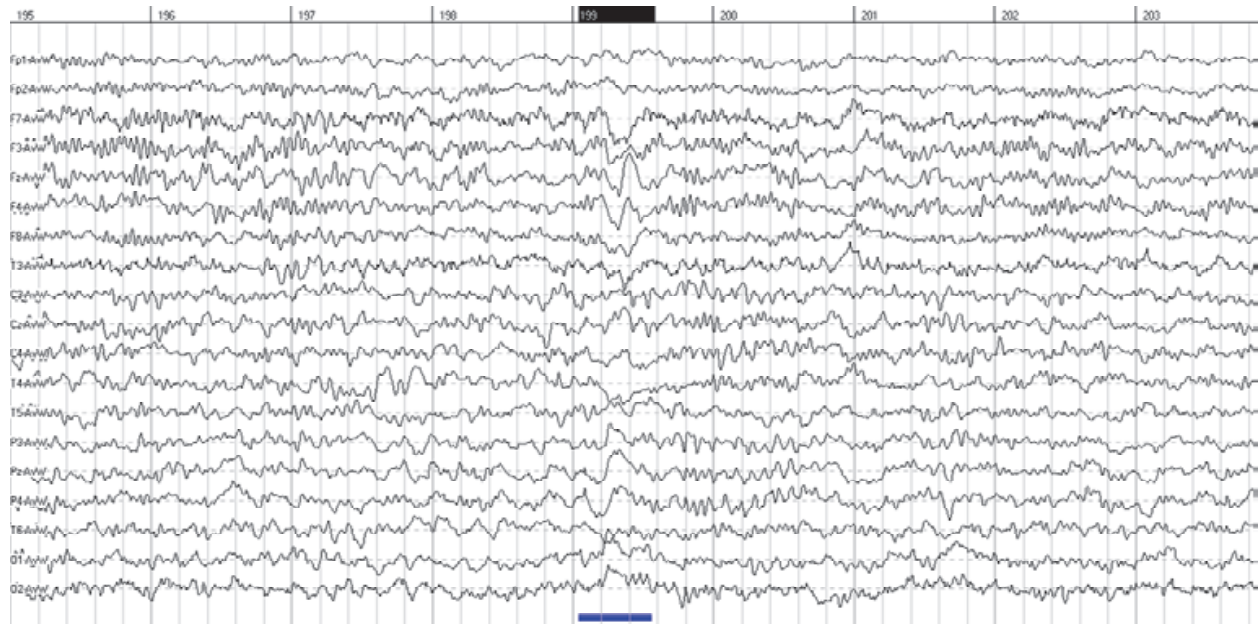
Fig. 4. Subtype II - row EEG recording

Fig. 5. Subtype III – over activated beta in frontal, central and parietal cortex

(Note fast brain waves over all cortex)

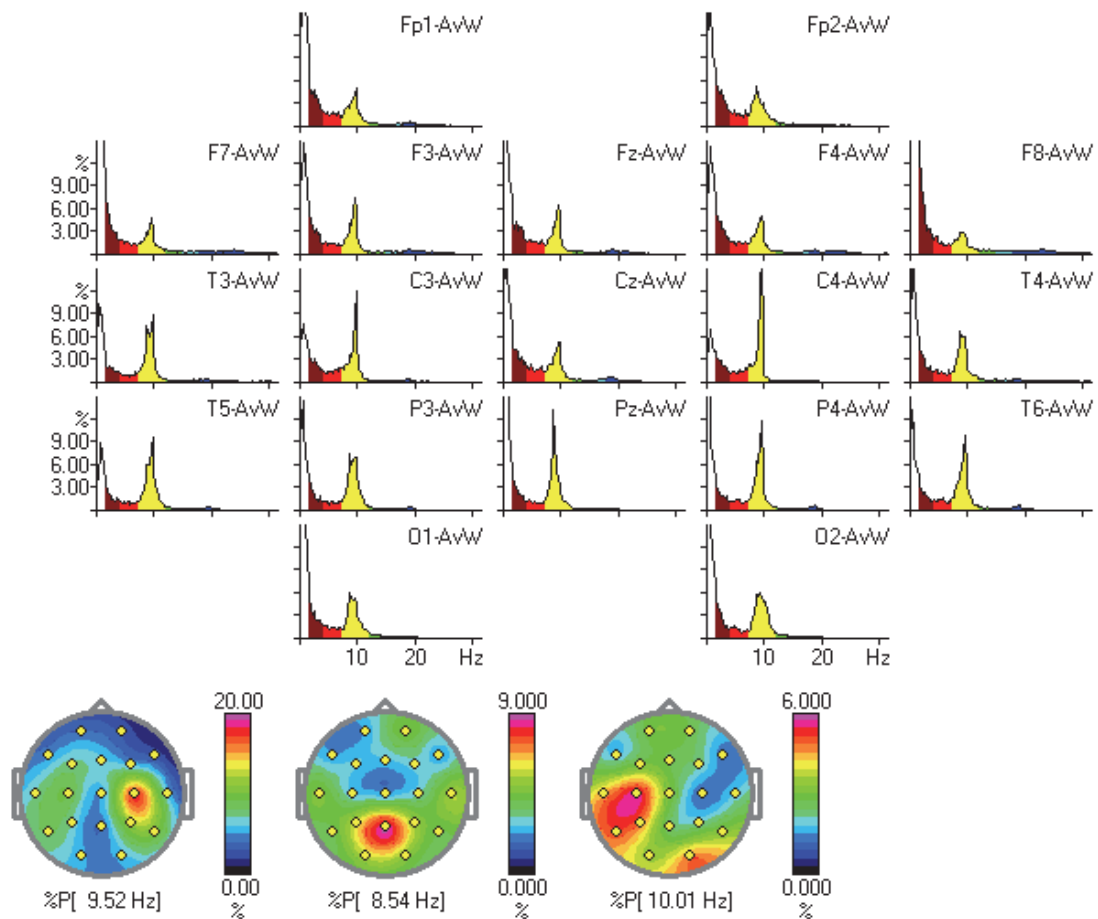Fig. 6. Row EEG recording - overactive cortex
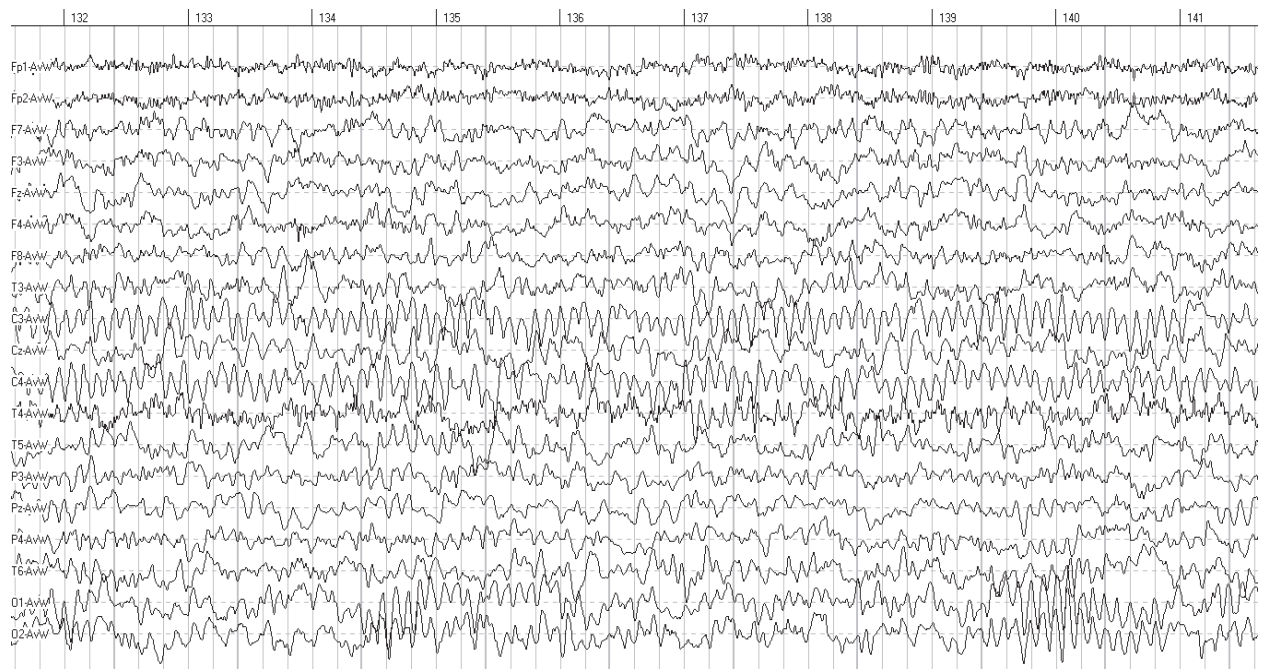

Fig. 7. Subtype IV – alpha excess

Fig. 8. Subtype IV- Row recording alpha excess

The evidence is not sufficient to permit conclusions about the benefits of SPECT imaging in the diagnosis and treatment of ADHD. A significant number of published studies are focused on investigating differences in regional cerebral perfusion in response to drug therapy and on serotonin and dopamine receptor and transporter activity. These studies are only preliminary. On the other side, the risks associated with SPECT imaging include exposure to low-dose radiation which is not recommendable in children.

4. Event related potentials

As we said previously, the term "executive functions" refers to the coordination and control of motor and cognitive actions to attain specific goals. The executive control is needed for optimizing behavior. The need for an executive control mechanism has been postulated for non-routine situations requiring a supervisory system (e.g. selection of appropriate action from variety of options, inhibition of inappropriate actions, and keeping in working memory the plan of the action as well as the outcome).

The executive system comprises a complex brain system such as several cortical and sub cortical structures interconnected with each other. The cortical structures include the prefrontal areas interconnected with the corresponding thalamic nuclei. The striatum is the most important in the subcortical circuits and it is considered as a cognitive map of cortical representations of actions. Together with basal ganglia the prefrontal cortex performs executive functions associated with engagement, disengagement, monitoring operations and working memory.

These operations of executive system are reflected in event related potentials (ERPs) evoked in different paradigms like Go/NoGo, oddball and working memory tasks. In our practice with ADHD children, we use the Human Brain Institute (HBI) normative database for comparing the obtained ERPs from the patients and norms.

The following executive components in the Go/NoGo stimulus tasks could be obtained:

- the motor and action suppression components associated with frontal negativivities at 200 millisecond (the conventional N2 inhibition component)
- the engagement component associated with parietal positivity at 300 millisecond (the conventional P3b component)
- the monitoring component associated with frontal-central positivity at 400 millisecond (P400).

The N2 motor inhibition component is generated in the ipsi-lateral premotor cortex, the P3b component is generated in the parietal cortical area, and the P400 monitoring component is generated in the cingulated cortex. It is supposed that dopamine is the main mediator of the executive system.

For the psychometric assessment of the executive functions in ADHD patients most frequently we use the Stroop Color Word Task – SCWT (Stroop 1935), and Wisconsin Card Sorting Test – WCST (Berg 1948).

The obtained results for a group of 30 children diagnosed as combined form of ADHD, aged 7-14 years are presented on Table 1 and Table 2 (Zorcec and Pop-Jordanova, 2010).

WCST	T-score ADHD	Significance of the test	T-score controls	Significance of the test	P
N categories	42	Low average	55	average	0,32
N perseverations	31	below average	51	average	0,00001*
N mistakes	32	below average	50	average	0,00000*
carts total	30	below average	52	average	0,00001*
M categories	31	below average	51	average	0,00001*

* statistical significance

Table 1. T-score and statistical significance for WCST obtained for ADHD children compared with healthy control

SCWT	T-score ADHD	Significance of the test	T-score controls	Significance of the test	P
Mistakes (St) II	50	average	55	average	0,1
Mistakes III	29	Very low	50	average	0,00001*
Mistakes III/II	28	Very low	53	average	0,00000*
St III-St II	50	average	53	average	0,02

*statistical significance

Table 2. T- score and statistical significance for SCWT obtained for ADHD children compared with healthy control

In the electrophysiological evaluation of ADHD children we used VCPT (visual cognitive performance task) with two stimulus Go/NoGo task developed specifically for the HBI database. The task consisted of 400 trials. The duration of stimuli is equal to 100 ms. Trials consisted of presentation of a pair of stimuli with inter stimulus interval of 1.1 sec. Interval between trials is equal to 3,100 ms and response interval from 100 to 1,000 ms. 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 (NoGo condition).

The VCPT during QEEG for ADHD children showed very high ommission and commission errors, shorter reaction time (RT) and higher variation of the reaction time (var RT), compared with the results obtained for control healthy children.(Table 3)

VCPT	ADHD	Norm	*t*-test	P
omission errors (Go)	32, 25	4	15, 65	0, 00001*
commission errors (NoGo)	4, 75	1	7, 58	0, 0000*
RT (ms) Go	456, 89	486	- 9, 17	0, 00001*
var RT	18, 97	11, 7	8, 78	0, 00000*

*statistical significance

Table 3. Statistical significance for VCPT forADHD children compared with tests norms

For the P3Go component (activation processes) we did not obtained significant differences for the latency as well as for the amplitude, while for P3NoGo component (inhibition processes) we obtained not significant differences for the latency, but significant differences concerned to the amplidude. (Tabl. 4)

	ADHD	norm	*t*-test	p
P3Go (ms)	327, 15	327, 89	- 0, 12	0, 9
P3Go (mV)	9, 73	8, 55	0, 77	0, 44
P3NoGo (ms)	402, 05	415, 78	- 0, 69	0, 49
P3NoGo (mV)	4, 67	6, 23	- 2, 89	0, 006*

*statistical significance

Table 4. Statistical significance for P3Go and P3NoGo for ADHD children compared with tests norms

Generally, our research (Zorcec and Pop-Jordanova 2010) dedicated to the psychometric and electrophysiological evaluation of children diagnosed as ADHD showed significant presence of the perseverative mistakes and difficulties in the mental flexibility. The results obtained for VCPT showed significantly higher ommission and commission errors, lower reaction time (RT) as well as higher variation of time reaction (var RT) compared to the tests norms. The P3Go component values in tle latency and amplitude did not differ from the norms, but the P3NoGo component showed significant difference in the amplitude.

5. Brain rate evaluation

Reviewing the EEG studies of patients with ADHD it can be concluded that most of them have generalized or intermittent spectrum shift. It is the reason that we introduced the brain rate calculation (Pop-Jordanova and Pop-Jordanov, 2005) in addition to theta/beta ratio for both aims, in the assessment procedure and as a neurofeedback parameter.

The brain rate (EEG spectrum weighted frequency) can be considered as an integral state attribute correlated to brain electric, mental and metabolic activity. In particular, it can serve as a preliminary diagnostic indicator of general mental activation (i.e. consciousness level), in addition to heart rate, blood pressure or temperature as standard indicators of general bodily activation.

In our research it was shown that brain rate can be used to discriminate between the groups of under-arousal (UA) and over-arousal (OA) disorders, to assess the quality of sleep, as well as to indicate the IQ changes caused by some environmental toxins (Pop-Jordanova 2009; Pop-Jordanov and Pop-Jordanova 2009, 2010). Brain rate is also suitable to reveal the patterns of sensitivity/rigidity of EEG spectrum, including frequency bands related to permeability of corresponding neuronal circuits. Based on all this findings, the individually adapted neurofeedback protocols can be elaborated.

The main characteristic of the integral (polychromatic) EEG spectrum is its mean frequency, weighted over the whole spectrum (brain rate - f_b), defined as

$$f_b = \frac{1}{V} \int f V(f) df, \quad V = \int V(f) df$$

or

$$f_b = \sum_i f_i P_i = \sum_i f_i \frac{V_i}{V}; \quad V = \sum_i V_i$$

where, i denotes the frequency band (for delta $i=1$, theta $i=2$, etc.), and V_i - the corresponding mean amplitude of the electric potential. (Pop-Jordanova N., Pop-Jordanov J., 2005)

In the following I will present some results obtained for brain rate (Demerdzieva, 2011) calculated for a group of 50 patients diagnosed as ADHD (age 119. 98; SD = 25.32 months, two females and 48 males) compared with a group of 50 healthy controls (mean age 117.84; SD = 24.89 months, and the same gender ratio as the ADHD group) (Table 5).

		Frontal	Central	Posterior	Left	Midline	Right
Group effect	Normal's vs. ADHD		0.000000	0.000000	0.000000	0.029686	0.000082
Condition effect	EC vs. EO	0.033569	0.015872	0.000000	0.000083	0.000000	0.000014
	EO vs. VCPT	0.000001					
	EC vs. VCPT	0.000000	0.007530	0.000000	0.014954	0.000000	
	EC vs. ACPT	0.000005	0.000196	0.000000	0.000004	0.000000	0.000089
	VCPT vs.ACPT	0.000005					

Table 5. Summary of significant interactions between groups, conditions and regions for brain rate results (evaluated with post hoc Bonferroni test)

Maximum values of f_b for sagittal topography were obtained in central and posterior regions, which is statistically significant, F (3, 390) = 24.849, p =.00000 (Fig. 9, left panel). Anyway these results are lower than those in healthy controls. According to the different conditions, obtained results were also statistically significant, F (9, 949.31) = 72.294, p = 0.0000. Maximum values for f_b were obtained in the posterior region during EC and minimum values in the frontal region again during EC condition for both ADHD and healthy groups..
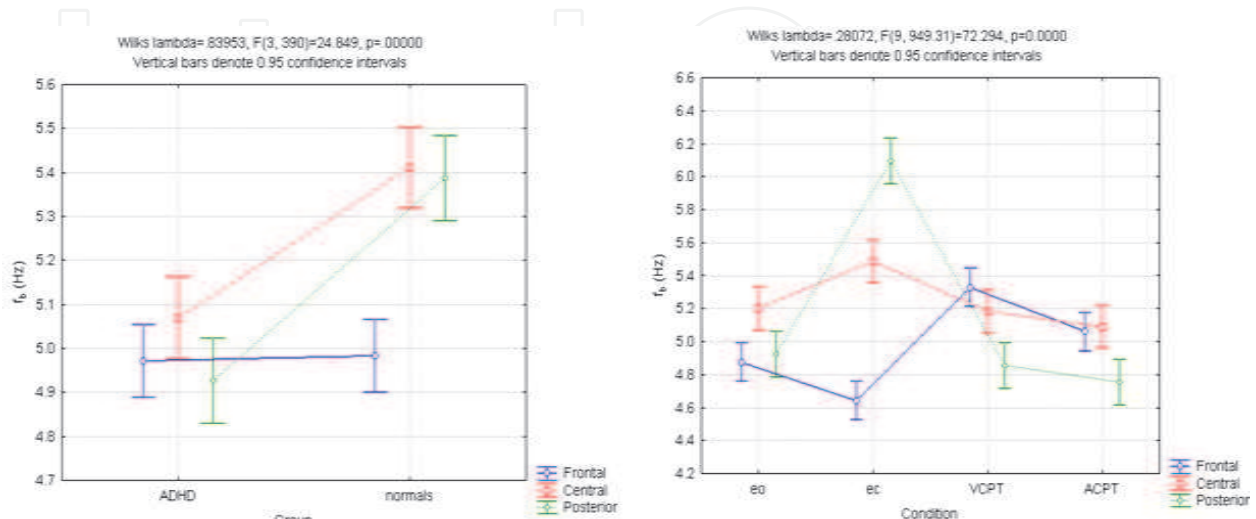

Fig. 9. Results for f_b values for sagittal topography according groups-left panel and according conditions-right panel (EC-eyes closed, EO-eyes opened, VCPT– visual continuous performance test, ACPT- auditory continuous performance test)

Maximum values of f_b for lateral topography are obtained in the left and right sides (Fig.10, left panel), which indicates higher excitability of lateral regions. The results are again significantly higher in normal group which indicates under arousal (UA) in children with ADHD (corresponding to subtype I prevalence). According different conditions in lateral topography the lower f_b values were obtained in midline for all four conditions (Fig.10, right panel).
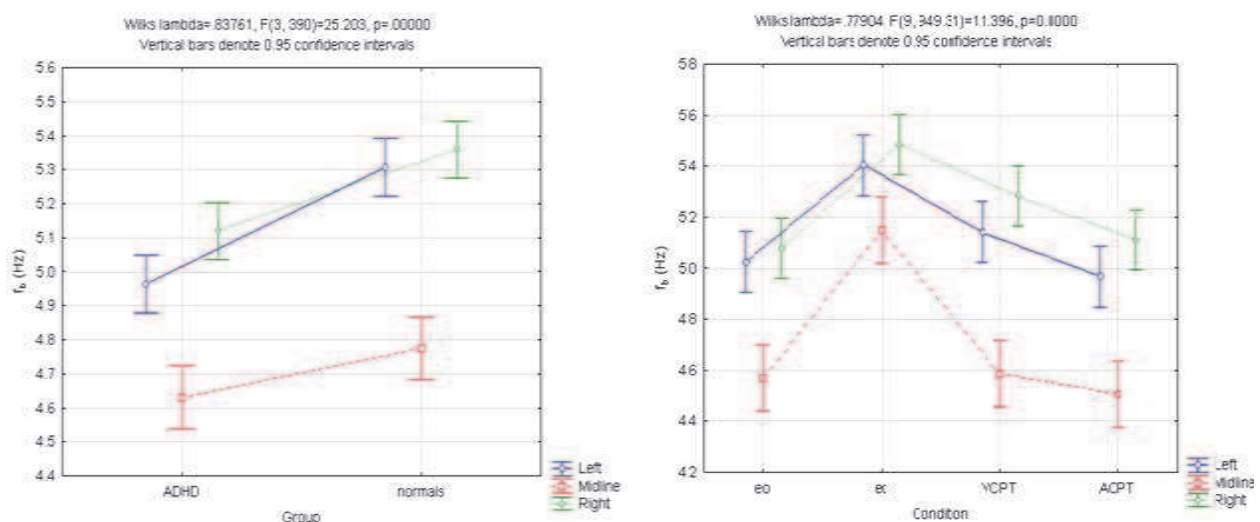

Fig. 10. Results for f_b values for lateral topography according groups - left panel and according conditions - right panel (EC-eyes closed, EO-eyes opened, VCPT-visual continuous performance test, ACPT- auditory continuous performance test)

The brain rate cocept is shown to be useful in the case of ADHD adults as well (Markovska-Simoska and Pop-Jordanova, 2011). Maximum values of *fb* for sagittal topography are obtained in central region, while the minimum in frontal region, corresponding to increased arousal (which is in agreement with the neurophysiological considerations). Maximum values of *fb* for lateral topography are obtained in the left and right sides, while the minimum in the midline region, which indicates higher excitability of lateral regions. As expected, a positive correlation between *fb* values and the QEEG spectra subtypes was obtained. Lower values were found for first and second subtype, and higher for the third and fourth subtype. This can be explained by the comparable arousal level for first and second subtype, and higher arousal in the third and fourth subtype. On the other hand, there was no correlation between behavioral symptoms (obtained with Barkley's scale) and *fb* values (i.e. spectrum gravity), as well as between QEEG ADHD subtypes and behavioral symptoms, illustrating the heterogeneous and multifactorial character of ADHD.

Generally we can summarize that through different clinical experiments and pediatric practice concerning brain rate it was shown that:

- Brain rate may serve as an indicator of general mental arousal level, similar to heart rate (Kaniusas et al, 2007), blood pressure and temperature as standard indicators of general bodily activation.
- By comparing eyes closed and eyes open brain rate values the diagnoses of inner arousal can simply be achieved (Pop-Jordanov and Pop-Jordanova, 2009).
- As a measure of arousal level, brain rate can be applied to discriminate between subgroups (clusters) of "mixed" disorders (e.g. ADHD, OCD, headache) (Pop-Jordanova, 2007, 2008, 2009).
- Brain rate can be more useful for selecting patients which need neurofeedback training (Pop-Jordanova, 2009).

6. Biofeedback treatment

Most prevalent approaches in the treatment of ADHD involve the use of stimulants, occasionally supplemented by tricyclic antidepressants, alpha-blockers and, in rare cases, antipsychotic drugs or selective serotonin reuptake inhibitors. In addition, the extensive behavior management, cognitive-behavioral therapy, individual psychotherapy and family system approaches have been applied. In the last two decades, biofeedback modalities have been offered in the treatment of different conditions and diseases (Schwartz 1987).

Biofeedback modalities can be divided into peripheral (based on electromyography, electrodermal response, heart rate, temperature, blood volume pulse) or central i.e. neurofeedback (based on electroencephalography). In what follows, we will concentrate on electrodermal response and neurofeedback.

Electrodermal response (EDR) is a complex reaction with a number of control centers in CNS. Three systems related to arousal, emotion and locomotion are responsible for the control of electrodermal activity (Bouscin 1992). The reticular formation controls EDR in connection to states of arousal, the limbic structures (hypothalamus, cingulated gyres and hippocampus) are involved in EDR activity related to emotional responses and thermoregulation, while the motor cortex and parts of the basal ganglia are involved in locomotion. In particular, skin potential and skin conductance used as parameters in EDR

biofeedback are related to both sympathetic and parasympathetic arousal (Andreassi 2000; Mangina 1996).

Treatment by EDR biofeedback is generally based on training patients in strategies for lowering arousal and maintaining a healthful sympathetic/parasympathetic tone. Consequently, EDR biofeedback modality is a first choice for introvert persons, where high inner arousal is a typical finding and biofeedback training is supposed to lower sympathetic activity. Changes in electrodemal activity can be reliably detected within one second of stimulus presentation, often following a single event. It is important to know that electrodermal conductance precede any other signals related to neuroimaging such a positron emission tomography (PET), blood oxygen level-dependent functional magnetic resonance (BOLD), single photon emission computerized tomography (SPECT) etc. In other words, the changes of electroderamal activity can be registered before the changes obtained by the other neuroimaging techniques.

Neurofeedback (NF) i.e. EEG biofeedback refers to a specific operant-conditioning paradigm where an individual learns how to influence the electrical activity (frequency, amplitude or synchronization) of his brain. It involves teaching skills through the rewarding experience of inducing EEG changes reflected in a perceivable signal (light or sound). Neurofeedback has been shown to be particularly useful in reference to pathologies characterized by dysfunctional regulation of cortical arousal, such as epilepsy and attention deficit hyperactivity disorder (Lubar 1991, 1997; Birbaumer 1999; Mann et al. 1992; Monastra 2001; Pop-Jordanova et al 2005). Our team also used EEG biofeedback in anorectic girls (Pop-Jordanova 2000, 2003), posttraumatic stress disorder - PTSD (Pop-Jordanova 2004), headaches (Pop-Jordanova 2008), as well as for optimal school (Pop-Jordanova, Cakalaroska, 2008) and music performance (Markovska-Simoska et al. 2008).

As we explained previously, the application of spectral analysis to EEG shows that in some brain dysfunctions the EEG amplitude in certain frequency bands significantly differs from the EEG amplitude of healthy subjects. For example, a relatively large group of children with ADHD reveals an excess of the theta/beta ratio i.e. decrease of fb in central – frontal leads. This EEG abnormality is associated with hypo activation of frontal lobes. Neurofeedback provides a best tool for correcting such deviations from normality.

Neurofeedback is based on three scientific facts. First, EEG parameters reflect brain dysfunction in a particular disease (in the case of specific subgroup of ADHD children this means the corresponding changes of theta beta ratio and of fb). Second, subject can voluntarily change the state of his/her brain so that changes can be associated with increasing or decreasing the relevant parameter. Third, the brain can memorize this new state and keep it for longer time not only in lab conditions but also in other environments, such as school, home etc.

For applying neurofeedback therapy, QEEG evaluation of each patient is needed. In our studies the QEEG is obtained by standard MITSAR EEG recordings (21 electrodes), with the administration of standardized tests: eyes-open (EO), eyes-closed (EC), visual continuous performance (VCPT), auditory continuous performance (ACPT), reading test and math test. EEG data are analyzed for frequency content using the fast Fourier transformation. Statistical analysis compares subject's data with a normative database corrected for time-of-day variations. Data are also evaluated for percentage change across states and compared

with a normative database for state modulation. The obtained topographic maps show covariance between all sites at relevant frequencies compared with a normative database, illustrating functional cortical interactions.

Many studies of QEEG for the ADHD group confirmed an increased theta activity predominantly in frontal regions, and a decreased beta activity in comparison to normal children (Mann et al 1992). In this context increased theta/beta ratio is reported as a typical finding in ADHD children (Lubar 1991; Monastra et al. 2001; Muller, 2006). So, the typical ADHD finding can be underarousal. As we said previously, the recent cluster analysis identified several subgroups of ADHD based on different EEG topographies. As a consequence, manly four distinct subgroups of ADHD with regard to electrophysiology are defined (Kropotov, 2009).

Neurofeedback treatment is particularly indicated in ADHD patients who show excessive EEG slowing in the superior frontal cortex or the midline central cortex (i.e. the first two subtypes) The most relevant neurological EEG correlate in these ADHD cases is usually assumed in the place where the highest ratio of theta/beta activity or lowest *fb* is seen, so that placement of the electrode between Cz and Fz is the best for training. We followed two consecutive treatment protocols. (1) Training to increase the SMR EEG rhythm (11 - 13 Hz) and at the same time, starting to inhibit (decrease) slow activity in the theta range (4 - 8 Hz); this approach is primarily used for the hyperactive component of ADHD. (2) Training to focus attention aiming at increasing higher beta activity (16 - 20 Hz), while training for decreasing the slow activity continued. The training is performed with 40 sessions, 60 min duration per session, one per week. To obtain stress diminishing, before neurofeedback we use peripheral biofeedback for all children.

Practically all neurofeedback interventions can be roughly reduced to the need of mastering flexibility in increasing or decreasing the general mental activation, i.e. mental arousal (which is somehow coupled with metabolic activity). Thereby, in practice, whenever a certain band is trained, the other bands are affected too (it may even appear that e.g. "…the changes that occurred as a result of stimulating in the alpha frequency were not in alpha but were in beta…"(Lubar 1997). Therefore, the introduced brain rate f_b could be employed as a complementary biofeedback parameter, characterizing the whole EEG spectrum (as distinct from e.g. theta-beta ratio). The rationale is that, according to the mentioned empirical results, the EEG frequency shifts are related to mental activation / deactivation, as the main objective of the treatment.

Using brain rate as a neurofeedback parameter for a group of ADHD children (N=50 mean age 11.11 years) Pop-Jordanova et al. (2005 and 2008) obtained the shifting of the spectrum from under-arousal to normal mental arousal, and it corresponded to improved attention and cognition as well as better school performance. Thereby obtained change of brain rate (i.e. arousal level) appeared to be more realistic in respect to the changes of psychological state of children than the drastic reduction of theta/beta ratio, which appeared to be even halved.

If we introduce brain rate as a general indicator of mental arousal in ADHD example, we can see that the first two subtypes are correlated with lower brain rate, (underarousal-UA) the third subtype with higher brain rate (overarousal-OA), while the four subtype is related to excess of alpha activity and "normal" arousal state. In the first three subtypes of ADHD the protocol for UA and OA is clear, while for the "normal" arousal it is not.

The detailed analysis of QEEG after the neurofeedback training with brain rate as a parameter could detect which bands have been most changed. For instance, in some cases shifting the brain rate to higher values could result in increasing high alpha or beta frequencies; in other, the same change can appear due to diminishing the power of theta or delta bands. As a result, the QEEG comparison before and after the brain rate training can be informative for assessing the individual spectrum band sensitivity.

7. Conclusions

The frontal regions are most likely to show deviations from normal development in the case of ADHD, with disturbed thalamo-cortical and septal-hippocampal pathways, altogether named as executive system.

Application of spectral analysis to EEG shows that the EEG amplitude in certain frequency bands significantly differs from the EEG amplitude of healthy subjects. For example, a relatively large group of children with ADHD reveals an excess of the theta/beta ratio i.e. decrease of brain rate in central – frontal leads. This EEG abnormality is mostly associated with under activation of frontal lobes.

For the exact diagnosis of ADHD, it is recommendable QEEG to be combined with DSM-IV (or ICD-10) behavioral based approach.

There are four main endophenotypes in ADHD population: I subtype (abnormal increase of delta-theta frequency range centrally or centrally-frontally), II subtype (abnormal increase of frontal midline theta rhythm), III subtype (abnormal increase of beta activity frontally), and IV subtype (excess of alpha activities at posterior, central, or frontal leads). Thereby, we consider the second subtype as a subgroup of the first subtype.

The dysfunction of the executive system can be evaluated by event related potentials (ERP's) as well. Children with ADHD showed significant presence of the perseverative mistakes and difficulties in the mental flexibility. The results obtained for visual cognitive performance test (VCPT) showed significantly higher ommission and commission errors, lower reaction time (RT) as well as higher variation of time reaction (var RT) compared to the tests norms.

Distribution of brain rate values for sagittal and lateral topographies reflects the arousal levels in the corresponding conditions. There is a positive correlation between brain rate values and the QEEG spectra subtypes.

Neurofeedback provides a tool for correcting deviations from normality, especially for the subtypes I, II and III. For obtaining better therapeutic results, before neurofeedback, the use of peripheral biofeedback (such as electrodermal activity) aiming to obtain stabilization of sympathetic/parasympathetic system is recommended for all patients.

Brain rate can be used as a multiband biofeedback parameter in mediating the under arousal or over arousal states, complementary to few-band parameters and the skin conduction

Follow-up research is needed in order to determine more precisely the specificity and sensitivity of QEEG and brain rate approach related to neurophysical substrates of ADHD.

8. References

Amen, DG. (1997) Brain SPECT imaging: Implication for EEG biofeedback. Keynote address presented at 28th annual meeting of the Association for Applied Psychophysiology and Biofeedback, San Diego, CA.

Amen DG, Hanks C, Prunella J. (2008) Preliminary evidence differentiating ADHD using brain SPECT imaging in older patients, *J Psychoactive Drugs*. 40(2):139-46.

Andreassi, JL. (2000) Psychophysiology. Human behavior and physiological response. LEA, London.

Anokhin, AP, Heath AC, Myers E. (2006) Genetic and environmental influences on frontal EEG asymmetry: A twin study. *Biol. Psychol.* 71 (3): 289-295

Barkley, R. (1990) Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, Guilford Press, New York

Berg, A. (1948) A simple objective technique for measuring flexibility in thinking, *J. Gen. Psychol.* 39: 15-22

Birbaumer, N, Roberts LE, Lutzenbrger W, Rockstroh B, Elbert T. (1999) Area-specific self-regulation of slow cortical potential on the sagittal midline and its effects on behavior. *Electroencephalogr Clin Neurophysiol* 84:352–361

Boucsein, W. (1992) Electrodermal activity. Plenum, New York.

Crosbie J, Schachar R. Deficient inhibition as a marker for familial ADHD. *Am J Psychiatry*. 2001; 158:1884-1890.

Culbert, TC, Kajander RL, Reaney JB. (1996) Biofeedback with children and adolescent: clinical observations and patient perspectives. *J Dev Pediatr* 17(5):342–350

Demerzieva, A. (2011) EEG spectra power characteristics of Attention Deficit Hyperactivity Disorder in childhood, *Epilepsija:* 124-136

Gottesman I I. and Shields J., (1972) Schizophrenia and Genetics: A Twin Study Vantage Point. Personality and Psychopathology Series, New York and London, Academic Press.

Kaniusas, E, Varoneckas G, Alonderis A, Podlipsky A. (2007) Heart rate variability and EEG during sleep using spectrum-weighted frequencies – a case study, COST B27. EU/ESF, Brussels.

Kropotov, J. (2009) Quantitative EEG, ERP's and neurotherapy. Elsevier, Amsterdam

Lubar JF. (1991) Discourse on development on EEG diagnostics and biofeedback treatment for attention deficit/hyperactivity disorders. *Biofeedback Self-Regul* 16: 201–225

Lubar JF. (1997) Neurocortical dynamics: Implications for understanding the role of neurofeedback and related techniques for the enhancement of attention. *Appl Psychophysiol Biofeedback* 22(2):111–126

Mann, C., Lubar J., Zimmerman A., Miller C., and Muenchen R. (1992) Quantitative analysis of EEG in boys with attention-deficit/hyperactivity disorder: A controlled study with clinical implications. *Paediatric Neurology*, 8: 30-36

Mangina CA, Beuzeron-Mangina JH. (1996) Direct electrical stimulation of specific human brain structures and bilateral electrodermal activity. *Int J Psychophysiol* 22:1–8

Markovska-Simoska S, Pop-Jordanova N, Georgiev D. (2008) Simultaneous EEG and EMG biofeedback for peak performance in musician. *Prilozi* 1:239–253

Markovska-Simoska S., Pop-Jordanova N. (2011) Quantitative EEG Spectrum-weighted Frequency (Brain Rate) Distribution in Adults with ADHD, *CNS spectr* 16 (5): 579-587

Monastra VJ, Lubar JF, Linden M. (2001) The development of quantitative electroencephalographic scanning process for attention deficit-hyperactivity disorder: reliability and validity studies. *Neuropsychology* 15(1):136–144

Muëller A. (2006) Neurobiological diagnostics and therapy in ADHD, in: *News in Pediatrics.* University of Skopje, Skopje, pp 135–147

Pop-Jordanova N. (1999) Electrodermal response based biofeedback in pediatric patients. *Paediatr Croat* 43:117–120

Pop-Jordanova N. (2000) Biofeedback mitigation for eating disorders in preadolescents. *Int Pediatr* 1:76–82

Pop-Jordanova N. (2003) Eating disorders in the preadolescent period: psychological characteristics and biofeedback mitigation, Chapter III. In: Swain P (Ed) Focus on eating disorder research. Nova Biomedical books, New York .

Pop-Jordanova N, Zorcec T. (2004) Child trauma, attachment and biofeedback mitigation. *Prilozi* 1–2:103–114

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

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

Pop-Jordanova N. (2006) Biofeedback modalities for children and adolescents. In: Columbus F. (Ed) New research on biofeedback. Nova Biomedical Book, New York.

Pop-Jordanova N., Muller A., Zorcec T., Markovska-Simoska S. (2007): QEEG subtypes of Macedonian ADHD children, Applied Neuroscience for Healthy Brain Function, Nijmegen, Netherlands, Book of abstracts, p.60

Pop-Jordanova N. (2008) EEG spectra in pediatric research and practice. *Prilozi* 1: 221–239

Pop-Jordanova N, Cakalaroska I. (2008) Biofeedback modalities for better achievement in high school students school students. *MJM* 2:25–30, also *Revista Espanola de Neuropsicologia*, 1:97–98

Pop-Jordanov J, Pop-Jordanova N. (2009) Neurophysical substrates of arousal and attention. *Cogn Process*. 10(Suppl.1), S71-S79

Pop-Jordanova N. (2009) Biofeedback application for somatoform disorders and attention deficit hyperactivity disorder (ADHD) in children. *Int J Med Sci* 1(2):17–22

Pop-Jordanov J. Pop-Jordanova N. (2010) Quantum transition probabilities and the level of Consciousness. *Journal of Psychophysiology*, 24(2):136-140

Schwartz MS (1987) Biofeedback: a practitioner's guide. Guilford Press, New York.

Scott F (1998) EEG biofeedback for children and adolescent: a pediatrician's perspective. *Biofeedback* 26(3):18–20

Smith and Jonides (1999) Storage and executive processes in the frontal lobe, *Science* 283 (5408): 1657-1661.

Stroop R. (1935) Studies of interference in serial verbal reactions, *Journal of Experimental Psychology*, 18: 643-662

Zorcec T, Pop-Jordanova N, Müller A.(2007) Attention Deficit Hyperactivity Disorder in three family generations (case report). *Neuroscience today: neuronal functional diversity and collective behaviors*, COST B27. EU/ESF Florence, Italy, Book of abstracts p. 25.

Zorcec T., Pop-Jordanova N., Muller A. (2007) QEEG characteristics of children with ADHD, *Epilepsy*: 111-120

Zorcec T., Pop-Jordanova N., Mueller A., Gjoneska B. (2008) The Role of Q-EEG in Comprehensive Classification of ADHD Children; 2nd Neuromath Workshop, Jena. 28-29 April: 42-43

Zorcec T., Pop-Jordanova N. (2010) ADHD as executive dysfunction, *Prilozi*, 31 (2): 171-181
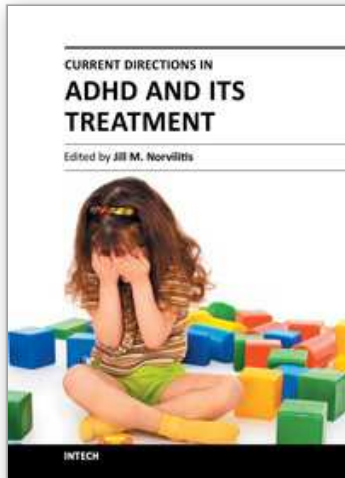
Current Directions in ADHD and Its Treatment

Edited by Dr. Jill M. Norvilitis

The treatment of Attention Deficit Hyperactivity Disorder is a matter of ongoing research and debate, with considerable data supporting both psychopharmacological and behavioral approaches. Researchers continue to search for new interventions to be used in conjunction with or in place of the more traditional approaches. These interventions run the gamut from social skills training to cognitive behavioral interventions to meditation to neuropsychologically-based techniques. The goal of this volume is to explore the state-of-the-art in considerations in the treatment of ADHD around the world. This broad survey covers issues related to comorbidity that affect the treatment choices that are made, the effects of psychopharmacology, and non-medication treatments, with a special section devoted to the controversial new treatment, neurofeedback. There is something in this volume for everyone interested in the treatment of ADHD, from students examining the topic for the first time to researchers and practitioners looking for inspiration for new research questions or potential interventions.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

INTECH
open science | open minds