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ALPHA ASYMMETRY IN QEEG RECORDINGS IN YOUNG PATIENTS WITH ANXIETY

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A b s t r a c t: Anxiety is defined as a subjective sense of worry, apprehension, fear and distress. When severe, it can affect a child's thinking, decision-making ability, perceptions of the environment, learning and concentration. Basal instability in cortical arousal, as reflected in measures of quantitative electroencephalography (qEEG), is common in most of the anxiety disorders.

Subjects and methods: The sample was composed of 26 children and teenagers aged 11.73 ± 4.03 years, F: M = 1 : 2. The group was diagnosed as having Generalized Anxiety Disorder (GAD). EEG was recorded with Quantitative EEG equipment – Mitsar-amplifier with 19 electrodes with 250 Hz sampling rate in the 0.3–70 Hz frequency range in the following conditions: eyes opened and eyes closed, at least 5 minutes each.

Results and conclusions: A statistically significant difference of spectra power in alpha band between left and right hemisphere was obtained. The right frontal asymmetry is specific to the right-handed. In eyes-open condition the percentage of children manifesting right asymmetry is up to 92.31% and in the eyes-closed condition it is 88.46%. Left frontal asymmetry was typical of left-handed children. We did not confirm the posterior right asymmetry suggested by other authors. The correlations between asymmetry and hand preference of children was very strong ($r = 0.68–0.85$) and statistically significant ($p < 0.05$) only for frontal regions of the brain. For parietal regions this was weak and statistically not significant.

Key words: General Anxiety Disorder, quantitative EEG (electroencephalography), Alpha spectra power, alpha asymmetry.

Introduction

Anxiety is defined as a subjective sense of worry, apprehension, fear and distress. When severe, it can affect a child's thinking, decision-making ability, and perceptions of the environment, learning and concentration. Brain imaging and functional studies have shown some evidence of abnormal function in several regions of the brain.

Among the techniques of functional brain imaging, quantitative electroencephalography (qEEG) offers many advantages. The ideal temporal resolution in the millisecond time domain characteristic of neuronal information processing, no ionizing radiation, noninvasive images, both excitatory and inhibitory cortical neuronal activity rather than secondary haemodynamic processes, and relatively inexpensiveness and portability are the advantages. [1].

Many authors have reported specific electrophysiological patterns for anxiety disorders. The basal instability in cortical arousal, as reflected in measures of qEEG, is common to most of the anxiety disorders. Resting electroencephalographic (EEG) measures tend to correlate with symptom sub-patterns and be exacerbated by condition-specific stimulation [2].

Bruder *et al.* (1997), investigated a model of asymmetric hemispheric activity in depression and anxiety, and reported that anxious and nonanxious depressed patients differ on electroencephalographic (EEG) measures of parietotemporal activity. As predicted, depressed patients with an anxiety disorder differed from those without anxiety in alpha asymmetry. Nonanxious depressed patients showed an alpha asymmetry indicative of less activation over right than left posterior sites, whereas anxious depressed patients showed evidence of greater activation over right than left anterior and posterior sites. [3].

Frontal EEG asymmetry has been studied as a state related to acute affective response. Authors have used experimental factors to induce emotions, like evocative film clips, and produced asymmetric patterns of EEG activation. In these experiments, a negative affect was associated with relatively higher right frontal activation, whereas positive emotional states were associated with greater left frontal activation [4–6].

Frontal brain asymmetry has been conceptualized as a biological substrate for the fundamental dimensions of emotion, approach and withdrawal [7–8]. There was very interesting work by Fox, 1991, [9] related to brain asymmetries (as measured by scalp-recorded EEG activity) localized to the frontal region and associated with the generation of emotions even in infants.

The goal of our study was to evaluate EEG alpha power and alpha asymmetry in children with anxiety from 7–18 years of age. OUR HYPOTHESIS is that there is a significant difference in spectral power in the alpha activity between the left and right sides of the brain in children with anxiety disorders.

In addition, the asymmetric alpha activity was found to be associated with relatively higher right frontal activation predominant in the frontal but not the posterior regions in children with anxiety disorders.

Methods and patients

Subjects

The sample comprised 26 children and teenagers, average age 11.73 ± 4.03 years; 65.28% (or 17) of patients were males and 34.62% (or 9) were females. The diagnosis as GAD (Generalized Anxiety Disorder) was made according to ICD-10 criteria. The manifested symptoms comprised:

- ✓ Excessive concerns about the quality of one's performance in areas such as schoolwork, sports or everyday life;
- ✓ Excessive concerns about physical health (despite good health);
- ✓ Excessive concerns about non-health themes (money, family, disasters…);
- ✓ Free floating anxiety unrelated to specific situations;
- ✓ A frequent need for reassurance;
- ✓ Marked feelings of tension, inability to relax or to concentrate, nervousness, difficulty falling asleep, autonomic symptoms (such as palpitations, sweating, dry mouth, etc.);
- ✓ Recurrent somatic complaints.

Inclusion criteria were: age between 7 and 18 years; absence of actual neurological or mental impairments and absence of the use of psychoactive or psychotropic substances (screened by a previous anamnesis and clinical examination). EEG was recorded with qEEG equipment (Mitsar, Ltd.) amplifier from 19 electrodes (on the International 10–20 system) with 250 Hz sampling rate in 0.3–70 Hz frequency range in the following conditions:

1) eyes open (EO) – at least 5 minutes, and

2) eyes closed (EC) – at least 5 minutes.

Recorded results were referred and analysed as data base montage.

Scale: 50 mcV/cm, speed – 30 mm/sec, time constant – 0.3 sec, low frequency filter – 30 Hz. The analysis was made after eliminating artifacts resulting from movements, large scale muscle tension, sweat, and large eye movements. Vertical and horizontal eye movement artifact correction was done by means of Independent Component Analysis (ICA). ICA is an information maximization algorithm that derives spatial filters by blind source separation of the EEG signals into temporally independent and spatially fixed components.

Then recordings for two conditions – eyes closed and eyes open – are sufficient for calculation of spectra power values for every 19 electrodes for all 5 bands: delta, theta, alpha, beta1 and beta2.

Table 1

Results for spectra power in eyes-open condition for 11-year-old girl

Montage	**Delta μV²**	**Theta μV²**	**Alpha μV²**	**Beta 1 μV²**	**Beta 2 μV²**
Fp1-AvW	11.86	3.68	3.02	1.57	3.02
Fp2-AvW	11.68	3.58	3.43	2.79	9.26
F_7-AvW	6.07	2.09	1.97	1.01	2.18
F_3-AvW	6.58	2.73	2.78	2.00	2.89
Fz-AvW	8.96	3.41	2.74	1.42	1.24
F_4-AvW	7.48	2.72	3.02	2.77	4.54
F_8-AvW	7.08	2.19	2.19	1.26	2.30
T_3-AvW	8.04	3.33	3.77	4.22	3.16
C_3-AvW	6.71	3.11	4.83	3.25	1.61
Cz-AvW	11.39	4.22	4.22	1.70	1.18
C_4-AvW	2.72	1.18	1.62	0.68	0.68
T_4-AvW	7.78	3.30	3.96	2.74	2.45
T_5-AvW	9.31	3.93	6.35	2.81	4.64
P_3-AvW	8.34	3.45	5.58	1.53	1.77
Pz-AvW	7.39	2.96	3.40	1.13	0.73
P_4-AvW	7.26	3.30	7.27	2.22	1.15
T_6-AvW	9.09	3.71	9.54	2.93	1.60
O_1-AvW	11.70	4.86	12.32	3.99	2.40
O_2-AvW	15.73	5.96	18.45	4.98	4.98

The spectra power or spectral analysis is computed using fast Fourier transformation (FFT) algorithm. The averaged (over time of recording) spectra are calculated for each EEG channel separately. EEG rhythms are expressed in the form of spectra peaks.

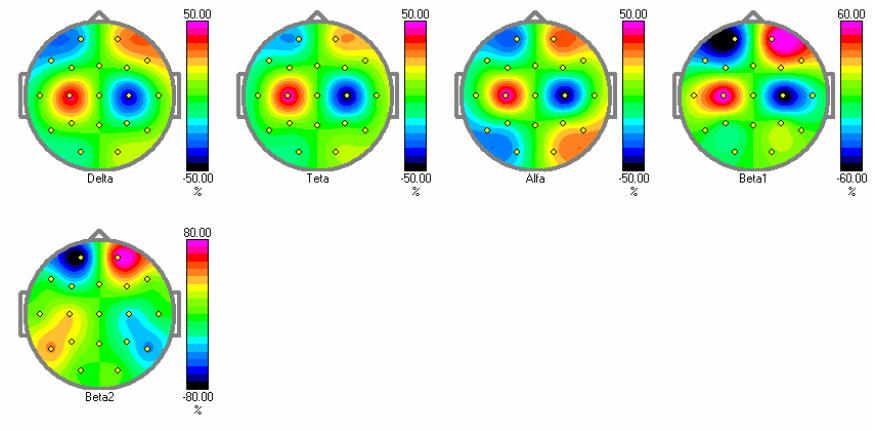

Figure 1 – Alpha asymmetry for 11-year-old girl, eyes-open condition

Asymmetry is defined as a functional difference between the left and right hemispheres measured from absolute amplitude which exists between the homologous electrodes located on these hemispheres [10]. It was calculated from the equation:

$$P(L) – P(R) / P(L) + P(R),$$

where P(L) corresponds to the alpha power of the electrode located on the left hemisphere, and P(R) to the alpha power on the right hemisphere. These asymmetry data were submitted to statistical analysis.

EEG asymmetry scores can be computed either as the difference between natural logarithm (ln) of EEG alpha power at the right recording site and the left recording site (ln (right) – ln (left); e.g. F3/4 = ln (F4) – ln (F3).

Brain activity is an inverse measure of alpha power activity, meaning less alpha power represents more brain activity and vice versa [11]. Consequently left EEG asymmetry values indicate greater left relative to right brain activity, and right EEG asymmetry values yield the opposite activity pattern. EEG asymmetries were evaluated for mid frontal (F3, F4), lateral frontal (F7, F8), and parietal (P3, P4) pairs of sites.

The qEEG spectra power data and data for alpha asymmetry were analysed using Statistica software (version 7.0). The results were calculated for two condition s- eyes closed and eyes open.

Results

A statistically significant difference was found in E.C. condition from calculated alpha power in frontal (F_3/F_4; F_7/F_8), parietal (P_3/P_4), temporal (T_5/T_6) and occipital region (O_1/O_2).

Table 2

Difference in spectra power in alpha band for paediatric anxious patients in E.C.

Variables	t-value	p
Fp1 vs. Fp2	0.942731	0.350352
F_3 vs. F_4	**2.709538**	**0.009204***
F_7 vs. F_8	**3.668533**	**0.000592***
C_3 vs. C_4	0.151996	0.879802
T_3 vs. T_4	1.656083	0.103969
P_3 vs. P_4	**2.310308**	**0.025036***
T_5 vs. T_6	**4.098149**	**0.000153***
O_1 vs. O_2	**4.859354**	**0.000012***

*significance level $p < 0.05$

In E.O. no statistically significant difference was found.

Table 3

Difference in spectra power in alpha band for paediatric anxious patients in E.O.

Variables	t-value	p
Fp1 vs. Fp2	– 0.990310	0.326791
F_3 vs. F_4	0.144898	0.885374
F_7 vs. F_8	0.932772	0.355420
C_3 vs. C_4	– 0.803280	0.425615
T_3 vs. T_4	0.027787	0.977943
P_3 vs. P_4	– 1.34584	0.184425
T_5 vs. T_6	– 0.810602	0.421436
O_1 vs. O_2	– 0.435178	0.665306

Alpha asymmetry was calculated using formula: P(L) – P(R) / P(L) + P(R) in 26 patients:

Table 4

Results from alpha asymmetry in frontal and parietal regions for 26 patients

Patients	**F_3/F_4 eo**	**F_7/F_8 eo**	**P_3/P_4 eo**	**F_3/F_4 ec**	**F_7/F_8 ec**
1.	0.034	0.04	0.026	0.069	0.182
2.	0.267	0.088	– 0.249	0.025	0.045
3.	0.043	0.048	– 0.131	0.1	0.125
4.	0.111	0.125	– 0.031	0.129	0.166
5.	0.026	0.203	0.071	0.1	0.075
6.	0.001	0.266	– 0.117	0.0007	0.189
7.	0.252	0.252	– 0.771	0.203	0.229
8.	0.38	0.105	– 0.584	0.401	0.096
9.	– 0.029	0.313	– 0.127	– 0.062	– 0.073
10.	0.084	0.512	0.179	0.198	0.263
11.	0.075	0.092	0.117	0.054	0.053
12.	0.046	0.008	0.044	0.04	0.131
13.	– 0.116	– 0.104	– 0.101	– 0.121	– 0.079
14.	0.069	0.043	– 0.294	0.044	0.132
15.	0.326	0.165	– 0.016	0.123	0.136
16.	0.008	0.062	0.064	0.013	0.038
17.	0.057	0.261	0.196	0.056	0.261
18.	0.029	0.025	– 0.203	0.019	0.049
19.	0.098	0.196	– 0.131	0.094	0.275
20.	– 0.086	0.119	– 0.163	0.059	0.031
21.	0.061	0.151	0.031	0.078	0.321
22.	0.007	– 0.183	– 0.092	0.012	– 0.053
23.	0.109	0.019	0.034	0.069	0.019
24.	0.081	0.396	– 0.116	0.044	0.365
25.	0.119	0.428	– 0.163	0.084	0.202
26.	0.048	0.019	– 0.16	0.02	0.057

These results showed that in eyes-open condition asymmetry was as follows:

Table 5

Percentage of patients with right and left alpha asymmetry in E.O.

F_3/F_4 eyes-open condition	
92.31% (24 patients)	Right Asymmetry
7.69% (2 patients)	Left Asymmetry
F_7/F_8 eyes-open condition	
92.31% (24 patients)	Right Asymmetry
7.69% (2 patients)	Left Asymmetry
P_3/P_4 eyes-open condition	
65.38% (17 patients)	Left Asymmetry
46.15% (9 patients)	Right Asymmetry

In E.C. condition the results are as followed:

Table 6

Percentage of patients with right and left alpha asymmetry in E.C. condition

F_3/F_4 eyes-closed condition	
92.31% (24 patients)	Right Asymmetry
7.69% (2 patients)	Left Asymmetry
F_7/F_8 eyes-closed condition	
88.46% (23 patients)	Right Asymmetry
11.54% (3 patients)	Left Asymmetry
P_3/P_4 eyes-closed condition	
50% (13 patients)	Left Asymmetry
50% (13 patients)	Right Asymmetry

Table 7

Correlations between alpha symmetry during E.O. and E.C. conditions (all of calculated results show strong positive correlations significant at $p < 0.05$)

Asymmetry	F_3/F_4 e.c.
F_3/F_4 e.o.	**r = 0.74**
Asymmetry	F_7/F_8 e.c.
F_7/F_8 e.o.	**r = 0.62**
Asymmetry	P_3/P_4 e.c.
P_3/P_4 e.o.	**r = 0.67**

Obtained results showed a strong positive correlation between alpha asymmetry in E.C. and E.O. conditions.

Correlations between results for alpha asymmetry and left- or righ- handed side of the child.

Table 8

Correlations between alpha symmetry in E.O. and E.C. related to hand preference

CORRELATIONS	RH/LH
F_3/F_4 e.o.	**r = 0.85**
F_7/F_8 e.o.	**r = 0.68**
P_3/P_8 e.o.	r = 0.31
F_3/F_4 e.c.	**r = 0.68**
F_7/F_8 e.c.	**r = 0.85**
P_3/P_8 e.c.	r = 0.21

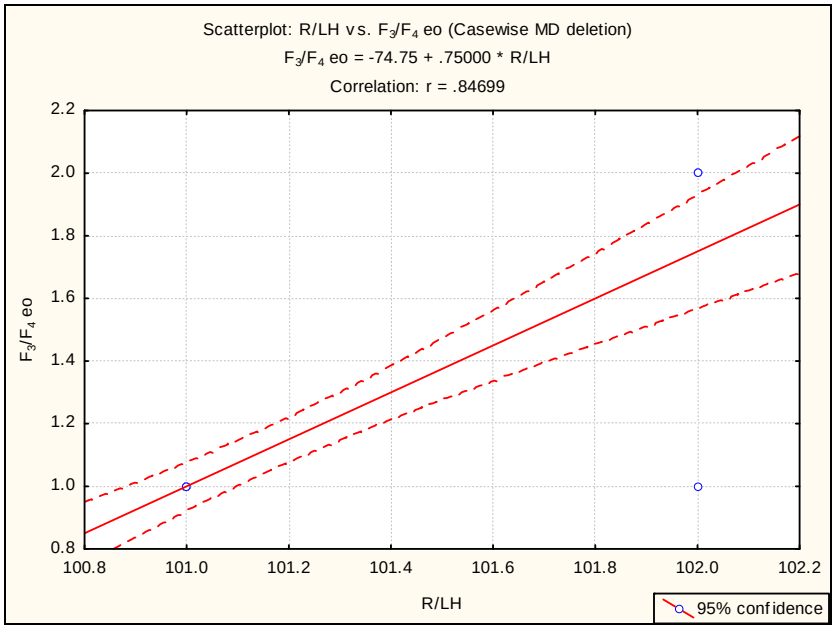

Figure 2 – Correlation (r = 0.85) between hand preferance and alpha asymmetry in eyes – open condition in frontal region (F_3/F_4)

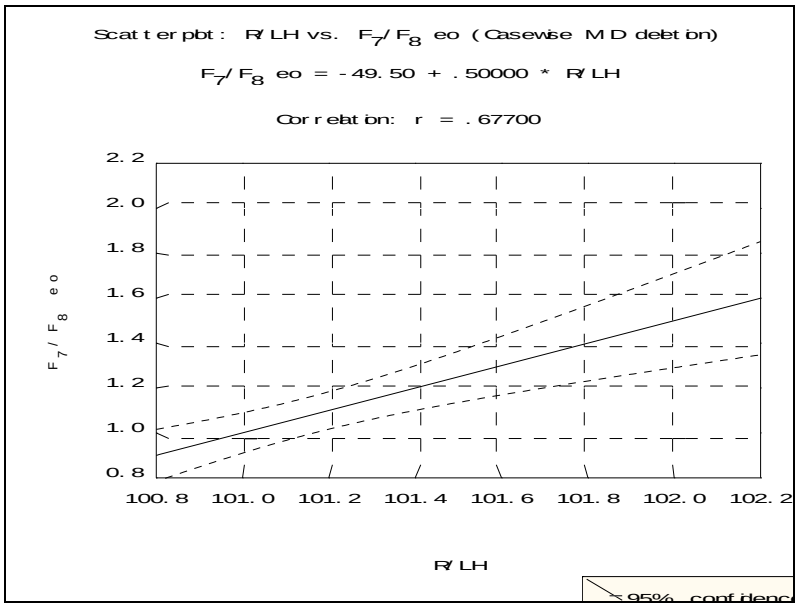

Figure 3 – Correlation (r = 0.68) between hand preferance and alpha asymmetry in eyes – open condition in frontal region (F_7/F_8)

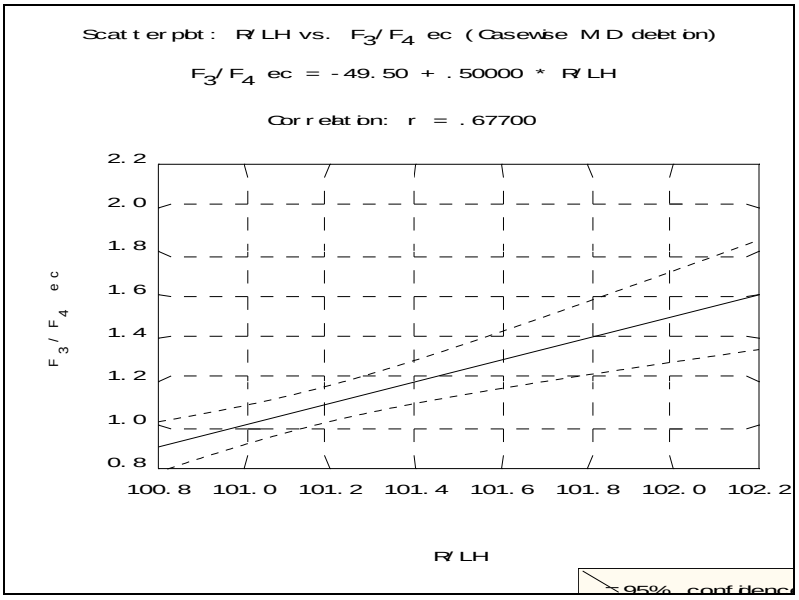

Figure 4 – Correlation (r = 0.68) between hand preference and alpha asymmetry in eyes – closed condition in frontal region (F_3/F_4)

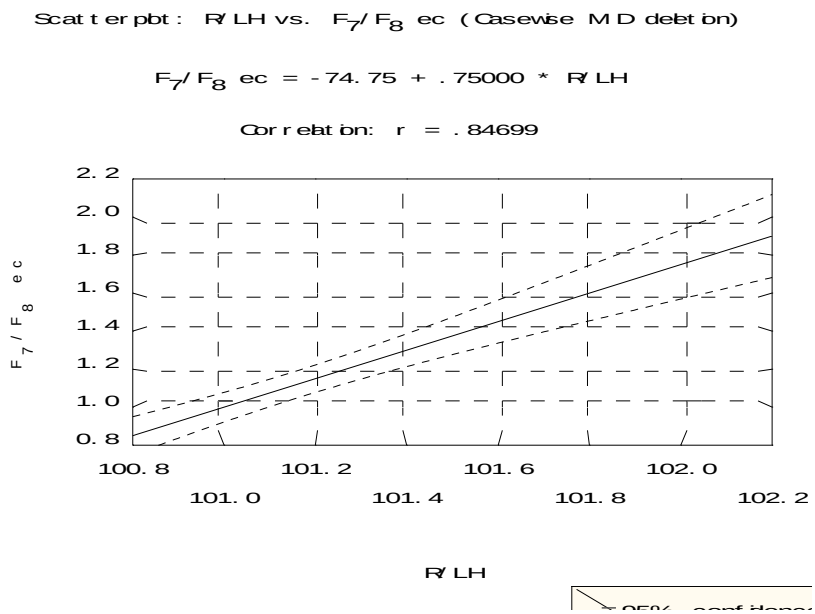

Figure 5 – Correlation (r = 0.85) between hand preference and alpha asymmetry in eyes – closed condition in frontal region (F_7/F_8)

For the parietal region correlation is weak and statistically not significant. However, for frontal regions correlation between localization of alpha asymmetry and hand preference is very strong and statistically significant.

Discussion

Kropotov J. [12] found that the grand average spectra are quite symmetrical, but it is not uncommon for a healthy individual to reveal an asymmetry at the range of 10–50%. Asymmetry larger than 50% might be an indication of pathology. Some researchers have suggested that approach-related positive emotions are associated with greater left frontal brain activity and contrasting withdrawal-related negative emotions are associated with greater right frontal brain activity [13].

EEG studies used a specialized set of approaches for reducing raw EEG signals to metrics that provide the correlations between frontal brain activity and emotions. We used published methods from Allen *et al*. (2004), for data processing in this field of research, with a focus on statistical and methodological issues.

Functional interpretation of frontal EEG asymmetry in all studies relies upon a fundamental assumption that EEG alpha band power is an inverse measure of cortical activation underneath the recording electrode. These findings generally support the utility of EEG alpha power as an inverse indicator of regional cortical activation.

The finding that alpha band (8 ± 13Hz) has been inversely related to the activation of the corresponding region of the brain provoked Davidson (1992) to conclude that anterior alpha asymmetry measurements reflect relative differentces in activity between the left and right hemispheres [4]. In general, lower alpha power correlated with higher activation in the right hemisphere is related to a more negative affective response.

After qEEG assessment in two conditions – e.o. and e.c. – we found that a statistically significant difference between left and right sides in alpha spectra power was found in frontal, parietal, temporal and occipital regions. There is also asymmetric alpha activity associated with relatively higher right frontal activation predominant in frontal but not in parietal (posterior) regions in children with anxiety disorders. Right frontal asymmetry was specific for all assessed children except for left-handed ones in the two conditions, e.c. and e.o. For parietal regions there was no specific predominant side for alpha asymmetry in our group of patients.

The results obtained in our study are in agreement with others who found that EEG asymmetry of parietal sides has larger variability than EEG asymmetry of frontal sites.

It is very important that frontal EEG asymmetry appears to serve as an individual variable related to emotional response in emotional disorders like anxiety. It corresponds to the hypothesis of Kim (2006), that regulatory skills and behaviours developed rapidly during childhood play a critical role in linking frontal EEG asymmetries to emotional reactivity in children.

Ginette *et al.* (2006) found that children with relatively greater right anterior EEG activity at baseline manifested significantly more anxiety one year later. It was supposed that greater relative right anterior EEG activity may predispose a person to thedevelopment of anxiety symptoms in the future. Does this mean that alpha asymmetry in the frontal region obtained during the assessment of a child with another problem can be indicative for anxiety disorder or anxiety symptoms in future?

Santesso *et al*. 2006 [20], reported that children with externalizing behaviours exhibited significantly greater relative right frontal EEG activity at rest compared with children with no externalizing behavioural problems. Higher relative right-sided activity during the experience of negative withdrawal related emotions was reported also by De Raedt *et al.* in 2008 [21].

There are few studies concerned with the correlations between alpha asymmetry and hand preference in children. In our group for frontal regions correlation between localization of alpha asymmetry and left – or right-handed of the analysed children is very strong and statistically significant ($r = 0.68–0.85$ $p < 0.05$). For the parietal region correlation is weak and statistically not significant ($r = 0.21–0.31$).

This study has some limitations. First, the assessment of alpha asymmetry was based on a relatively short EEG recording (a total of 10 min – a 5 minutes' eyes open and 5 minutes' eyes closed period). However, obtaining longer recordings for children with GAD are practically impossible according to their emotional state, especially fears and worries which are constantly present. Some authors suggest [22, 23] that even much shorter intervals (2 minutes) provide reliable information for further analysis. In addition, in the present study anxiety levels were not assessed, and investigations such as correlation with frontal EEG asymmetry remain for the future. Further, future investigations might continue to explore the relations between frontal EEG asymmetry and attachment, as associations between cognition, emotions and psychopathology.

Conclussions

- There is a difference in the spectra power of the alpha band between left and right hemispheres which is statistically significant in the e.c. condition in frontal, parietal, temporal and occipital regions in children with GAD. In e.o. condition the difference is not statistically significant.
- Right frontal asymmetry is specific to right-handed children with anxiety disorders, especially with GAD. In e.o. conditions the percentage of children who have right asymmetry is up to 92.31%, and in eyes-closed conditions is 88.46%. Left frontal asymmetry was typical of left-handed children. Although many authors suggested that children with anxiety have not only frontal but either posterior right asymmetry it was not specific for our group.
- Correlations between asymmetry and hand preferance of children was very strong and statistically significant only for frontal regions of the brain ($r = 0.68–0.85$; $p < 0.05$). For parietal sides correlation was weak and statistically not significant ($r = 0.21–0.31$).

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Резиме

АЛФА АСИМЕТРИЈА ВО КВАНТИТАТИВНИТЕ ЕЕГ ЗАПИСИ КАЈ ДЕЦА СО ГЕНЕРАЛИЗИРАНА АНКСИОЗНОСТ

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Апстракт: Анксиозноста се дефинира како субјективно чувство на загриженост, вознемиреност, страв и тага. Кога е многу интензивна може да влијае врз размислувањето на детето, неговата способност да донесува одлуки, перцепциите на околината, учењето и концентрацијата. Најголемиот број на анксиозни нарушувања имаат базална нестабилност во кортикалната активност претставена со мерките добиени од квантитативната електроенцефалографија (qEEG).

Пациенти и методи: Примерокот го сочинуваа 26 деца и тинејџери на просечна воздраст од 11,73 ± 4,03 години, од двата пола. Целата група на педијатриски пациенти беше дијагностицирана како генерализирано анксиозно нарушување (GAD – Generalized Anxiety Disorder). EEG-то беше снимано со

опрема за квантифицирано ЕЕГ-Митцар амплифиер со 19 електроди со 250 Hz семплинг и 0,3–70 Hz фреквентен ранг (опсег) во следните услови: очи отворени и очи затворени, од секоја состојба по 5 минути.

Резултати и заклучоци: Разликата во спектралната моќ на алфа спектарот помеѓу левата и десната хемисфера е статистички сигнификантна во фронталните, париеталните, темпоралните и окципиталните регии во состојба на затворени очи. Десна фронтална асиметрија е специфична за деснораките. Во состојба на отворени очи процентот на деца кои манифестираат десна асиметрија е 92,31%, а во состојба на затворени очи тој процент е 88,46%. Лево фронтална асиметрија беше типична за левораките деца. Ние не ја потврдивме десната асиметрија во постериорните регии што ја докажуваат други автори. Корелациите помеѓу асиметријата и доминантноста на раката кај децата беше многу силна ($r = 0,68–0,85$) и статистички сигнификантна ($p < 0,05$) само за фронталните регии на мозокот. За париталните регии корелациите беа слаби и статистички несигнификантни.

Клучни зборови: генерализирано анксиозно нарушување, квантитативна ЕЕГ (електроенцефалографија), алфа спектрална моќ, алфа асиметрија.

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