Izvorni znanstveni članak/Original scientific paper

Spectrum-weighted EEG frequency as an indicator of mental arousal in patients with anorexia

Analiza frekvencijskog spektra EEG-a kao pokazatelj mentalne pobude u bolesnika s anoreksijom

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Sažetak. ***Cilj:*** Anoreksiju karakterizira gubitak tjelesne težine koji dovodi do tjelesne težine od najmanje 15 % ispod normalne za dati uzrast. Cilj ovog rada bio je analizirati spektar usrednjenih frekvencija kao pokazatelj opće mentalne pobude u anoreksičnih preadolescenata, te usporediti rezultate sa zdravom populacijom iste dobi i istog spola. ***Metode:*** Dijagnoza je postavljena suglasno s dvama statističkim priručnicima (DMS-IV-R i ICD-10), medicinskom poviješću, neuropsihološkom procjenom, biokemijskom analizom i QEEG-om. Rezultati spektralne snage za četiri uvjeta (zatvorene oči, otvorene oči i ERP za vizualne i auditivne podražaje) obrađeni su u programu za procjenu aktivnosti mozga. ***Rezultati i diskusija:*** Računajući faktorsku ANOVU otkrili smo da postoji jaka statistička značajnost između rezultata aktivnosti mozga u kontrolne skupine zdravih ispitanika u odnosu na skupinu anoreksičnih preadolescenata ($p < 0.001$). *Post-hoc* analizom utvrđeno je kako su samo f_b vrijednosti u centralnim odvodima QEEG-a statistički značajne ($p = 0.005$). *Post-hoc* analiza koja se odnosi na opisano stanje pokazuje značajnu razliku u vrijednosti f_b za zatvorene oči *vs.* otvorene oči, zatvorene oči *vs.* ACPT u stražnjim odvodima i za zatvorene oči *vs.* VCPT za frontalne regije (svi $p < 0,05$). ***Zaključak:*** f_b dobar je pokazatelj opće mentalne aktivnosti – pobude, ali potrebna su daljnja istraživanja kako bi parametar QEEG postao dijelom rutinske analize u procjeni duševnih bolesti u djetinjstvu.

Ključne riječi: anoreksija, kvantitativni EEG, spektar usrednjenih frekvencija

Abstract. ***Aim:*** Anorexia is characterized by weight loss leading to a body weight of at least 15% below the normal. The aim of this study was to analyze the spectrum weighted frequency- f_b (brain rate) as an indicator of general mental arousal in anorectics and to compare the results with healthy preadolescents of the same age and gender. ***Methods:*** The diagnosis was made according to two statistic manuals (DMS-IV-R and ICD-10), medical history, neuropsychological assessment, biochemical analysis and quantitative electroencephalography. Results from spectra power for four conditions (eyes closed, eyes open, visual continuous performance test – VCPT and auditory continuous performance test – ACPT) were exported to brain rate software. ***Results and Discussion:*** Using factorial ANOVA we found that there is a strong statistical significance between results of brain rate for control group of healthy subjects vs. observed anorectic group ($p<0.001$). The post hoc Bonferroni test (summary of significant difference of groups) showed that only the f_b values for central region are statistically significant. The post hoc analysis regarding condition found a significant difference in f_b values for EC vs. EO and EC vs. ACPT for posterior region and for EC vs. VCPT for frontal region (all $p<0.05$). ***Conclusions:*** Brain rate – f_b is a good indicator for general mental activity but, further investigations are needed in order to add f_b as an indicator of mental arousal in assessment of mental diseases in childhood.

Key words: anorexia, QEEG, spectrum weighted frequency – f_b (brain rate)

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BACKGROUND

Anorexia is characterized by weight loss leading to a body weight of at least 15% below the normal. The weight loss is self-induced by avoidance of “fattening foods”. Preadolescents usually have self-perception of being too fat, with an intrusive dread of fatness, which leads to a self-imposed low weight threshold[1]. Abnormalities in brain functioning in anorectic patients are very often persistent. Thalamic pathways have been implicated in the control of normal eating. The smaller size of thalamus[2] and thalamic perfusion changes in anorexics[3] suggest that the thalamus plays an important role in anorexia nervosa.

> Anorexia has a specific psychopathology due to intense fear of becoming obese. Abnormalities in brain structure and function are among the most common, but it is hard to differentiate the effects of starvation on the brain from any long-standing characteristics.

Hyperphagia has been reported with a variety of lesions in the thalamus, hypothalamus and frontal lobe. Lesions in these areas have also been implicated in the onset of anorexia nervosa. Anorexia has also been associated with dorsomedial thalamic infarction[4].

Many authors reported specific electrophysiological patterns for mental disorders. For example, the basal instability in cortical arousal, as reflected in measures of quantitative electroencephalography (QEEG) is common to most of the mental disorders[5]. Results from QEEG assessment in anorectics suggest that differences in brain dynamics might explain difficulties in their social functioning.

Among the techniques of functional brain imaging, QEEG offers many advantages,such as ideal temporal resolution in the millisecond time domain characteristic of neuronal information processing, no ionizing radiation and relatively inexpensiveness[6].

Many authors made investigations in the field of QEEG assessment. Banaschewski T and Brandeis D. in one of their last articles wrote: ”In the future, EEG/ERP parameters will increasingly characterize the interplay of neural states and information processing. They are particularly promising tools for multilevel investigations of etiological pathways and potential predictors of clinical treatment response”[7].

Patients with anorexia have poor cognitive flexibility, particularly linked to the function of the ***frontal lobes*** and ***executive system***[8]. Hatch and colleagues show that some EEG abnormalities like reduced alpha/increased beta power in anorexia nervosa patients normalizes with refeeding, while increased theta power persists in parietal-occipital regions in an eyes closed condition[9]. According Grunwald and colleagues the results of EEG-power changes indicate a cortical dysfunction and deficits in somatosensory integration processing in anorexia nervosa patients[10]. The same author two years later found that theta power was lower in anorectic patients than in the healthy controls over the right hemisphere and right parietal regions[11].

According to the fact that anorectic patients have the same specific spectra power results in comparison with healthy subjects we expected that there would be deviations in brain rate values in comparison with healthy controls, either. So, the aim of this study was to analyze brain rate as an indicator of general mental arousal in anorectic patients and to compare the results with healthy preadolescents at the same age and the same gender.

After analysis of QEEG spectra power we introduced the calculation of spectrum weighted frequency or brain rate which is correlated to brain electric and metabolic activity. In particular, brain rate – in further text- f_b 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[12].

Brain rate is calculated by following formula:

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

where the index i denotes the frequency band (for delta i = 1, for theta i = 2, etc.) and V_i is the corresponding mean amplitude of the electric potential or power. Following the standard five-band classification, one has f_i = 2, 6, 10, 14 and 18 respectively[12].

If we start from the assumption that different brain rate values are somehow coupled with metabolic activity in different disorders, then it is very interesting to compare it with the same parameter in normal subjects.

PATIENTS AND METHODS

Subjects

The first group of anorectic preadolescents and teenagers was comprised of 22 individuals mean age (14±3) years, 21 female and 1 male patient. The group of healthy controls had 22 youngs with a mean age of (14±2) years, and the same gender as the anorectic group.

All subjects were patients attending the Department for Psychophysiology at University Pediatric Clinic in Skopje, in the period from January 2008 until December 2010. The diagnosis was made according two statistic manuals: DMS-IV-R (13) and ICD-10[1]. Also medical history, neuropsychological assessment, biochemical analysis as well as QEEG have been realized in all preadolescents. Inclusion criteria were: age between 7 and 18 years, absence of actual neurological impairments, and absence of the use of psychoactive or psychotropic substances (screened by previous anamnesis and clinical examination).

The control group were youngs without history of any psychopathological or neurological symptoms, assessed through personal interview and self report. All subjects had normal or corrected to normal vision.

"Informed consent" for QEEG recording has been appropriately obtained from all participants. All of them were assessed with psychological testing (personality questionnaires: MMPI and EPQ in a single session which lasted approximately 2 hours). Subjects were without any medication for 48-hours before testing and were asked to have a good night sleep before testing. All of them must have a good meal before testing to avoid effects of hypoglycemia on brain function. They were seated in a comfortable chair with a backrest and were instructed not to move their eyes during testing.

METHODS

EEG was recorded with Quantitative EEG equipment (Mitsar, Ltd.) amplifier from 19 electrodes, referenced to linked ears (on the International 10-20 system) with 250 Hz sampling rate in 0.3 – 70 Hz frequency range in the following conditions:

QEEG assessment including brain rate suggest that differences in brain dynamics might explain difficulties in the social functioning of patients with eating disorders. For example, theta activity in the right parietal region is responsible for inappropriate body image. Brain rate as indictor for general mental activity shows low brain rate (f_b) or state of underarousal in all conditions (e.o., e.c., VCPT and ACPT).

1) eyes opened (EO) – 5 minutes,
2) eyes closed (EC) – 5 minutes,
3) visual continuous performance task (VCPT) – 20 minutes.
4) auditory continuous performance task (ACPT) – 20 minutes.

The ground electrode was placed between Fpz and Fz. The impedance levels for all electrodes were set to 5 KΩ. We used two stimulus GO/NOGO task developed specifically for HBI (Human Brain Institute) database. VCPT consisted of 400 trials and ACPT of 1000 trials. Subjects were instructed to press a button with index finger of their right hand for GO condition and not to press a button for NOGO condition.

Recorded results were referred and analyzed as data base montage. The 19 electrode positions were allocated to three sagittal regions:

Frontal – Fp1, Fp2, F_3, Fz, F_4, F_7 and F_8.

Central – T_3, T_4, C_3, Cz and C_4.

Posterior – T_5, T_6, P_3, Pz, P_4, O_1 and O_2.

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

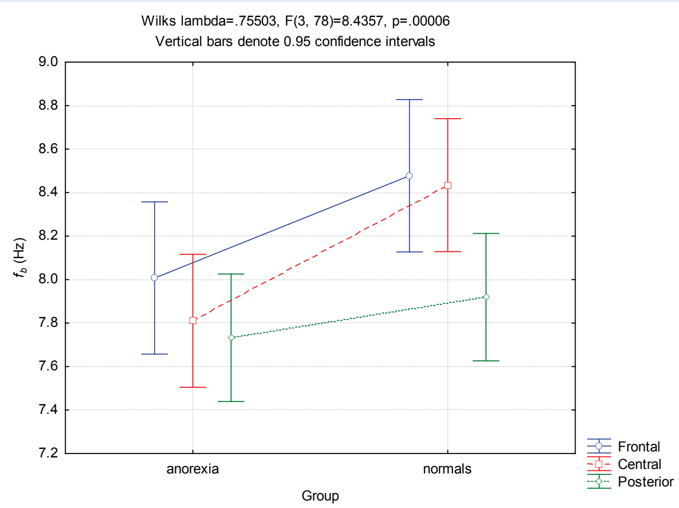

Figure 1. f_b values for sagittal topography in anorectic patients and the group of normal controls *(the results are presented as Mean values ±SD; F=8.44, P<0.001.)*

algorithm that derives spatial filters by blind source separation of the EEG signals into temporally independent and spatially fixed components.

Then recordings for four conditions (eyes closed, eyes open, VCPT and ACPT) were sufficient for calculation of spectra power values for all 19 electrodes. Obtained results were exported to brain rate software and then calculated for each region separately.

Statistical analysis

The QEEG spectra power data and data for brain rate were analyzed using Statistica software (version 7.0). A series of repeated measures analysis of variance – Factorial ANOVA was performed using the factors:

- sagittal topography (frontal, central and posterior region),
- measurement condition (EO, EC, VCPT and ACPT) and
- group (anorectic's and controls) for brain rate values.

Then post hoc Bonfferoni test was performed to explain significant interactions. p-level <0,05 was considered as significant..

RESULTS

In the anorectic group, the mean f_b for frontal region was 8.007±1.619 Hz, for central region 7.810±1.302 and for posterior region 7.732±1.280 Hz. In the control group the mean f_b for frontal region was 8.477±0.865 Hz, for central region 8.419±0.583, and for posterior region 7.919±0.638 Hz. Calculated factorial ANOVA for brain rate results for anorectic preadolescents vs. group of normal healthy controls in EO, EC, VCPT and ACPT condition for three regions (frontal, central and posterior) were F=8.44 p<0.001 (Figure 1). Results were statistically significant between groups in three different regions (Figure 2-4).

Results from ANOVA regarding sagittal topography have shown statistically significant difference between f_b values in four different conditions (EO-eyes opened, EC- eyes closed, VCPT-visual continuous performance test, ACPT - auditory continuous performance test) – F=13.59, P<0.001 (Table 1).

The post-hoc Bonferroni test (summary of significant difference of groups) showed that only the f_b values for central region were statistically significant – p=0.005 (or values of f_b in normal group are statistically significant higher than values of f_b in anorectic group but only for central region). The post hoc analysis regarding condition showed a significant difference in f_b values for EC vs. EO

Table 1. Summary of significant post-hoc Bonferroni P-values for brain rate difference between groups, regions and conditions.

		Frontal	Central	Posterior
Group effect	Normal's vs. Anorectic		0.005	
Condition effects	EC vs. EO			0.046
	EC vs. VCPT	<0.002		
	EC vs. ACPT			0.022

EO - eyes opened, EC - eyes closed, VCPT - visual continuous performance test,
ACPT - auditory continuous performance test

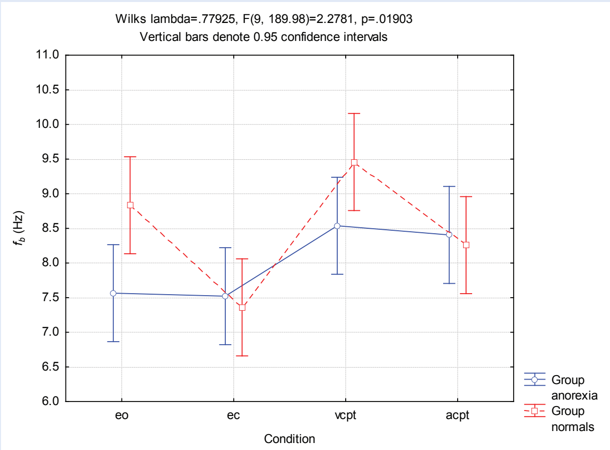

Figure 2. f_b values in frontal region for anorectic patients and the group of normal controls according to recorded conditions (EO-eyes opened, EC- eyes closed, VCPT-visual continuous performance test, ACPT- auditory continuous performance test); the results are presented as Mean values±SD; F=2.28, P<0.05.

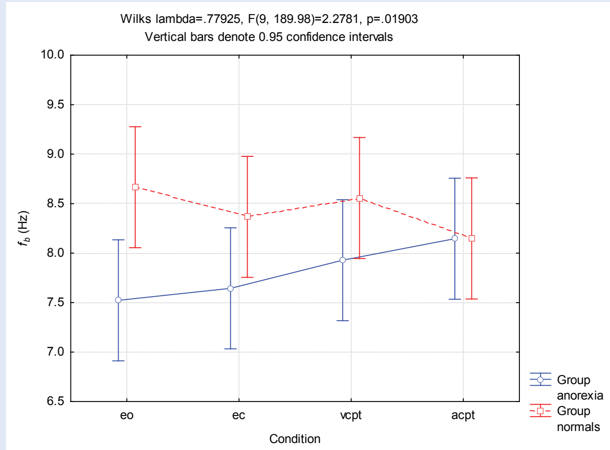

Figure 3. f_b values in central region for anorectic patients and the group of normal controls according to recorded conditions (EO-eyes opened, EC- eyes closed, VCPT-visual continuous performance test, ACPT- auditory continuous performance test) ; the results are presented as Mean values±SD; F=2.28, P<0.05.

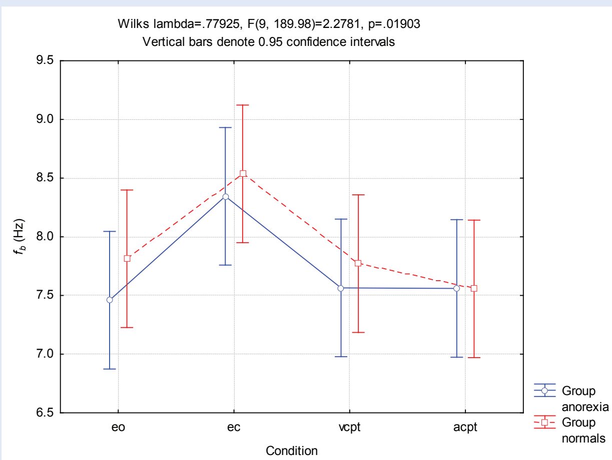

Figure 4. f_b values in posterior region for anorectic patients and the group of normal controls according to recorded conditions (EO-eyes opened, EC- eyes closed, VCPT-visual continuous performance test, ACPT- auditory continuous performance test); the results are presented as Mean values±SD; F=2.28, P<0.05.

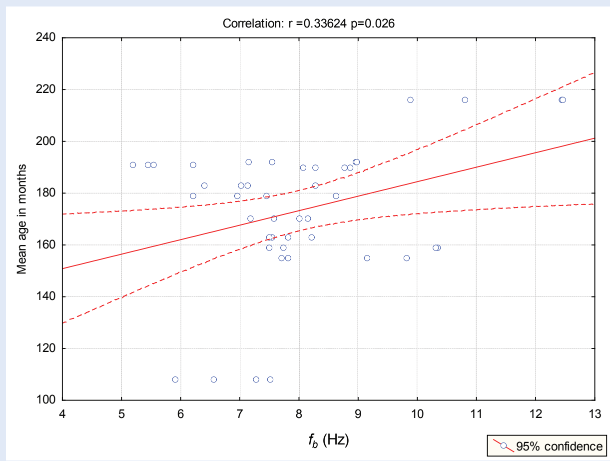

Figure 5. Correlation between the f_b values in anorectic group vs. mean age of anorectic patients in months for frontal region (Solid line represented line of correlation and dashed line represented 95% CI of it)

and EC vs. ACPT for posterior region and for EC vs. VCPT for frontal region (or values of f_b for EC condition are statistically significant higher than values of f_b in EO and ACPT for posterior region and values of f_b for EC condition are statistically significant higher than values of f_b in VCPT for frontal region).

Correlations between the f_b values in anorectic group vs. mean age of anorectic patients in months were: for frontal region is r =0.34, p=0.026; for central region r =0.37, p=0.014; for posterior region r =0.46, p= 0.002 (Figure 5-7).

In conclusion, there is a statistically significant correlation between f_b values in anorectic group vs. mean age of same patients in months for all three regions (all p<0.05). So, as preadolescents became older they have higher values of f_b in all three regions of the brain.

It is clear that brain rate as an indicator of general mental activation/arousal in general, is lower

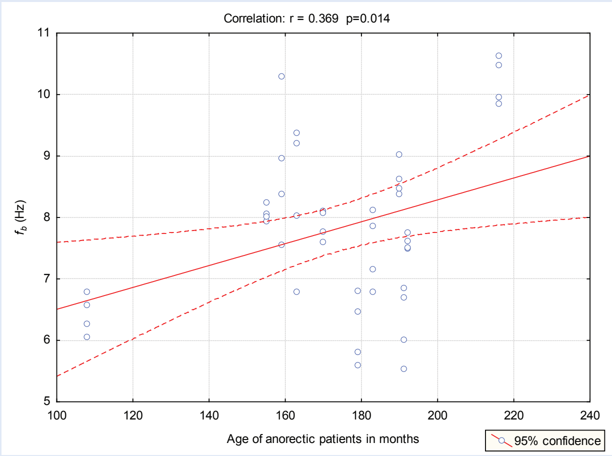

Figure 6. Correlation between the f_b values in anorectic group vs. mean age of anorectic patients in months for central region (Solid line represented line of correlation and dashed line represented 95% CI of it).

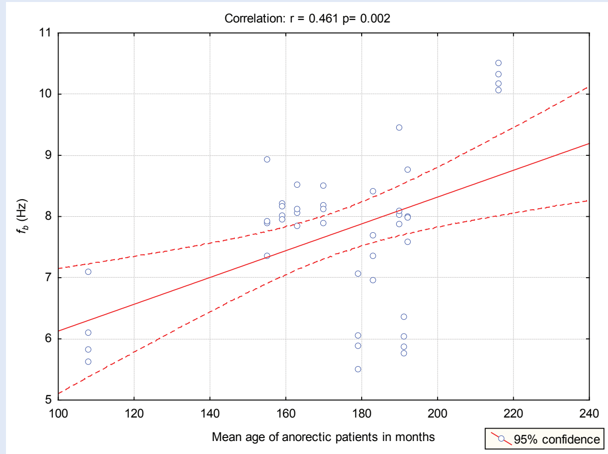

Figure 7. Correlation between the f_b values in anorectic group vs. mean age of anorectic patients in months for posterior region (Solid line represented line of correlation and dashed line represented 95% CI of it).

in patients with anorexia in comparison with brain rate of normal controls. Exception from this are results of f_b – mean value for ACPT condition for anorectics is 8.03 and for normal group 8.01 but, the difference is so small that we can say that results for brain rate in ACPT-condition are nearly the same for two groups.

DISCUSSION

In addition to the analysis of QEEG characteristics of anorectic preadolescents we introduced the calculation of spectrum weighted frequency or f_b as an indicator of general mental activity. It was shown that f_b can be used to discriminate between the groups of underarousal and overarousal disorders, as previous authors[12] have reported in their article. Brain rate – f_b, also can be used to assess the quality of sleep, as well as to indicate the IQ changes caused by some environmental toxins[14].

According to their studies, Pop-Jordanova N. and Pop-Jordanov J.[12] explained that same values of this parameter are specific for some mental states. For example they mentioned that "f_b = 4.59 would correspond to a very drowsy state (or mental retardation) for an adult, and a relaxed state for a child, while f_b= 9.58 would correspond to a relaxed state for an adult, and a very attentive (or anxious) state for a child".

According to these numbers, the anorectic group assessed during this study are not so far from relaxed state during baseline recording, but they became anxious during psychological testing. What is more interesting in many of these preadolescents during QEEG assessment in EO condition dominant EEG band was alpha and in group of normal healthy subjects dominant activity in EO condition was beta. This corresponds to research of Rodriguez, Babiloni and their colleagues[15] who found that eating disorders are related to altered mechanisms of cortical neural synchronization, especially in rolandic alpha rhythms.

Calculating factorial ANOVA we found that there is big difference between results of brain rate in control vs. anorectic group which is statistically significant. Further we calculated post hoc Bonferroni test (summary of significant difference of groups) and showed that only the f_b values for central region are statistically significant. The post hoc analysis regarding condition found a significant difference in f_b values for EC vs. EO and EC vs. ACPT for posterior region and for EC vs. VCPT for frontal region. Still these are first investigations in this field so we must be careful and further investigations are needed.

There is statistically significant correlation between f_b values in anorectic group vs. mean age of same patients in months for all three regions. These means that in older patients f_b have higher values in all three regions of the brain.

Interesting was founding that there is no statistically significant difference between results of BR in different conditions (EO, EC, VCPT and ACPT) in anorectic group. There was strong statistical significance (p=0.022) between calculated values of brain rate in normal controls vs. anorectic group only in eyes open condition. The dominant activity which in anorectic group is alpha and in control group is beta could be the explanation. During assessment it was very obvious that preadolescents became anxious in EC condition, which is presented with big difference between f_b in EC vs. f_b in VCPT (for frontal region) and between f_b in EC vs. f_b in EO and ACPT condition (for posterior region). Brain rate was much higher in EC condition, probably because of the fact that preadolescents became more anxious with close eyes which means that faster frequencies became dominant. But in generally for all three regions f_b has much higher value during VCPT and ACPT vs. EO and EC condition. Explanation of this is in high perfectionism in anorectic patients who became more anxious during psychological testing (VCPT and ACPT) with dominant fast activity so, they didn't make any errors. These correspond to results of Pieters GL and colleagues[16] in which study anorectic patients made significantly less errors than controls.

We started from the assumption that different brain rate values are somehow coupled with metabolic activity in brain region. Low metabolic activity specific for anorexia is explanation for lower values of brain rate in comparison with normal controls. At the end in light of all this findings about meaning of some EEG markers in assessment of brain functions in childhood we would like to promote brain rate – f_b as an indicator of general mental activity which can allow us to put anorexia in group of underarousal disorders. Of course, further investigations are needed.

CONCLUSIONS

Brain rate is good indicator of general mental activity. Assessed preadolescents with anorexia, have specific electrophysiological patterns. There is a strong statistical significance between results of brain rate in control group vs. anorectic group of healthy subjects calculating factorial ANOVA. Distribution of f_b values for sagittal topography reflects the arousal levels in corresponding regions. These are first calculations of f_b in groups of preadolescents with mental disorders. Further investigations are needed in order to add f_b as indicator of mental arousal in assessment of mental diseases in childhood.

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