The Correlation of PANSS Scores and P100 Latency in Patients with Schizophrenia and Migraine Headache Using Visual Evoked Potentials (VEPs) According to Gender and Age

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ABSTRACT

Background: The VEPs provide an objective measure of brain function, analyzing integrity of visual processing. With patients affected with schizophrenia, the changes with the implementation of VEP are evident, such as symmetrical deceleration of the impulse and the continuance of latency, which points to a degenerative illness, suggesting the presence of optical neuritis or hemianopsia conjoined with mentioned intracranial illness.

Objective: The aim of the study was to determine the correlation of positive and negative symptoms (PANSS scores) and P100 latency between patients with schizophrenia and patients with migraine headache according to gender and age. Visual evoked potentials (VEPs) were applied. Methods: The sample included 80 subjects: a) S group- 40 patients with schizophrenia (21 males; 19 females); b) H group-40 healthy subjects with migraine headache (10 males; 30 females). The study was conducted at the Department of Psychiatry and Neurology University Clinical Center Sarajevo. Results: Our research revealed positive correlation of the P100 latency and the PANSS score of negative symptoms, which means that the subjects of the observed group with a higher latency of the P100 wave of the entire visual field in both eyes have higher PANSS scores of negative symptoms. The correlation is significantly higher in female subjects (37% shared variance) than in male subjects (12% shared variance). All male subjects have a PANSS negative symptoms score of 17 or higher, while all female subjects have a PANSS negative symptoms score of less than 17 positive correlations were registered in P100 latency in left view field of both eyes and in P100 amplitude in the region of right eye (p=0.01) in comparison with left eye region (p=0.05) in patients with schizophrenia. Conclusion: Results imply that the cognitive impairment seen in schizophrenia is not just due to deficits in higher order aspects of cognition but also encompasses significant deficits in early sensory processing. Our study is useful to initiate new questions and recommendations for further studies, specifically on changes in the occipital lobe in the schizophrenic patient’s brain.

Keywords: schizophrenia, early visual dysfunction, visual evoked potentials (VEPs), PANSS.

1. BACKGROUND

Schizophrenia is a complex mental disorder where environmental factors interacting with the genetic susceptibility and early neurodevelopmental aberrations, precede the onset of psychotic symptoms. It remains one of the most intriguing psychiatric research topics with a worldwide prevalence of 1% leading to lifelong disability in more than 50% of the sufferers. As a pathological entity, schizophrenia reflects the specific existential context of an individual, while maintaining a consistent core in regard to all stable and diagnostically relevant characteristics. It remains one of the most intriguing psychiatric research topics. In terms of content, schizophrenic manifestations display an abundance of individual differences, while the pattern related to symptoms and the course of the disease remains the same (1). No other disease can so radically damage the personality of the patient and potentially destroy the very foundations of what we consider to be the essential part of every human being. In medical terms, it is primarily a neurocognitive or neurobiological disorder. While...
leading to significant changes and damaging the cognitive functions, it also transforms the will, emotional expression and behavior of the afflicted. A lot of research has confirmed the presence of neurodegenerative processes such as excessive apoptosis, gliosis and demyelination in the brains of patients with schizophrenia. There are indications that neurodegenerative changes occur in the dopaminergic pathways in the cortex and glutamatergic pathways from the cortex to subcortical structures (2, 3).

Dysfunctional neuronal networks are involved in the pathophysiology of the disease and related to symptom dimensions. Neurodevelopmental disturbances and additional neurodegenerative processes in subgroups of patients are hypothesised to be underlying pathophysiological mechanisms (4). Synaptic pathology, oligodendrocyte dysfunction and decreased neurogenesis may lead to disconnection syndrome as a basis of symptoms and cognitive deficits. On the functional level, deficits are evident in symptom dimensions, a subtle loss of volumes in specific brain regions, and in the activation pattern of neuronal networks (5).

2. OBJECTIVE

The aim of the study was to determine the correlation of positive and negative symptoms (PANSS scores) and P100 latency between patients with schizophrenia and patients with migraine headache according to gender and age.

3. PATIENTS AND METHODS

Patients and study design

This prospective, comparative study had been conducted at the Department of Psychiatry and Department of Neurology, Clinical Center of the University of Sarajevo. The study included 80 patients of both sexes, 21–67 years old, classified into two groups: S group included 40 patients with schizophrenia (21 males and 19 females) and H (control) group with 40 patients with migraine headache (10 males and 30 females). The Ethics Committee of the University Clinical Center Sarajevo gave an ethical consent to perform the study. All subjects signed a written informed consent for the use of the results obtained for publication before the enrollment. Patients (S group) included in the study were 18 to 67 years old, who were on the hospital treatment and under antipsychotic drugs at the Department of Psychiatry, and had been diagnosed with schizophrenia according to the ICD-10 criteria (8). Patients were included into the research on the basis of consecutive admissions, taking into account that all of them were with a long psychiatric history (at least 5 years of hospital treatment) with signed information consent within clinical research. The criteria for the exclusion referred to publications before the enrollment. Patients included in the study were 18 to 67 years old, who were on the hospital treatment and under antipsychotic drugs at the Department of Psychiatry, and had been diagnosed with schizophrenia according to the ICD-10 criteria (8). Patients were included into the research on the basis of consecutive admissions, taking into account that all of them were with a long psychiatric history (at least 5 years of hospital treatment) with signed information consent within clinical research. The criteria for the exclusion referred to the appearance of psychotic phenomenology within neurological disease, organic psychosyndrome, somatic disease, neurological disorder (head trauma, brain insult, epilepsy), information on drug or alcohol abuse, or those who did not sign informed consents for voluntary participation. For the group of patients with schizophrenia, the average age was 41.50 (SD±10.44; range 22–67) years.

The control group (H group) represented patients 18 to 55 years old, based on admissions at the Department of Neurology, diagnosed with migraine headache criteria (9), and were tested with the test scales of assessment with the signed informed consent for voluntary participation. This group included subjects who had never suffered from psychotic or severe neurological disorders (head injuries, epilepsy) or diseases, and in whose medical history there was no information on drug or alcohol abuse, with no metal content in the body and who signed informed consent for voluntary participation. The average age of the control group was 38.50 (SD±26.59; range 30–53) years. The groups were equal according to age (p=0.691).

Neurophysiological method - Visual evoked potentials (VEPs)

Patients were subjected to examination by Visual evoked potentials (VEPs) and patterns for psychophysical and electrophysiological experiments were generated using a Medelec Synergy, Version 10.1 (Oxford Instruments Medical, United Kingdom), applying a unipolar montage technique where reference electrode (surface gold electrode) was placed 5–9 cm above the nasion point on the sagittal line between the nasion and Cz point, the active electrode was placed 2–4 cm above the posterior external protuberance on the line between the latter and Cz, while the ground surface electrode was placed on the chin to reduce artifacts. The pattern used was alternate pattern, each evoked potential recorded right and left eyes was recorded and processed, then the evoked potential was recorded from both eyes, and processed to calculate P100 latency. Recording was repeated 3 times for each patient and the mean was taken for recordings measured for each patient to minimize recording artifacts. For all experimental runs, the stimulus consisted of a checkerboard pattern with equal numbers of light and dark checks (16 black and 16 white, size 2x2 cm). Luminance was 50 cd/m2, Michelson contrast = 80%. Each check subtended a visual angle of 0.65° both horizontally and vertically, while the checkerboard as a whole subtended visual angle of 5.25° vertically and horizontally. In all experimental runs the checkerboard was presented in the center of a monitor with a gray background. Visual-evoked potentials were recorded from the occipital site relative to the vertex site reference by means of gold-cup electrodes placed on the midline of the scalp. The ground was placed at the paramedian site. Visually evoked potentials elicited by flash stimuli can be recorded from many scalp locations in humans. Visual stimuli stimulate both primary visual cortices and secondary areas. Clinical VEPs is usually recorded from occipital scalp overlying the calcarine fissure. This is the closest location to primary visual cortex (Brodmann's area 17).

A common system for placing electrodes is the "10-20 International System" which is based on measurements of head size (10). The mid-occipital electrode location (OZ) was on the midline. The distance above the inion calculated as 10% of the distance between the inion and nasion, which is 3-4 cm in most adults (the inion is the most prominent projection of the occipital bone at the posteroinferior part of the skull) (lower rear). Lateral occipital electrodes are at similar distance off the midline. Another set of locations was the "Queen Square system" in which the mid-occipital electrode is placed 5 cm above the inion on the midline and 5 cm lateral from that location for lateral occipital electrodes (11).

There is a prominent negative component at peak time of about 75 msec (N75), a larger amplitude positive component at about 100 msec (P100) and a more variable negative com-
ponent at about 145 msec (N145). The major component of the VEPs are the large positive wave peaking at about 100 milliseconds. The VEPs waveform, amplitudes and peak times depend upon the parameters of the stimulus. Steady state VEPs are those recorded using stimulation rates of 3 or more per second. Transient VEPs were recorded using rates of less than 3 per second. For all experimental runs, the stimulus consisted of a checkerboard pattern with equal numbers of light and dark checks. Each check subtended a visual angle of 0.65° both horizontally and vertically, while the checkerboard as a whole subtended visual angle of 5.25° vertically and horizontally. In all experimental runs the checkerboard was presented in the center of a monitor with a gray background. The stimulation of the entire field of view with both eyes, then the whole field of view individually for left and right and for the halves of the visual fields of both eyes. Eye that was not watching was covered. Average values of latency (the entire eye field both eyes) of the healthy population for the comparison were as follows- P100 latency (ms): entire field of view (both eyes) 96.60, left eye: 96.60, right eye 99.30, right field of view (left eye) 103.50, right eye 103.50, left field of view (left eye) 105.00, right eye 105.00.

**PANSS**

The Positive and Negative Syndrome Scale (PANSS) is an established psychiatric rating system that is an operationalized, drug-sensitive instrument that offers balanced representation of positive and negative symptoms and estimates their relationship to one another and to global (or general) psychopathology. It is the most widely used measure of symptom severity in schizophrenia and this 30-item scale is typically administered by trained clinicians who evaluate patients’ current severity level on each symptom (item) by endorsing 1 of 7 options (weights) numbered 1 through 7. The PANSS has demonstrated high internal reliability and good construct validity.

**Statistical analysis**

The research task was to define the differences between patients with schizophrenia and patients with migraine headache according to PANSS scores and VEPs of both groups. For the purposes of correlation and associative analysis multivariate analysis of variance, Pearson’s correlation coefficient and Point-biserial correlation was applied using χ² test, T-test, multivariate analysis of variance, Pearson’s correlation coefficient. For the purposes of correlation and associative analysis multivariate analysis of variance, Pearson’s correlation coefficient and Point-biserial correlation was applied using χ² test, T-test, multivariate analysis of variance, Pearson’s correlation coefficient. For the purposes of correlation and associative analysis multivariate analysis of variance, Pearson’s correlation coefficient and Point-biserial correlation was applied using χ² test, T-test, multivariate analysis of variance, Pearson’s correlation coefficient.

**4. RESULTS**

**Demographic data of subjects**

The study was conducted on a group of 80 subjects divided into two groups: patients with schizophrenia (40) and control group (40) with migraine headache.

**Demographic data of subjects divided according to gender**

The sample consisted (schizophrenic patients) of 21 (52.5%) male and 19 (47.5%) female, control group of 10 (25.0%) male and 30 (75.0%) female. Analysis regarding gender demonstrated statistically significant difference in control group (χ²=6.173; df=1; p=0.012). More subjects in that group were women with higher prevalence of migraine headache in female population (15%-17% female instead male of 6%; 2:1-3:1) (Table 1).

**Analysis of subjects according to age**

Average age of patients in the time of study was 41.50±10.43 years, and of controls 38.50±9.48 years. The youngest subject in schizophrenia group was 22, and the oldest one 67 years, in the control group the youngest was 20, and the oldest 55 years (Table 2.). Comparative analysis regarding age in both groups demonstrated that there was not a statistically significant difference in the investigated sample (t=1.346; p=0.1821).

**Comparative analysis of positive and negative symptoms (PANSS) in patients according to gender**

The correlation of positive and negative symptoms in patients according to gender was examined in 40 patients with schizophrenia using psychiatric rating system (PANSS). The T test for independent samples tested whether there is a statistically significant difference in the presence of positive and negative symptoms (PANSS) in male and female subjects of the observed group. In the group of male and female patients,
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There is no statistically significant difference in the variances of the PANSS symptom score. While the difference in the variances is not statistically significant, the results show that the difference in the average values of the PANSS symptom score between male and female subjects is statistically significant for both positive and negative symptoms (p=0.026) (Table 3., Table 4.)

The average PANSS score is higher in male subjects in both positive and negative symptoms. While for positive symptoms male subjects have a 16% higher average score, for negative symptoms they have a 53% higher average score. (Graph 1.)

Comparative analysis of positive and negative symptoms and P100 latency in patients using PANSS and visual evoked potentials (VEPs)

The following table (Table 5) shows Pearson correlation coefficients between PANSS positive and negative scores with P100 latencies of both visual fields in both eyes. The presented table shows that only the PANSS score negative symptoms have a positive statistically significant correlation with the P100 latency of the entire visual field in both eyes. Other correlations are not statistically significant, and the PANSS score of positive symptoms is less than 0.20, while the PANSS score of negative symptoms is up to 0.40, but they are statistically insignificant. The PANSS score of negative symptoms can explain about 22% of the variance of the P100 wave latency (ms) of the entire visual field in both eyes. The scatter diagram (Graph 2.) shows that there is a positive correlation of the P100 latency and the PANSS score of negative symptoms, which means that the subjects of the observed group with a higher latency of the P100 wave of the entire visual field in both eyes have higher PANSS scores of negative symptoms. The correlation is significantly higher in female subjects (37% shared variance) than in male subjects (12% shared variance). All male subjects have a PANSS negative symptoms score of 17 or higher, while all female subjects have a PANSS negative symptoms score of less than 17.

Graph 2. Correlation of the P100 latency of the entire visual field of both eyes with the negative symptoms PANSS score

5. DISCUSSION

Widespread alterations in connectivity are present in the brains of chronic schizophrenia patients and there is some evidence that patterns of reduced connectivity cut across the different stages of the disorder, including those with an increased risk of developing the illness. Patients with schizophrenia show severe neurophysiological deficits in brain information processing not only at cognitive (6-8), but also at perceptual levels (9-13) and perceptual deficits have been particularly well-documented in the visual system (14-25). The Positive and Negative Syndrome Scale (26-28) was developed.
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In our study, in regard to the age of patients, the minimum age in both groups was around 20 years, while the maximum age in the group of patients with schizophrenia was 67, and in the control group 55. Members of the group diagnosed with schizophrenia were on average 3.5 years older than those in the control group. Our research revealed the correlation between the presence of positive and negative symptoms (PANSS) and the P100 latencies of both visual fields, both eyes, was observed. It is evident that there is a positive correlation of the P100 latency and the PANSS score of negative symptoms, which means that subjects of the observed group with prolonged P100 latency of the entire visual field in both eyes have higher PANSS scores of negative symptoms. The correlation is significantly higher in female subjects (37% of shared variance) than in male subjects (12% of shared variance). The correlations between the P100 latencies are all statistically significant and very high, with a prolonged latency in negative symptoms, i.e., a reduction in positive symptoms.

### 6. CONCLUSION

The principal assumption is that normal brain development is disrupted in specific ways at critical periods and the resulting lesion produces the symptoms of schizophrenia only through interaction with the normal maturation processes in the brain, which occur in late adolescence or early adulthood. Schizophrenia is associated with the volume changes of...
the occipital lobe, and findings of our study support the view that schizophrenia is associated with impairment of early visual stream processing. Little is known about the association of schizophrenia with the occipital lobe or whether the visual symptoms exacerbate if the occipital lobe is severely damaged or not yet known. Also, if the whole occipital lobe is involved in schizophrenia or just some part of it is involved also remains an unsolved mystery. Our study is useful to initiate new questions and recommendations for further studies, specifically on changes in the occipital lobe in the schizophrenic patient’s brain.

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