Evaluation of the evoked brain potentials of patients with asthenia and anxiety symptoms and the partial lost of sight

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Abstract

Background. Vision loss, even partial, especially in adulthood, is accompanied by emotional, motivational and social consequences that directly affect the psychophysiological state of the individual himself, his communication in society and, often, the social status of the subject.

Methods. From the group of patients-volunteers (n=15) with a partial loss of sight of traumatic genesis two groups were formed for carrying out neurophysiological evaluation: with predominant asthenia and anxiety. The control group (CG) consisted of patients with the same age (n=20) without psychiatric comorbidity. A study of acoustic event-related potentials of the brain (ERP) was carried out in the oddball paradigm with the recording of the time and correctness of a simple sensorimotor reaction.

Results. Comparative analysis of the asthenia group with the comparison group revealed a sufficient number of ERP's, which have significant statistical differences. The correctness of the sensorimotor reaction in this group was 98.3 ± 2.44%, whereas in the CG - 92.5 ± 5.74% (U = 62.5, p<0.01). The P1 initial positivity amplitude values in the asthenia group were 4.25 ± 3.12 µV and in the CG -4.15 ± 7.933 µV (U = 50, p<0.001). The early negativity in that group was -2.78 ± 2.377 µV, and in the CG it was 10.55 ± 7.466 µV (U = 75; p<0.05).

Conclusion. In the anxiety group, significant differences were noted in: P1 latency, P1N1, and N2P3 interval latencies, amplitude swing in P1N1. A specific marker of the asthenia group, distinguishing it from the CG, was the more positive values of the amplitude for the components P1, N1, P2, N2. Taking into account the low-frequency nature of the amplitude modulation in these components (circa 2 Hz), it can be assumed that nonspecific brainstem systems are involved in the process.

Keywords: loss of sight, trauma, nonpsychotic, mental disorders, asthenia, anxiety, neurophysiology, cognitive, evoked potentials, brain, sensorimotor reaction
1 Background

The visual system is the main sensory channel for humans that connects them with the environment. And therefore, loss of sight, especially in adulthood, is accompanied by emotional, motivational and social consequences that directly affect the psychophysiological state of the individual himself, his communication in society and, often, the social status of the subject [1]. In 90% of vision loss cases, this condition is accompanied by depression due to disability [2], and in case of loss of sight with a traumatic genesis, this process is further exacerbated by negative psychopathological manifestations, caused by the additional aggravating effect of posttraumatic stress on the state of mental health [3, 4]. The obvious relevance of the problem implies the involvement of various approaches to its solution, and the neurophysiological approach, as we hope, will allow us to identify new neurophysiological predictors for effective diagnosis and treatment of these disorders, on the one hand, and on the other hand - to elucidate the physiological mechanisms of these conditions. Earlier our group carried out neurophysiological studies of patients with nonpsychotic mental disorders due to a partial loss of sight owed to trauma [5]. However, later we assumed that the group of patients, that was studied by us was not homogeneous, which made us take a more differentiated approach. The results of these studies are presented in this paper.

2 Methods

Comprehensive studies were carried out at the Eye Microsurgery Center, Kyiv, Ukraine during 2010-2013. Study was conducted according to the principles of bioethics and deontology. The volunteer patients were informed of the nature and purpose of the study and have signed an informed consent. A randomized group of patients was formed in the period after the ophthalmologic intervention and determination of the volume and prognosis of visual impairment. A total of 600 people with partial loss of sight of traumatic genesis (PLVTG) underwent a screening examination. The manifestations of an acute stress reaction were recorded in all patients. Within one to three months after discharge from the hospital, when patients underwent MSE, we conducted an in-depth patients’ clinical-psychopathological examination. As a result, two groups of research were formed: the main group (MG) - 200 Patients who, after a traumatic event that caused a partial loss of sight, were diagnosed with nonpsychotic mental disorders (NPD), and a comparison group (CG) - 200 people whose mental state was consistent with the so-called "conditional norm". The criteria for exclusion from the study were lack of informed consent, history of mental and behavioral disorders, and the presence of severe somatic diseases, during which the patient's mental state may be affected.

Clinical-psychopathological research was conducted through an in-depth clinical standardized interview using ICD-10 diagnostic criteria. A subjective evaluation of the existed clinical and psychopathological manifestations was carried out using the Beck Depression Inventory [6], Diagnostic Techniques for Self-Assessment of Reactive (R) and Personal (P) Anxiety (Ch. D. Spielberger-Y. L. Khanin) [7]. The analysis of objective manifestations of psychopathological symptoms was carried out using Hamilton's clinical rating scales of depression (D) and anxiety (A) HAM-A and HAM-D [8]. The nosological structure of diagnosed NPD was represented by mental and behavioral disorders from cluster F43 - "response to stress and adaptive disorders" (22%), adaptation disorders with a predominant disturbances of other emotions F43.23 (14.5%); Post-traumatic stress disorder F43.1 (11.5%), adaptation disorder with mixed emotions and behavior disorder F43.25 (3.5%).

Two groups were formed to carry out electrophysiological examination to identify the developmental characteristics of neurophysiological mechanisms of the of NDP due to PLVTG from the MG: asthenia and anxiety, which included 15 men aged 22 to 57 years, and a CG comprised of 20 men of the same age. The asthenia group included patients with an asthenia, in whom asthenic-depressive and asthenic-hypochondriac syndromes were identified. The anxiety group included patients with a clinical prevalence of anxiety with anxiety-depressive, anxious-phobic, and obsessive-phobic syndromes.

Electrophysiological studies were carried out using the diagnostic complex "Amplaid MK15" (Italy). To study brain electrical activity, the method of event-related evoked potentials (ERP) was used with auditory modality. The subjects were binaurally exposed to a series of stimuli in the pseudorandom (with a predetermined probability of the significant stimuli appearance) sequence – oddball paradigm. A significant stimulus - a tone with a frequency of 4000 Hz was presented with a probability of 20%, a background stimulus - tone with a frequency of 1000 Hz was presented with a prob-
ability of 80%. The sound intensity was 100 dB above the audibility threshold [12]. The interval between stimuli was 2 seconds. The subject was instructed to react to the appearance of a significant signal by pressing the button, background stimuli were ignored. When the button was pressed, registration of the induced brain electrical activity occurred, as well as the time and correctness of a simple sensorimotor reaction. The ERP registration was carried out from the head surface with standard electroencephalographic electrodes located in the 10/20 (Jasper) system at the points: Cz - active electrode, A1 + A2 - common refractive electrode, Fpz – grounding electrode. The averaging of evoked potential was carried out based on 100 records [13]. Elimination of artifacts, including eye movement artifacts, was hardware-based. The P1, N1, P2, N2, P3 and N4 components were marked out on the ERP curve registered for a significant stimulus (Fig. 1). The positive component in the range of latent periods from 30 to 80 ms was regarded as P1, negativity from 80 to 140 ms - as N1, the positive component of P2 was differentiated in the time interval 120-200 ms, N2 - between 180 and 320 ms from the start of the scan, the late positive component P3 was detected in the range of 270-550 ms, and the next maximum negative bias potential was considered as component N4. Statistical software package Statistica 5.5 (StatSoft, USA) was used for statistical processing of the obtained experimental results. When checking statistical hypotheses, the values of criteria with significance level p <0.05 were considered reliable. The comparative analysis was carried out by nonparametric methods: the Wilcoxon T-test and the Man-Whitney U test, and the Pearson-Spearman correlation analysis [14].

3 Results

3.1 The results of psychological testing in asthenia and anxiety groups

The results of psychological testing show the differences between the groups in all indicators: RA, PA, Ds, Do, Ao (Fig. 2). At the same time, the values of the three parameters - RA, PA and Do in the anxiety group were higher than in the asthenia group. Thus, the RA index in the anxiety group (59.3 ± 2.13) was greater (U = 50; p <0.001) than in the asthenia group (49.7 ± 2.12). PA in the anxiety group (46.7 ± 3.81) also exceeded (U = 50, p <0.001) the values of the asthenia group (35.0 ± 6.92), and the Ao values in the anxiety group (22.0 ± 0.85) were almost twice as large (U = 0, p<0.001) than in the asthenia group (13.3 ± 2.97). The two remaining indicators: Ds (16.0 ± 0.84) and Do (17.7 ± 1.76) in the anxiety group were lower than in the asthenia group - 20.3 ± 2.58 (U = 12.5, p <0.001) and 24.67 ± 1.76 (U = 0; p <0.001) respectively.

The indices of psychological testing of asthenia and anxiety groups showed significant exceeding values (U values from 0 to 25, p<0.001) of RA, PA, Ds, Do and Ao of both groups relative towards the comparison group (Fig. 2).

3.2 ERP in the asthenia and anxiety groups

Comparative analysis of cognitive evoked potentials in anxiety and asthenia groups revealed a number of statistically significant differences (Fig. 3). The time of the sensorimotor reaction in the anxiety group was 337.3 ± 9.31 ms, which was significantly higher (U = 50; p <0.05) than in the asthenia group (308.7 ± 31.28 ms). The latent period of the P1 component of the ERP in the anxiety group (76.0 ± 23.42 ms) significantly exceeded (U = 50, p<0.05) the latent period of this component in the asthenia group (52.3 ± 31.28 ms).
The amplitude of the negative N2 component in the anxiety group (-6.54 ± 2.261 μV) had more negative values than in the asthenia group (-1.23 ± 1.644 μV) (U = 0; p < 0.001). The temporal indices of the ERP, such as the intervals P1N1 and P3N4, were smaller than in the asthenia group. Thus, the values of the P1N1 interval in the anxiety group were 31.0 ± 12.76 ms, and in the asthenia group, they were 47.7 ± 17.94 ms (U = 50, p<0.05). And the interval of the later P3N4 complex in the anxiety group was longer than in the early complexes and equaled 126.0 ± 12.68 ms, which was less than in the asthenia group 139.0 ± 11.43 ms (U = 62.5, p < 0.05).

3.3 ERP in asthenia and anxiety groups compared to the control group

Comparative analysis of the asthenia group with the comparison group revealed a sufficient number of the ERP indicators, which had significant statistical differences. The correctness of the sensorimotor reaction in this group was 98.3 ± 2.44%, whereas in the CG - 92.5 ± 5.74% (U = 62.5, p<0.01). Also in this group, there were differences in the amplitudes of the components: P1, N1, P2, N2 (Fig. 4, Fig. 5).

So, the values of the amplitude of the early positivity of P1 in the asthenia group were 4.25 ± 3.312 μV, and in the CG - 4.15 ± 7.933 μV (U = 50, p <0.001). The early negativity in that group was -2.78 ± 2.377 μV, and in the CG it was 10.55 ± 7.466 μV (U = 75; p <0.05). Differences between late P2 and N2 have the same trend of differences for the compared groups. The P2 values were 3.40 ± 2.029 μV in the asthenia group and -3.08 ± 8.287 μV in the CG (U = 75; p <0.05), the N2 value was -1.23 ± 1.644 μV, and in the CG it was 7.23 ± 5.754 μV (U = 75; p <0.05). In the anxiety group, there were other, different from the asthenia group, significant indica-

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*The values for reactive anxiety (RA), personal anxiety (PA), subjective assessment of depressive manifestations (Ds), an objective assessment of depression severity by the D. Hamilton scale (Do) and an objective evaluation of anxiety by the Hamilton scale (Ao) in the main asthenia and anxiety groups and in comparison group. Medium values (in points) and standard deviations are presented. * - differences with significant level of p<0.05. # - significant differences (p<0.05) in comparison with the asthenia group and * - with the comparison group.
of the ERP. Basically, these were time indicators, such as
the latency period of the P1 component, which values in
the anxiety group were 76.0 ± 23.42 ms, while in the CG - 49.3 ±
4.38 ms (U = 0; P <0.001), as well as P1N1 intervals of 31.0 ±
12.76 ms in the anxiety group and 58.8 ± 7.447 ms in the
CG (U = 0; p <0.001).
The interval of late N2P3 components in the anxiety
group was 103.0 ± 24.09 ms, and in the CG it was 150.0 ±
48.812 ms (U = 75; p<0.05). In addition to the P1N1 in-
terval in the anxiety group, significant differences from the
CG showed the P1N1 amplitude swing, which was 31.0 ±
12.76 μV, whereas in the CG it was 6.39 ± 1.110 μV (U =
50; P<0.001). Among the ERP indicators were also those
that had statistically significant differences from CG in both
groups.
These include such ERP indicators as latent periods of
P3 and N4 components, amplitude N4 and amplitude ranges
of N1P2 and P3N4. The latent periods of the P3 component
and in the asthenia group are 312.0 ± 33.16 ms (U = 50;
p <0.001), and in the anxiety group 320.0 ± 34.61 ms (U
[15]; [16] = 87.5, p <0.05) were lower than in the CG (368.3 ±
37.15 ms) (Fig. 6). The latent periods of component N4
and in the asthenia group (451.0 ± 33.09 ms, (U = 25; p
<0.001)), and in the anxiety group (446.0 ± 25.52 ms, (U =
50; p <0.001)) were lower than the values of this component
in the CG (498.8 ± 32.67 ms). Amplitudes of this component
had more negative values: -6.36 ± 1.44 μV (U = 75; p<0.05).
and anxiety group (4.75 ± 2.538 μV (U = 50; P <0.001)) were
smaller than the CG (7.47 ± 2.599 μV), when the amplitude of
the later P3N4 was 18.69 ± 5.525 μV (U = 25; p<0.001) and
18.75 ± 0.873 MV (U = 75; p <0.05), respectively, exceeded
the values of CG (11.04 ± 5.965 μV).

4 Discussion

It should be noted that depressive and anxious manifesta-
tions were detected not only in anxiety and asthenia
groups, formed as subgroups from the MG but also among the
comparison group. However, upon evaluation of CG, only a
single symptom was detected that did not constitute a signif-

Figure 4: Amplitudes of ERP P1, P2, N1P2, P3N4 positive
components in the anxiety, asthenia and comparison groups.

*Significant differences (p<0.05) of the indicators compared
to the comparison group

Figure 5: Amplitudes of ERP N1, N2, N4 negative components
in anxiety, asthenia and comparison groups.

*Significant differences (p<0.05) of the indicators compared
to the comparison group.
significant clinical picture of the mental disorder and had a lesser degree of severity. Alongside, in MG patients depressive and anxiety symptoms were diagnosed with a severity of small (72.5%) or severe (11.5%) depressive episode, as well as anxiety (56.0%) or anxiety disorder (32.5%). For persons with NPD, subjectively and objectively significant depressive manifestations were primary disturbances of the cognitive-affective and somatic spheres, as well as a high "dynamically stable" pathological anxiety with a negative drift of reactive anxiety. As a background was seen the presence of a high-level personality anxiety. Among the respondents from the MG, on the contrary, according to their subjective assessment the manifestations of depression were either absent or had a slight degree of severity. Present individual depressive symptoms characterized the process of the person’s response to trauma. The assumption of heterogeneity in the MG was initially evaluated by available clinical and psychopathological manifestations, both subjective and objective (Figure 2). Both groups showed statistically significant differences, both intergroup and in comparison to the CG. And these differences were noted for objective (Do and Ao), as well as for subjective indicators (RA, PA, and Ds).

Later, upon analysis of ERP data, we found differences in the nature of brain activity. Thus, higher values of the sensorimotor reaction time in the asthenia group in comparison with the anxiety group were combined with the higher values of the latency period of the P1 component. It points to a significant contribution to the process of early sensory perception mechanisms and attention mechanisms, and the whole brain activation level upon examination [17]. In the anxiety group, this process was less rapid than in the asthenia group. The reason for this seems to be a decrease in the efficiency of the inhibition mechanisms of the sensor gates, which screen out irrelevant information, projected through the medial geniculate bodies into the projection sections of the auditory cortex [18], [19]. And the implementation of this mechanism, in the context of P1 component, is associated with cholinergic nonspecific brain systems [16], [20]. The interval between P1 and the subsequent negative N1 components was also increased in the asthenia group. Despite its poly-generational nature, [21] it is also associated with selective attention mechanisms [22] and with N1 generators - such brain structures, as associative cortex regions, the nucleus of the medial and dorsal thalamus, hippocampus, tonsils and structures of the reticular formation of the midbrain [23].

The P3N4 interval is formed by the two late ERP components - P3 and N4, that are poly-generators. The main P3 wave generators are localized in such structures of the central nervous system as the hippocampus, frontal and parietal parts of the cerebral cortex [24], as well as a number of subcortical structures and primarily thalamic nucleus [25]. Neurons generating N4 late negativity refer to novelty detectors that are activated with explicit, non-automatic recognition of deviations in audio signals. The positive component of P3 is generated when any deviations of audio signals from standard signals are perceived [26]. Thus, the P3N4 complex can be interpreted as an electrophysiological correlate of the significant acoustic stimuli recognition and an increase in this interval in the asthenia group, compared with the anxiety group (Fig. 3). It can point to an increase in the necessary time for the realization of this process.

Summarizing the results of a ERP comparative analysis in asthenia and anxiety groups with CG, it should be noted that in these groups were identified two types of indicators. The first type is the ERP components, which had statistically significant differences compared to the CG in both the asthenia and the anxiety groups. These are the latent periods of
the P3 and N4 components, N4, N1P2, and P3N4 amplitudes. Changes in the second component are unique for each group, distinguishing them from the CG.

In the asthenia group, this is the sensorimotor reaction correctness and the amplitude of the P1, N1, P2, and N2 components. In the anxiety group, such indicators were: P1 latency period, P1N1 and N2P3 intervals, P1N1 amplitude swing. The N1P2 complex is part of the so-called V-wave (or complex P1-N1-P2), which, in fact, reflects the response of auditory cortex to the stimulus [27],[28],[29]. Complex N1P2 is associated with a conscious distinction of any discrete changes in acoustic signals (tonality, loudness, modulation, duration, localization in space, etc.) [30]. It has multiple cortical and subcortical generators in the serotoninergic system of the brain, which are modulating the primary auditory cortex [31],[32]. And a significant role in this is played by nonspecific brainstem systems [33]. The decrease in the N1P2 amplitude swing in both the asthenia group and, to a greater extent, in the anxiety group, should be interpreted as a reduction in the modulating effects of the suture nuclei in the auditory cortex. The changes in the N1P2 amplitude were observed in the experiments on the effects of sedatives on healthy subjects, and during deep sleep phases [34]. As it is known, during deep sleep the activity of serotoninergic neurons of the raphe nuclei is increased, and regarding to the amplitude of the late P3N4 complex in the asthenia and anxiety groups, we observe the opposite effect. It exceeds the values of the CG, which can be interpreted as a compensatory mechanism of active recognition, implemented in the late stages of the cognitive process, which allows successful solving the experimental task, even with the reduced effectiveness of early recognition mechanisms. This mechanism, probably, can also explain the decrease in the latent periods of P3 and N4 components in asthenia and anxiety group.

A specific marker of the asthenia group, distinguishing it from the CG, was the more positive amplitude values of the P1, N1, P2, and N2 components. Taking into account the low-frequency nature of these changes (circa 2 Hz), we assume the nonspecific brainstem systems contribution to this process.

In the anxiety group, the most significant neurophysiological markers were: the P1 latency period, P1N1 complex interval and amplitude range. A significant increase in the latency period P1, which resulted in the shortening of the P1N1 interval and a decrease in its amplitude, should be interpreted as a reduction in the effectiveness of early selective attention mechanisms, which provide the subtraction of relevant information from irrelevant and are implemented mostly by cholinergic mediator systems. Despite this, the sensorimotor reaction in this group remained at the level of the CG values, which reflects the activation of compensatory mechanisms at the later stages of sensory information processing. The N2P3 interval correlates with these processes and it became much shorter in the anxiety group compared to CG. It is known that the N2P3 complex occurs only when the auditory stimuli are identified, and not only heard [34]. This complex is registered on the scalp points, projected on the frontal and anterior temporal region of the cortex; it is associated with the extensive activation in these brain areas during the selective attention tasks.

5 Conclusion

Regarding to present study, were revealed changes in neurophysiological activity in patients with nonpsychotic mental disorders due to a partial loss of sight of traumatic genesis. Unique neurophysiological markers in patients with asthenia and anxiety distinguish them from the healthy individuals. These differences are associated with changes in brain areas, which provide sensory information processing, explicit stimuli recognition and late stages of cognitive processes.

Competing interests

The authors declare that no competing interests exist.

References


