Evaluation of Nonspecific Brain Systems in Patients with Panic Disorders by the Method of P300 Cognitive Evoked Potentials

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Measuring of the amplitude of auditory cognitive evoked potentials P300 showed its changes (decrease and increase) in patients with panic disorders compared to healthy individuals. The authors hypothesize that the decrease in P300 amplitude reflects increased activity of the cerebral reticulothalamic structures, while its increase is associated with activation of the septohippocampal limbic system in patients with panic disorders. P300 recording can serve as a valuable diagnostic method.

Key Words: *P300 cognitive evoked potentials; nonspecific systems of the brain; panic disorders*

The method of recording of P300 endogenous cognitive potentials is widely used for the study of cognitive functions, which are realized in humans through nonspecific systems of the brain (temporal-limbic and stem-reticular structures). P300 reflect processes associated with stimulus recognition and differentiation, concentration, decision making, reception of information or resolution of uncertainty, cognitive evaluation of the stimulus, memorization or operative memory [4]. There is no universal opinion about the main structures participating in the generation of P300 potentials: some authors believe that P300 are generated in the hippocampus, frontal and parietal lobes [10], others note appreciable effects of subcortical structures, primarily nonspecific thalamic nuclei [7]. N2 wave is believed to be associated with stimulus recognition in the medial temporal lobe with participation of associative parietal lobes. P300 peak (P3 component) is formed with participation of the frontal lobes. These data are confirmed by the results of mapping and 3-dimensional location of P300 sources by means of analysis of electrical and magnetic signals [3,4,11].

The method of cognitive evoked potentials is now widely used in practical neurology. Changes in P300 peak amplitude were detected in patients with obsessive-compulsive disorders [6,12], in military personnel with posttraumatic stress disorders [8]. Studies of P300 in patients with panic disorders (PD) showed increased amplitude of P300 peak [2,9] or increase of only early N1 and N2 components of the cognitive evoked potential.

We evaluated the cognitive functions and nonspecific systems of the brain in patients with PD.

MATERIALS AND METHODS

Forty-two patients (28 women and 14 men, mean age 30.5 years) and 23 healthy volunteers (15 women and 8 men, mean age 29 years) took part in the study. The clinical picture of PD included dyspnea, palpitations, sweating, flushes/chills, chest pain or discomfort, internal strain, and fear of dying. In addition, the majority of patients had depressive, anxious, agoraphobic, and alexithymic disorders. Hyperventilation syndrome was detected in all patients.

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The method of P300 auditory cognitive evoked potentials was used as a neurophysiological method of examination. Auditory stimuli were presented according to the oddball paradigm, *i.e.* presentation of rare (target) stimuli and frequent (non-target) stimuli. Binaural stimulation with pulses (50 msec duration, 80 dB intensity, 2.1 Hz frequency) was used. The frequency of the target stimulus was 2000 Hz, probability 30%; the frequency of the non-target stimulus was 1000 Hz, probability 70%. The emergence of the target or the non-target stimulus was a pseudoaccidental event. The examinee counted (in mind) only rare (target) stimuli. Monopolar leads were used. "Active" electrodes were placed in C3, C4 points according to the International 10-20 System, the reference electrodes were placed on the mastoid processes, and the grounding lead in the Fpz point. The Neiro-MVP complex device was used for P300 amplification and averaging. The amplitude and temporal parameters of N2-P3-N3 complex (the cognitive component of the response) were evaluated. Habituation was evaluated by comparing the amplitudes of successive P300 blocks consisting of 2-3 cycles.

The following psychometrical tests were used: Beck Depression Inventory, Speilberger State-Trait Anxiety Inventory for evaluating reactive and personal anxiety, Toronto Alexithymia Scale for detecting cognitive emotional disorders associated with alexithymia. Schulte tables were used for evaluating attention and working capacity; the selectivity of attention was evaluated using Munsterberg test. Signs of autonomic dysfunction were detected using Autonomic Inventory and Hyperventilation Questionnaire. The results were processed using Student's parametrical *t* test and Statistica software.

RESULTS

A significant decrease in P300 amplitude and changes in its habituation in both hemispheres were detected in patients with PD in comparison with healthy volunteers. In healthy individuals P300 amplitude decreased between averaging cycles 1 and 2, while in the pa-

TABLE 1. Psychoneurophysiological and Clinical Characteristics of Patients with PD ($M \pm m$)

Parameter		Healthy volunteers (n=23)	Patients with PD (n=42)
P300 amplitude, mcV	left hemisphere	12.2±0.7	8.3±1.2
	right hemisphere	12.0±0.7	8.1±1.1
Habituation, mcV	left hemisphere	2.2±0.2	-1.2±0.6
	right hemisphere	2.3±0.3	-1.4±0.6
Level of depression, score		6.2±0.3	15.4±1.1
Level of reactive anxiety, score		30.3±0.9	55.0±1.6
Level of personal anxiety, score		32.2±0.9	51.3±1.3
Toronto alexithymia score, score		53.2±0.5	68.3±1.8
Schulte tables (mean time), sec		26.1±0.5	41.7±1.2
Munsterberg test, number of layers		21.0±0.1	13.2±0.4
Vegetative questionnaire, score		19.1±0.6	46.1±2.6
Hyperventilation questionnaire, score		3.8±0.5	41.4±2.6

Note. All differences between patients with PD and healthy volunteers are significant (p<0.0001).

TABLE 2. Psychoneurophysiological Parameters in Patients with PD (Subgroups 1 and 2, $M \pm m$)

Parameter		Subgroup	
		1 (n=28)	2 (n=13)
P300 amplitude, mcV	left hemisphere	5.0±0.4*	15.9±2.6
	right hemisphere	5.1±0.4*	15.2±2.4
Habituation, mcV	left hemisphere	-1.7±0.7***	0.4±1.2
	right hemisphere	-1.8±0.6***	0.4±1.3
Schulte tables (mean time), sec		42.6±1.1**	36.7±2.6
Munsterberg test, number of words		11.8±0.5***	13.6±0.8

Note. *p<0.0001, **p<0.01, ***p<0.05 compared to subgroup 2.

tients with PD P300 amplitude increased with presentation of further blocks of stimuli. Moreover, significantly more pronounced reactive and personal anxiety, depression, vegetative dystonia, hyperventilation, and alexithymia were detected in patients with PD. Significant disorders in attention selectivity and stability were also found in these patients (Table 1).

Evaluation of the amplitude and temporal parameters of P300 potential prompted us to distinguish two subgroups in the group of patients with PD. Patients of subgroup 1 (n=28) differed significantly from normal subjects and patients of subgroup 2 (n=13) by lower P300 amplitude, distortions in its habituation, and more pronounced disorders in the selectivity and direction of attention in comparison with subgroup 2. Patients from subgroup 2 exhibited higher P300 amplitude (in comparison with healthy volunteers and patients of subgroup 1) and its slower (but not distorted) habituation (Table 2). Other psychophysiological and clinical characteristics of patients in the two subgroups were similar.

The results suggest that changes in P300 amplitude in patients with PD reflect dysfunction of nonspecific limbico-reticular structures playing an important role in the formation of emotionally motivated behavior, short-term memory, and cognitive functions such as recognition, differentiation, decision making, directed attention, *etc.* The data of electrophysiological studies closely correlate with the results of psychometrical tests, indicating high anxiety and easy distraction of patients with PD, depression, disorders in selectivity and stability of attention in comparison with healthy volunteers.

The decrease in P300 amplitude in subgroup 1 patients can be explained by high level of activation of nonspecific reticulothalamic structures of the brain or arousal-1 systems (according to Routtenberg), which can be also seen from previously recorded depression of α-rhythm, enhanced β-activity [1], decreased contingent negative variation amplitude, and decelerated fading of galvanic skin response in patients with PD [5]. P300 habituation disordered in subgroup 1 also indicates the predominance of activating processes.

Higher amplitude of P300 in subgroup 2 can indicate hyperactivity of the septo-hippocampal limbic structures or arousal-2 systems, which is confirmed by the increase in EEG spectral power in the θ-range in some patients with PD [1].

Hence, the method of P300 cognitive evoked potentials can be used as an objective test for evaluating the status of various compartments of the cerebral nonspecific systems in patients with PD and as a valuable diagnostic method.

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