PHYSIOLOGY

Psychoneurophysiological Assessment of Recovery of Cognitive Function in Patients with Asthenia during Rehabilitation

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Forty patients with severe asthenia were subjected to clinical, neurological, psychometric, and neurophysiologic examination before and after Enerion therapy. Psychoneurophysiological assessment with cognitive evoked potentials P300 and psychometric tests revealed serious impairment of cognitive functions in patients before therapy (compared to healthy individuals). Enerion therapy decreased the degree of psychoautonomic syndrome and asthenia and improved cognitive functions.

Key Words: *endogenous evoked P300 potentials; cognitive functions; asthenia; psychoautonomic syndrome*

The incidence of asthenic disorders constantly increased in the last decade. Nearly 60% patients seeking medicinal advice have asthenic complaints. The prevalence of chronic fatigue syndrome varies from 7 to 45% depending on the method of assessment.

Asthenia is characterized by abnormal spontaneous fatigue and easy physical and mental fatigability that develops after minimal physical and mental work, persists for a long time, and does not disappear after rest. It also includes emotional lability, increased anxiety, reduced motivation, sleep and memory disorders, and impaired concentration. Asthenia violates physical and mental capacities and affects patient's life and social activity. Asthenia is often associated with psychoautonomic syndrome (autonomic dystonia) and underlies the development of somatic and neurological disorders [1]. As differentiated from physiological fatigue, asthenic syndrome requires medical treatment. Enerion is a promising antiasthenic drug. This preparation possessing lipophilic properties crosses the blood-brain barrier and is accumulated in the limbicoreticular complex, hippocampus, and dentate gurus. Dysfunction in these structures contributes to the pathogenesis of autonomic dystonia and leads to cognitive disorders [1].

Recording and analysis of endogenous evoked potentials P300 are widely used as an objective psychoneurophysiological test for the assessment of cognitive functions and state of nonspecific limbicoreticular structures [3,7]. Here we performed a neurophysiological and psychometric study of cognitive functions in patients with psychoautonomic syndrome and severe asthenia.

MATERIALS AND METHODS

We examined 26 healthy individuals (17 women and 9 men, 20-67 years, mean age 38.1 years) and 40 patients with psychoautonomic syndrome and severe asthenia (26 women and 14 men, 18-62 years, mean age 37.2 years) before and after 28-day treatment with Enerion.

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TABLE 1. Patient Questionnaire before and after Therapy ($M \pm m$, n=40)

Parameter, score		Before therapy	Day 28 of therapy
Symptoms of asthenia (asthenia questionnaire)		72.6±13.7	55.2±11.6*
Autonomic disorders (autonomic questionnaire)		44.8±11.1	33.2±10.1*
Beck inventory		16.3±7.1	10.6±4.5**
Spielberger inventory	personal anxiety	52.8±6.6	42.9±6.3**
	reactive anxiety	42.3±7.2	40.5±5.3

Note. *p<0.02 and **p<0.05 compared to parameters before therapy.

Examination included clinical and neurological study of the autonomic nervous system and asthenia with standardized questionnaires (score) and psychometric tests for the severity of reactive and personal anxiety (Spielberger State Anxiety Inventory), degree of depression (Beck Depression Inventory), short-term memory (visual memory for numerals and images and mediated memorization), concentration of attention, and working capacity (Burdon's test and Schulte's tables) [4,5].

Cognitive functions were assessed using auditory P300 event-related potentials (oddball paradigm). Recording was performed in unipolar C3 and C4 leads. Reference electrodes were fixed on the mastoid processes. Binaural stimulation included impulses with a duration, strength, and frequency of 50 msec, 80 dB, and 2.1 Hz, respectively. The probability of target (2000 Hz) and non-target stimuli (1000 Hz) was 30 and 70%, respectively. The stimuli were delivered pseudorandomly. The examinee counted only rare (target) stimuli. P300 were amplified and analyzed using a Neiro-MVP device. The mean evoked potential was calculated after presentation of 26-29 significant stimuli. We evaluated amplitude and temporal characteristics of N2-P3 (P300) components (cognitive complex). The results were analyzed by Student's t test.

RESULTS

Before the therapy the patients felt bad and had severe symptoms of asthenia (asthenia questionnaire), pronounced autonomic disorders (autonomic questionnaire), increased indexes of reactive and personal anxiety (Spielberger State Anxiety Inventory), mild depression (Beck Depression Inventory). Considerable differences were revealed between patients and healthy individuals ($0.001<p<0.005$). After 28-day therapy the patients felt better, the degree of asthenia, autonomic dystonia, personal anxiety, and depression markedly decreased (Table 1).

The study of cognitive functions by the method of endogenous evoked potentials showed that before therapy the amplitude of P300 component in patients was lower than in healthy individuals. Temporal characteristics (latency of peaks N2 and P3) were similar in patients and healthy individuals. After therapy the amplitude of P300 component in patients increased, but remained below the control level.

Psychometric study of cognitive functions showed that before the therapy the ability of patients to memorize numerals (short-term visual memory for numerals) and images (short-term visual memory for images) was lower than in healthy individuals, mediated memori-

TABLE 2. Cognitive Functions in Healthy Individuals and Patients before and after Therapy ($M \pm m$)

Parameter	Healthy individuals	Patients	
		before therapy	day 28 of therapy
P3 amplitude (P300), μV	11.7±0.5	4.3±0.4*	7.1±0.5^{+}
N2 latency, msec	220.3±5.1	226.2±4.9	224.6±4.4
P3 latency (P300), msec	304.6±6.1	306.2±5.8	305.7±6.2
Visual memory for numerals, number	7.3±2.2	5.2±1.3***	6.5±1.5^{++}
Visual memory for images, number	12.4±2.3	9.3±2.2***	11.4±2.5^{++}
Mediated memory storage, number	8.5±1.4	4.4±1.0**	7.6±1.6^{+}
Schulte tables (average time), sec	30.7±11.5	38.7±12.8***	32.4±12.6^{++}
Burdon test, number of missed lines	37.6±12.5	32.5±11.3***	35.6±9.5^{++}
Burdon test, number of mistakes	8.5±1.6	15.3±2.2**	9.4±1.8^{+}

Note. *p<0.001, **p<0.01, and ***p<0.05 compared to healthy individuals; ^{+}p<0.01, and ^{++}p<0.05 compared to parameters before therapy.

zation (ability to retain and manipulate information) and concentration (Burdon and Schulte tests) were impaired. After therapy these parameters were improved, but remained below the control level (Table 2).

Endogenous evoked potentials P300 are mainly generated in the hippocampus, medial temporal lobe, frontal and parietal areas [2,7,8], and nonspecific reticulothalamic systems [6] responsible for cognitive functions and involved in the pathogenesis of psychoautonomic disorders. Changes in the amplitude of P300 are an objective neurophysiological criterion of cognitive dysfunction resulting from functional insufficiency of limbicotemporal and reticulothalamic structures in patients with autonomic dystonia. Strict correlations were found between the results of neurophysiological and psychometric examination. Selective attention, mediated memorization, and short-term memory were impaired in asthenic patients. Enerion therapy reduced the severity of asthenic and autonomic disorders, normalized neurophysiological and psychometric indexes and, therefore, improved cognitive functions.

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