ISSN 0362-1197, Human Physiology, 2007, Vol. 33, No. 2, pp. 236–246. © Pleiades Publishing, Inc., 2007.
Original Russian Text © S.A. Gordeev, 2007, published in Fiziologiya Cheloveka, 2007, Vol. 33, No. 2, pp. 121–133.

REVIEWS

The Use of Endogenous *P*300 Event-Related Potentials of the Brain for Assessing Cognitive Functions in Healthy Subjects and in Clinical Practice

S. A. Gordeev

Brain Research Institute, Russian Academy of Medical Sciences, Moscow, 103064 Russia

Received March 22, 2006

Abstract—Assessment of higher mental functions, objective detection of cognitive impairments, and investigation of pathophysiological mechanisms underlying these impairments in various neuropsychological diseases are of great importance for neuropsychophysiology. The endogenous event-related potential (ERP) approach is one of the instrumental neurophysiological methods that are currently used for assessing these complicated processes because recorded potentials reflect the intrinsic brain activity and changes in these potentials are caused by endogenous factors of the brain activity. The *P*300 cognitive evoked potential, induced by selective attention to a stimulus, has been the most widely used endogenous ERP. This potential may be helpful for studying mechanisms of mental disturbances, as it reflects neuronal processes connected with nonspecific activating reticulothalamic systems, as well as with limbic and neocortical mechanisms of selective attention and short-term memory.

DOI: 10.1134/S0362119707020168

MECHANISMS AND SOURCES OF GENERATION OF THE ENDOGENOUS *P*300 POTENTIAL IN THE BRAIN AND ITS RELATIONSHIP WITH COGNITIVE FUNCTIONS

The famous Russian psychologist A.R. Luria described three blocks involved in fulfilling higher mental functions: (1) the first block, regulating the energy level, comprising subcortical and stem structures; (2) central mechanisms of information perception and processing, associative brain regions; and (3) the third block, the frontal lobes [1].

Cognitive impairments may result from dysfunction of any of these three structural and functional blocks of the brain [2]. An injury in some part of the first block (nonspecific structures of the mesencephalon and diencephalon or mediobasal parts of the frontal lobes) affects activation processes, causing neurodynamic disturbances, such as attention disorder, psychomotor delay, and modally nonspecific memory impairments. Failure of the functions of the second block (information perception, coding, and storage), comprising the parietal, temporal, and occipital cortical areas, leads to disorganization of behavioral processes, including modally specific processes related to processing of visual, auditory, and proprioceptive information. Injuries to the third block (involved in behavior program formation, regulation, and control), related to the prefrontal cortex, result in regulatory impairments, including impaired formation of intentions and goals, as well as impaired regulation and control of actions and behavior as a whole.

Methods for estimating the electrical activity of the brain, including the evoked potential (EP) approach, are of great importance for investigating brain mechanisms responsible for higher mental functions [3–5]. The current notion is that any EP reflects both sensory perception of information (early short-latency components of response) and information processing and storage and decision making (late long-latency components of response) [6]. Many authors think that analysis of parameters of long-latency responses yields important information on the brain activity and is important for assessing cognitive functions involving information perception and processing [4, 7].

Analysis of *P*300 endogenous cognitive EPs has been widely used since the mid-1960s for objective assessment of cognitive functions involving temporal–limbic and stem–reticular brain structures [8–10].

*P*300 has been recorded only as a response to significant attention-related stimuli and has been interpreted as a correlate of stimulus recognition or differentiation [11], the level of selective attention [3, 11, 12], decision making [13–15], obtainment of information or reduction of ambiguity [16], responses depending on stimulus significance [17, 18], cognitive assessment of a stimulus [19, 20], and storage or operative memory [21, 22]. On the other hand, *P*300 has been recorded as a response to sudden changes in an insignificant stimulus or when an oddball stimulus is presented to a subject during the performance of any task and has been interpreted as a correlate of an orienting reaction [23–25]. It has been hypothesized that the amplitude of the cognitive *P*300 potential depends on the degree to which a

probabilistic forecast (expectation) and a real event (stimulus or response) are not matched [26]. This hypothesis is compatible with the so-called noncognitive interpretation of the *P*300 potential, according to which an endogenous potential is the common denominator of different cognitive processes causing changes in the state in response to a stimulus, by which a certain change in activity is meant [27]. Speculations on the relationship between the *P*300 component and increased emotional tension [28], as well as the hypothesis that an endogenous potential is modulated by further activation of cortical neurons depending on the psychological significance of a stimulus [29], have come very close to this viewpoint.

Generally, the cognitive *P*300 EP is a complex potential that occurs in the selective attention paradigm and reflects the selection of a target stimulus [30]. Stimulus perception is characterized by early EP components, which reflect sensory processing connected with both physical parameters of a stimulus and the specific and nonspecific activation of specialized systems responsible for information perception and processing. A primary recognition of the stimulus occurs at the next stage, as evidenced by negativity recorded 100–250 ms after stimulus presentation, which is sometimes termed *N*2 in auditory and visual EPs [31]. The third stage is the final recognition of the stimulus, when it has to be compared to a template that is stored in the memory in order to organize the related action (ignore, remember, perform an action specified by instruction, etc.). Therefore, the *P*300 potential approach focuses on these events, with special emphasis on selective attention and short-term memory. That is why *P*300 parameters are so sensitive to the complicated and specific task of recognition and to a subject's cognitive functioning [32].

Some biological and psychological variables (factors) affect the *P*300 amplitude and time parameters. The psychological factors include the complexity of stimulus recognition, the level of attention to presented stimuli, the probability of occurrence of relevant stimuli, the stimulus nature and intensity, and the interstimulus interval [3]. The biological variables that have the greatest effect on *P*300 parameters are cognitive abilities (especially, a subject's memory), personality type (in my opinion, personality type is more likely a psychophysiological variable), age, arousal state [5], and gender [33].

*P*300 is the most marked in the vertex region as reported by most researchers. The *P*300 amplitude is the greatest in the frontocentral and less frequently the parietal areas [3, 32]. In females, the visual *P*300 EP has a shorter latency and a higher amplitude than in males [33]. The *P*300 peak amplitude of the response to verbal stimuli is significantly higher in the left hemisphere, and that of the response to nonverbal (image) stimuli, in the right hemisphere. Therefore, it can be used for testing verbal and nonverbal cognitive functions in neuropsychological studies [32].

During successive repeated trials, the *P*300 latency becomes shorter and the *P*300 amplitude decreases. There is an inverse relationship in the case of pathology: the *P*300 peak amplitude may be higher than that during the first trial (going into the task, which is typical of depression and suspense) [3].

There is a clear age dependence of *P*300 parameters, which allows plotting special aging curves. The *P*300 peak latency shows a downward tendency from the age of 7, when a child can properly follow instructions, until the age of 18–20. Then, the aging curve can be plotted: the *P*300 latency increases at a rate of 1–2 ms per year [34], and the *P*300 amplitude decreases at a rate of about 0.1 μV per year [35]. These changes in the amplitude–time parameters of cognitive EPs are associated with delayed memory processes [36] and with normal aging accompanied by a decreased number of dendritic spines and a reduced density of synaptic contacts at the level of cerebral neurons [33]. A relationship has been established between endogenous potentials and cholinergic and noradrenergic mechanisms of the brain [37].

A cognitive EP reflects nonspecific brain activation involving selective attention. *P*300 potentials recorded from the scalp during stereotactic operations in response to visual and auditory stimuli were accompanied by negative shifts in thalamic nuclei, indicating activation of nonspecific reticular systems, ascending afferentation from which led to a corresponding shift of brain electrical potential [38].

The *P*300 peak amplitude depends directly on the attention level and increases as the probability of a target stimulus decreases [39]. When a stimulus is ignored, the amplitude decreases and the latency increases. There is a negative correlation between the *P*300 amplitude and latency [40]. In healthy subjects, the *P*300 amplitude is directly proportional to the rate of response and task complexity [41].

The *P*300 amplitude depends on the size of the operative memory (it is likely that intensive attention rather than memory size is required, if necessary, to keep in the memory a great number of elements). When the number of letters in a stimulus combination increases from three to seven, the *P*300 amplitude increases proportionally [42]. Cognitive EPs depend on the cognitive content of the task performed, which is connected with a certain brain specialization involved in higher mental functions. When faces are used as visual stimuli, a correct recognition of repeatedly presented faces is accompanied by a positive wave, which is significantly more marked in the right hemisphere, in the area topically corresponding to the dipole at the posterior part of the superior temporal sulcus, i.e., where neurons are located that are specialized in analyzing complex visual images and faces, as reported in neuropsychological studies [43]. The *P*300 amplitude also depends on the cognitive content of a stimulus and memory size for verbal stimuli and is substantially independent of the

memory size for nonverbal stimuli, reflecting specific features of the processing of verbal (successive) information by the left hemisphere and of nonverbal (simultaneous) information by the right hemisphere [44].

According to neuropsychological examination, a shorter latency and a greater peak amplitude of *P*300 are typical of subjects with better cognitive abilities [5, 45]. It has been found that the amplitude is directly proportional to the level of task-related attention, while the latency reflects the rate of stimulus recognition in a series presented [46, 47]. The relationship has been established between *P*300 parameters and memory characteristics: the *P*300 peak latency increases as the size of the short-term and operative memories decreases [47, 48].

The fact that *P*300 parameters are correlated with the effectiveness of visual perception processes, short-term memory, and the abstraction function, estimated using neuropsychological methods, has been reported in many studies, indicating that an increase in the *P*300 peak amplitude is accompanied by the improvement of attention, calculation, and logical memory functions [49, 50].

From the 1960s until today, elucidation of the possible mechanisms underlying the generation of *P*300 and the search for brain structures involved in generating this potential have been important aspects of the study of *P*300. In this period, many hypotheses, often contradictory, have been made [51–54]. The main difficulty with locating the sources of long-latency activity is that long-latency EPs are widely spread, have an irregular pattern, and show a weak topical relation to specific brain regions.

It has been found that the *P*300 EP recorded by implanted electrodes from the hippocampus and nuclei of the amygdalar complex has a shorter latency and a greater amplitude than that recorded by scalp electrodes. This is explained by the fact that this potential is generated by the limbic structures. However, no substantial changes in *P*300 were found during examination of patients who underwent removal of individual limbic structures from one side, which contradicts the hypothesis that the primary source of this potential is located in the hippocampus or amygdala [53, 54].

The relationship between the late components of cortical potentials and deep brain structures is rather sophisticated; therefore, hypotheses have been put forward that there are several sources of the *P*300 potential [54, 55]. Some researchers believe that *P*300 is generated by several migrating subcortical and cortical sources [56], while others, on the basis of their findings, doubt the presence of cortical generators of *P*300, explaining *P*300 generation by electrical activity of hippocampal structures [57]. Cognitive *P*300 EPs have been recorded in the hippocampus, amygdala, and various subcortical structures. Data obtained using implanted electrodes indicate that late components of the *P*300 complex are generated by local postsynaptic potentials causing changes in the impulse activity of the globus pallidus and thalamic nuclei [54]. The authors think that the globus pallidus and ventrolateral thalamic nuclei are the elements of the system involved in cognitive processing.

Analysis of *P*300 topography and three-dimensional location showed an irregular pattern of the potential field, evidencing the presence of several sources [58]. A double-dipole model made it possible to identify certain phases in generating *P*300, with various brain structures involved. The first phase was immediately after the long-latency auditory response and included the *N*2 peak associated with stimulus recognition. It was found that the temporal and supraparietal brain regions were significantly involved in this phase. The second phase included the descending part of the *P*300 potential and reflected the involvement of the inferoparietal and frontal lobes. In the third phase, which included the peak of *P*300 and the beginning of its ascending part, the frontal lobes were involved. The fact that the frontal structures are involved in generating late components of the cognitive *P*300 complex is not unexpected because this area is associated with the final recognition of a stimulus and decision making [51, 59–61]. Thus, the *P*300 potential reflects the functioning of the central brain structures involved in recognition, differentiation, and storage of significant stimuli [46].

Finally, it may be concluded that the amplitude–time parameters of the *P*300 potential reflect the location and degree of activity of the brain structures involved in cognitive processing, allowing application of this method for assessing human psychophysiology, specifically, cognitive functions.

ANALYSIS OF ENDOGENOUS *P*300 EVENT-RELATED POTENTIALS IN THE CLINICAL PRACTICE OF PSYCHONEUROLOGY

In 1978, Goodin and Squires [62] for the first time suggested using the endogenous *P*300 EP test for assessing dementia, and since then this test has been widely used as a tool for objective assessment of cognitive functions in clinical studies [63, 64]. The *P*300 test was recommended for clinical practice by the International Federation of Clinical Neurophysiology and the American Association of Clinical Neurophysiology in 1993 [3].

Specific changes in *P*300 have been reported for both organic and mental disorders of the nervous system, aging, dementia, depression, schizophrenia, memory impairment, etc. *P*300 parameters such as a decreased amplitude, an increased latency, and the absence or instability of the response are of the highest diagnostic value [58, 65]. The fact that cognitive EPs are sensitive to structural and functional changes in the brain systems makes it possible to use the EP test for evaluating the effectiveness of treatment [32].

As noted above, many factors ensuring cognitive activity at a given moment, mainly, operative memory, decision making, and selective attention functions, affect the generation of the *P*300 potential [46, 66, 67]. A close correlation was established between the degree of prolongation of the endogenous potential latency and the intensity of cognitive impairments [46, 68–70]. For mild cognitive impairments and mild cortical-type dementia, the latency was 15–30% higher than that normal for a given age [3]. An increase in *P*300 latency was observed even for primary signs of impaired cognitive functions, i.e., at the preclinical stage of dementia. For pronounced cognitive impairments, the latency increased by 56% in patients with cortical-type dementia and by 38.5% in patients with subcortical-type dementia. Both the increase in the latency and the decrease in the amplitude of the cognitive potential were the greatest in patients with severe Alzheimer's dementia, exceeding those in patients with severe subcortical-type dementia [71]. The differences in *P*300 peaks between two types of dementia were the greatest for the *P*300 latency–amplitude ratios, indicating the intensity of cognitive impairments. This ratio was significantly higher in cortical-type than subcortical-type dementia [58]. Similar changes in *P*300 for two types of dementia were reported by other researchers [64].

The *P*300 test is widely used for objective differential diagnosis of subcortical (Huntington's chorea and Parkinson's disease) and cortical (Alzheimer's disease and vascular dementia) types of dementia [65]. In dementia of the subcortical–frontal type, there was an increase in the latencies of the early *N*1 and *P*1 components of the response to a stimulus, which were recorded up to 200 ms after the stimulus presentation and reflected the level of perception and physical properties of the stimulus, and of the late *N*2 and *P*3 (*P*300) components of the response, which were recorded 200 ms after the stimulus presentation and reflected the state of cognitive functions. In frontal-type (Alzheimer's) dementia, the latencies of only late components of the response were prolonged [64]. Patients with two types of cognitive impairments exhibited an increase in the *P*300 peak latency and a significant decrease in the amplitude of the cognitive components of this potential [58].

A close correlation was observed between the changes in *P*300 amplitude–time parameters and the degree of cognitive impairments: the greatest changes in *P*300 parameters (an increase in the latency and a decrease in the amplitude) were observed in patients with severe cognitive impairments [3, 59]. Accompanied by increasing severity of cognitive impairments, both an increase in *P*300 latency and a decrease in *P*300 amplitude were reported for Alzheimer's disease, vascular dementia, and Parkinson's disease [45, 70]. Analysis of *P*300 parameters [58, 63, 65] showed that the *P*300 test was helpful in detecting dementia and in differentiating dementia from functional disorders in patients with cognitive impairments caused by vascular or degenerative diseases of the brain, depression, head injury, and alcoholic intoxication [72].

A statistically significant decrease in *P*300 peak amplitude was observed in early Alzheimer's disease without pronounced clinical manifestations [73], and both an increase in *P*300 latency and a decrease in *P*300 amplitude were recorded for early cognitive subcortical- and cortical-type impairments caused by vascular diseases [58]. Similar results were observed in patients having cognitive impairments other than dementia, with hemodynamically relevant stenoses of the internal carotid artery [74]. The authors think that a smoothed shape of the wave and a decrease in the *P*300 amplitude are of additional diagnostic importance for detecting early cognitive impairments. Numerous studies showed a decrease in the amplitude and an increase in the latency of the *N*2 and *P*3 components of cognitive *P*300 in patients with Parkinson's disease without clinical manifestations of dementia [75–77]. Magnetic resonance imaging (MRI) and computer tomography scanning of the brain showed a decreased volume of the hippocampus and frontal lobe atrophy in the above patients [78, 79].

The *P*300 peak amplitude in early Parkinson's disease was abnormally increased as compared to that recorded in sex- and age-matched healthy subjects [49]. The authors explained this fact as reflecting a higher mobilization of attention and memory resources for performing a task in order to compensate the existing impairments of the brain function.

A number of researchers believe that latency prolongation can be observed only in dementia patients and cognitive abilities significantly decrease with age [80]. Neuropsychological data are consistent with an age-related increase in *P*300 latency [36].

EPs are most widely used in neurological diseases, mainly in multiple sclerosis. Cognitive *P*300 EPs are the most specific for investigating higher mental functions in disseminated sclerosis. Both visual and auditory stimulation led to a decrease in the amplitude and an increase in the latency of the *N*2 and *P*3 (*P*300) components. In patients with changes in *P*300 parameters, the number of mistakes and the response time exceeded those in both healthy subjects and multiple sclerosis patients whose *P*300 parameters were normal. In patients with pathological changes in cognitive potentials, brain damage was more extensive, as confirmed by MRI, and psychopathological symptoms (decreased intelligence and memory) were more pronounced [81]. It was found that a decrease in the *P*300 peak amplitude and an increase in the *P*300 peak latency were correlated with the impairment of nonverbal functions, abstract thinking, memory, and attention caused by a substantial impairment of the integrative cortical activity because of massive demyelination of thalamocortical systems [82].

Endogenous *P*300 EPs have been used for assessing higher cortical functions in cerebrovascular impair-

ments. The *P*300 peak latency was significantly increased relative to the normal value and the *P*300 peak amplitude was decreased, with a rather marked *N*2 peak, in a patient with transitory ischemic attack accompanied by hypomnesia and a 6-h episode of transitory global amnesia. The findings were interpreted as reflecting the impairment of cognitive functions caused by defective storage and a reduced volume of operative memory for current events rather than by the difficulty of recognition of a significant stimulus [58]. In patients with multiple lacunar dementia, prolongation of the *N*2 component was correlated with the response time. Considering the relationship between the *N*2 component and stimulus recognition, the reported data may indicate alteration of the relations between the frontal lobes and subcortical structures because of multiple lacunar infarcts [31].

In patients with Huntington's disease, a hereditary neurodegenerative disease characterized by cerebral and caudate nucleus atrophy, the *N*2 component was absent, the *P*300 peak latency was increased, and the *P*300 peak amplitude was substantially decreased, evidencing the impairment of cognitive functions related to stimulus recognition and differentiation (the absence of *N*2) and decision making and a decrease in operative memory [58].

In epileptic patients, changes in cognitive *P*300 EPs were explained by the impairment of the hippocampal mechanisms of memory [83]. The use of the endogenous *P*300 potential test in epilepsy is explained by two factors, one of which is substantial cognitive changes, especially in childhood. The other factor, no less important, is long-term administration of antiepileptic drugs, resulting in a decrease in cognitive functions. Therefore, the *P*300 test for monitoring side effects associated with antiepileptic treatment will be helpful in epilepsy [3].

Endogenous *P*300 potentials have been used in metabolic and neurotoxic disorders. Prolongation of the *P*300 latency is a sensitive indicator of uremic encephalopathy. The degree of prolongation of the *P*300 peak latency can be used for determining whether it is necessary to perform dialysis and for evaluating its effectiveness because the postdialysis improvement of health status was accompanied by a decrease in the *P*300 latency [84]. The *P*300 test can be used for detecting and estimating the severity of encephalopathic disorders in diseases leading to cirrhosis. Prolongation of the *P*300 peak latency was observed in patients with cirrhosis, and prolongation of the *N*1 and *N*2 component latencies was observed in severe cirrhosis [84]. In the double-choice test, a decrease in the amplitude was correlated with the degree of metabolic disorders [85]. Similar changes in the parameters of endogenous potentials, i.e., an increase in the *P*300 latency and a decrease in the *P*300 amplitude, were recorded for hepatolenticular degeneration (Wilson–Konovalov disease), characterized by concomitant damage to the internal organs and the brain. In patients with a long history of this disease, latency prolongation was similar to that typical of dementia (>500 ms) [58].

Fewer papers have focused on the effect of nootropic agents on the cognitive functions. Analysis of the effectiveness of treatment with Cerebrolysin and Tanakan showed that a decrease in the *P*300 latency and an increase in the *P*300 cognitive complex amplitude were the most marked in patients receiving Tanakan [86].

A passive perception task can be applied to assessing cognitive EPs in severe cognitive impairments [87]. This method is rather simple and significantly facilitates the assessment of cognitive functions in children with developmental delays.

Analysis of endogenous *P*300 EPs showed that the *N*2 and *P*3 components of the *P*300 complex depended on the age and state of cognitive functions, while the sensory part of the response (a long-latency auditory potential), which is related to stimulus perception, slightly depended on the age and did not depend on the state of cognitive functions. A decrease in the *P*300 amplitude and an increase in the *P*300 latency were statistically significant even in preclinical cognitive impairments. In patients with both cortical and subcortical types of impairments, the severity of cognitive impairments was correlated with more substantial changes in the *P*300 complex. With increasing cognitive impairments, the *P*300 latency increased and the *P*300 peak amplitude decreased.

Many papers deal with cognitive EPs in endogenous psychoses. Much attention has been focused on cognitive *P*300 EPs in schizophrenia because they may be helpful for objective assessment of certain aspects of information processing and thinking: subjective evaluation, classification, image recognition, memory, decision making, performing operations, etc. [88]. A decrease in the *P*300 peak amplitude was correlated with certain symptoms, specifically, negative symptoms in schizophrenic patients [89, 90]. In schizophrenic versus healthy patients, *P*300 was asymmetrical; i.e., the amplitude of its late components was lower in the left hemisphere [91]. A decrease in the *P*300 amplitude was observed in autistic patients [92]. Prospective family studies showed a decrease in the *P*300 peak amplitude and an increase in the *P*300 peak latency in relatives of schizophrenic patients. Prolonged latencies of the *N*200 and *P*300 components were recorded in children at risk for schizophrenia (one of the parents had schizophrenia) [93]. Although the *P*300 amplitude depends on the degree of interest in the task performed in both healthy and schizophrenic subjects, abnormal amplitudes of cognitive EPs are often considered to be attention disorders in schizophrenia [94]. Some authors tried to elucidate whether these abnormalities are caused by a lack of resources for information processing or by increased distractibility. For these purposes, they analyzed parameters of individual rather than averaged *P*300 responses in schizo-

phrenic patients. It was found that the *P*300 potential was absent in about 30 versus 18% of tests, the results of which are usually averaged, in schizophrenic and healthy subjects, respectively. In addition, a decrease in the *P*300 amplitude was observed in all individual tests in schizophrenic patients. The authors concluded that a decrease in the mean *P*300 peak amplitude showed that schizophrenic patients were more distracted and had fewer resources for processing target stimuli [95]. Changes in cognitive EPs were not specific for schizophrenic disorders and could be observed in some other psychic diseases [96]. For endogenous depression, the *P*300 peak amplitude was decreased in the *Fz* derivation and the *P*300 peak latency was increased in the *Pz* derivation [97]. Both endogenous and neurotic depressions are characterized by a decreased *P*300 peak amplitude, increased *P*300 peak latency, fuzzy peak shape, and abnormal topography. Moreover, in endogenous depression, there was a significant negative correlation between the *P*300 amplitude and the depression severity estimated by the Hamilton Anxiety Scale (HAS). In neurotic depression, no such correlation was observed [98].

Fewer papers have focused on cognitive *P*300 EPs in patients with anxiety disorders. When used for investigating psychophysiological features in panic disorders, the auditory event-related potential (ERP) test showed that, in panic patients, the amplitudes of the *N*1 and *N*2 components of the response to target stimuli and of the *N*1 component of the response to nontarget stimuli were significantly increased as compared to those in healthy subjects. There were no significant differences in the *P*300 amplitude and latency between these two groups. An increase in the amplitude of the early *N*1 and *N*2 components was interpreted as a change in early information processing in panic disorders [99]. In studies with panic patients and healthy controls, body-related (somatic) and nonsomatic words were presented tachistoscopically for correct identification. Fifty percent of the words were neutral [100]. Behavioral (the proportion of words correctly recognized) and electrocortical (event-related brain potentials) measures were recorded. Panic patients recognized more body-related than nonsomatic words and exhibited significantly larger *P*300 amplitudes and enhanced positive slow waves (600–800 ms after the stimulus presentation). In healthy controls, the number of correctly recognized words and the ERPs were not differently affected by the two word types. These results are consistent with cognitive models of panic disorders, assuming that certain bodily sensations are perceived and processed in an affective manner that differentiates panic patients from healthy controls [100]. A 1.5-year follow-up study showed that, although no significant correlations between neurophysiological and psychometric measures could be found at the onset of the study, there was a significant correlation between the improvement over the follow-up period and the neurophysiology. A decline in the HAS, which proved to be the best estimate of the improvement, was associated with the relative magnitude of the positive slow wave elicited by somatic stimuli. These findings support cognitive models of panic disorders, which stress that abnormal processing of bodily symptoms is relevant for the development and maintenance of the disorder [101]. An increase in the *P*300 amplitude was recorded in panic disorders (panic attacks) by other researchers and was interpreted as reflecting an increase in the excitability of cortical neurons and in orientation reaction [102].

Patients with obsessive–compulsive disorders showed either a decrease [103, 104] or an increase [105, 106] in the *P*300 peak amplitude in response to target stimuli. This was interpreted as hyperactivation of neurons of the frontal cortical area, which reflects a lack of cognitive functions (memory or selective attention) in these patients [107]. In veterans with combat-related posttraumatic stress disorder (PTSD), the *P*300 component amplitude was lower than that in military men without PTSD [108].

The cognitive EP test has been used for examining patients with pain syndromes. To examine the differences in cognitive processing between chronic and episodic pain sufferers, auditory ERPs were recorded in two consecutive trials from chronic lower back pain patients, episodic tension-type headache sufferers, and age- and sex-matched healthy subjects. The *P*3 latency and amplitude showed no differences between groups in the first trial. In an analysis of the *P*3 latency habituation, healthy controls and the episodic tension-type headache sufferers showed a significant change in the *P*3 latency, whereas the lower back pain sufferers failed to show such a change. The lower back pain sufferers significantly differed from the healthy controls in the amount of the *P*3 latency habituation. The *P*300 amplitude habituation was considerable only in the healthy controls. There were no differences in the *P*300 amplitude habituation between the groups. No correlation was observed between the *P*300 habituation, age, disease duration, and severity of symptoms. The authors suggest that the changes in the *P*300 peak latency point to attention disorders in chronic pain sufferers. They believe that, although cortical information processes are similar, brain structures involved in decision making and memory processes seem to work differently during repeated tasks in the chronic pain sufferers and episodic pain sufferers. Considering the reported abnormalities of the *P*3 habituation, the authors suggest that the involvement of temporal structures during migraine headache, rather than pain location, may cause attention disorder [109]. *P*300 ERPs were studied in migraine without aura sufferers and episodic tension-type headache sufferers during both pain-free periods and spontaneous headache attacks. No abnormalities of either *P*300 latency or *N*2–*P*3 amplitude were recorded in either group during the interictal period. Similarly, no abnormalities of the *P*300 parameters were recorded in the tension-type headache subjects during headache

attacks. However, an increase in the *N*2–*P*3 latency and amplitude was significant in migraine sufferers [110]. The authors discuss the data in terms of etiopathogenic theories of migraine and the hypothesis that acetylcholine and norepinephrine are the neurotransmitters capable of affecting *P*300 ERPs reflecting cerebral activity during sensory information processing and analysis [110]. Another study was performed in patients with a diagnosis of headache according to International Headache Society criteria: migraine without aura, migraine with aura, cluster headache, chronic paroxysmal hemicrania, episodic tension-type headache, and ergotamine headache. Age-matched healthy subjects served as a control group. ERPs were evoked by a visual oddball paradigm involving flashes of light (85% white light and 15% red light). The ERP parameters were evaluated separately for the first and the second 200 stimuli and for the whole series of stimuli. A decrease in the *P*300 latency was recorded during the second trial for migraine with and without aura, but not for other types of headache and not for healthy controls. A loss of cognitive habituation in migraine may serve as a specific diagnostic tool. Both migraine and cluster headache specifically modify cognitive processes, causing either a loss of cognitive habituation or an increase in the time of cognitive processes. These effects can be counterbalanced by antimigraine therapy [111]. In another study, visual *P*300 ERPs (two consecutive trials of 200 stimuli each) were recorded in children and adolescents suffering from migraine with or without aura, episodic tension-type headache, and ergotamine headache [112]. No statistically significant differences in *P*300 averaged parameters were found between all types of headache and healthy controls. However, a separate analysis of the first and second trials showed a highly significant loss of cortical habituation in migraine with and without aura as measured by the *P*300 amplitude and latency. This phenomenon increased with age and could not be observed in the healthy controls or the patients with tension-type headache or ergotamine headache. These findings suggest that cognitive processes are specific in migraine and similar in children and adolescents. Measurement of the habituation of the *P*300 latency and amplitude is a specific method for differentiating primary headaches in children and adolescents [112].

The relationship between the accuracy of cognitive processing and components of ERPs (*P*300) was analyzed in 21 young healthy subjects [113]. A benzodiazepine was used to manipulate the cognitive state of the subjects. The authors recorded serial changes in *P*300, choice reaction time (CRT), and error ratio before and after an oral administration of 0.4 mg of alprazolam. After the administration, the coefficient of variation of CRT tended to decrease in 9 subjects (group I) and to increase in 12 subjects (group II). Prolongation of the *P*300 latency was observed in all subjects after treatment but was more marked in group II than group I. In group I, there were neither errors nor significant differences in the *P*300 amplitude before and after the treatment. In group II, alprazolam caused a decrease in the *P*300 amplitude and an increase in the error ratio, which were significant. The findings suggest that both the accuracy and the *P*300 amplitude were unchanged when the central nervous system managed to reduce fluctuations in CRT, although both the *P*300 amplitude and the error ratio increased because of impairment of these processes [113].

Note that changes in amplitude–time parameters, specifically, the *P*300 component, are typical of the above diseases and are not unexpected because this component reflects the state of cognitive functions, including selective attention and short-tem memory [12, 46, 47, 50, 67], which are impaired to a certain extent in these diseases [58, 82, 94, 98].

Changes in *P*300 are not nosologically specific because an increase in the *P*300 peak latency, a decrease in the *P*300 peak amplitude, and abnormal habituation of the *P*300 peak are observed in various diseases accompanied by the impairment of cognitive functions. Generally, changes in the *P*300 component reflect the impairment of selective attention and short-term memory, which are of syndrome nature, and can be observed in diseases of various etiology.

CONCLUSIONS

The *P*300 ERP test is widely used for investigating the brain mechanisms of higher mental functions and for objective detection of cognitive impairments. *P*300 potentials are interpreted as a correlate of processes related to stimulus recognition and differentiation, the level of selective attention, decision making, storage or operative memory, orientation reaction, etc. The main structures that are involved in generating *P*300 are the hippocampus, frontal lobe, and parietal area; subcortical structures; and nonspecific thalamic nuclei. According to neuropsychological examination, a shorter latency and a greater peak amplitude of *P*300 are typical of subjects with better cognitive abilities: the amplitude is directly proportional to the volume of operative memory and the level of task-related attention, while the latency is inversely proportional to the same. In women, the visual *P*300 EP has a shorter latency and a greater amplitude than in men. There is a clear age dependence of *P*300 parameters, which allows special aging curves to be plotted.

Today, endogenous ERPs are widely used in clinical practice. A close correlation has been established between the degree of changes in endogenous potentials and the severity of cognitive impairments: the greatest changes in *P*300 parameters (an increase in the latency and a decrease in the amplitude of response) are observed in patients with severe cognitive impairments. The *P*300 test can be used for objective differentiation of subcortical (Huntington's and Parkinson's diseases)

and cortical (Alzheimer's disease and vascular dementia) types of dementia.

An increase in the *P*300 peak latency and a decrease in the *P*300 peak amplitude were recorded for early cognitive impairments of both cortical and subcortical types without pronounced clinical manifestations, making it possible to use the *P*300 test for early detection of preclinical dementia.

During the treatment of patients with vascular dementia and anxiety impairments, a significant positive correlation was established between the impairment of cognitive functions and normalization of *P*300 parameters, making it possible to use the endogenous EP test for objective evaluation of the recovery of cognitive functions during rehabilitation.

The amplitude–time parameters and *P*300 peak habituation can be used for differential diagnosis of dementia and depressive disorders, primary and secondary headaches, and primary headaches in children and adolescents.

Changes in *P*300 are not nosologically specific; they are of syndrome nature and are mainly associated with impairments of selective attention and short-term memory.

REFERENCES

1. Luria, A.R., *Osnovy neiropsikhologii* (Fundamentals of Neuropsychology), Moscow, 1973.
2. Luria, A.R., *Vysshie korkovye funktsii cheloveka i ikh narusheniya pri lokal'nykh porazheniyakh mozga* (Human Higher Cortical Functions and Their Impairments Caused by Local Brain Damage), Moscow, 1969, p. 433.
3. Gnezditskii, V.V., *Vyzvannye potentsialy mozga v klinicheskoi praktike* (Evoked Brain Potentials in Clinical Practice), Taganrog, 1997.
4. Shagas, Ch., *Vyzvannye potentsialy mozga v norme i patologii* (Evoked Brain Potentials in the Norm and Pathology), Moscow, 1975.
5. Polich, J., Cognitive Brain Potentials, *Curr. Dir. Psychol. Sci.*, 1993, vol. 2, no. 6, p. 175.
6. Ivanitskii, A.M., Human Brain Reflexes: from Stimulus to Recognition and from Decision to Action, *Zh. Vyssh. Nervn. Deyat.*, 1990, vol. 40, no. 5, p. 835.
7. Ciganek, L., The EEG Response (Evoked Potential) to Light Stimulus in Man, *EEG Clin. Neurophysiol.*, 1961, vol. 13, p. 165.
8. Davis, H., Enhancement of Evoked Cortical Potentials in Humans Related to a Task Requiring a Decision, *Science*, 1964, vol. 145, p. 182.
9. Haider, M., Spong, P., and Lindsley, D.B., Attention, Vigilance, and Cortical Evoked Potentials in Humans, *Science*, 1964, vol. 145, p. 180.
10. Sutton, S., Braren, M., and Zubin, J., Evoked Potential Correlates of Stimulus Uncertainty, *Science*, 1965, vol. 150, p. 1187.
11. Kostandov, E.A. and Genkina, O.A., Hemispheric Asymmetry of the Evoked Electrical Activity of the Cerebral Cortex to Letter and Non-Verbal Stimuli, *Zh. Vyssh. Nervn. Deyat.*, 1976, vol. 26, no. 1, p. 21.
12. Kostandov, E.A. and Vazhnova, T.N., Reflection of the Decision Making Process in Evoked Cortical Electrical Activity in Man, *Zh. Vyssh. Nervn. Deyat.*, 1976, vol. 26, no. 6, p. 1123.
13. Picton, T.W. and Hillyard, S.A., Auditory Evoked Potentials in Humans, *EEG Clin. Neurophysiol.*, 1974, vol. 36, p. 191.
14. Rohbaugh, J., Donchin, E., and Eriksen, C., Decision Making and the *P*300 Component of the Cortical Evoked Response, *Percept. Psychophys.*, 1974, vol. 15, p. 368.
15. Smith, D.B., Donchin, E., Cohen, L., et al., Auditory Averaged Evoked Potentials in Man during Selective Binaural Listening, *EEG Clin. Neurophysiol.*, 1970, vol. 28, p. 146.
16. Sutton, S., Tueting, P., Zubin, J., et al., Information Delivery and the Sensory Evoked Potential, *Science*, 1967, vol. 155, p. 1436.
17. Jenness, D.J., Auditory Evoked-Response Differentiation with Discrimination Learning in Humans, *Comp. Physiol. Psychol.*, 1972, vol. 80, no. 1, p. 75.
18. Sutton, S., The Sensitivity of the Evoked Potential to Psychological Variables, *EEG Clin. Neurophysiol.*, 1970, vol. 31, p. 302.
19. Harter, M.R. and Salmon, L.E., Intra-Modality Selective Attention and Evoked Cortical Potentials to Randomly Presented Patterns, *EEG Clin. Neurophysiol.*, 1972, vol. 32, p. 605.
20. Ritter, W. and Vaughan, H.G., Averaged Evoked Responses in Vigilance and Discrimination: A Reassessment, *Science*, 1969, vol. 164, p. 326.
21. Fabiani, M., Karis, D., and Donchin, E., *P*300 and Memory, *EEG Clin. Neurophysiol.*, 1986, vol. 38, p. 63.
22. McCarty G. and Donchin, E., A Metric for Thought: A Comparison of *P*300 Latency and Reaction Time, *Science*, 1981, vol. 221, p. 77.
23. Friedman, D., Simson, R., Ritter, W., et al., The Late Positive Component (*P*300) and Information Processing in Sentences, *EEG Clin. Neurophysiol.*, 1975, vol. 38, no. 3, p. 255.
24. Roth, W.T., Auditory Evoked Responses to Unpredictable Stimuli, *Psychophysiology*, 1973, vol. 10, p. 125.
25. Roth, W.T. and Kopell, B.S., An Orienting Reaction in the Human Auditory Evoked Responses, *Percept. Mot. Skills*, 1973, vol. 36, no. 1, p. 219.
26. Rutman, E.M., *Vyzvannye potentsialy v psikhologii i psikhofiziologii* (Evoked Potentials in Psychology and Psychophysiology), Moscow, 1979.
27. Karlin, L. and Martz, M.J., Response Probability and Sensory-Evoked Potentials, in *Attention and Performance. IV*, New York: Acad. Press, 1973, p. 175.
28. Vasil'eva, V.M. and Farber, D.A., Study of the Functional Importance of Late Evoked Potential in Response to Sound, *Fiziol. Chel.*, 1977, vol. 3, no. 2, p. 270.
29. Kostandov, E.A., *Vospriyatie i emotsii* (Perception and Emotions), Moscow, 1977.
30. Polich, J., Attention, Probability, and Task Demands as Determinants of *P*300 Latency from Auditory Stimuli, *EEG Clin. Neurophysiol.*, 1986, vol. 63, p. 251.

31. Tachibana, H., Toda, K., Aragane, K., and Sugira, M., Chronometrical Analysis of Event-Related Potentials and Reaction Time in Patients with Multiple Lacunar Infarcts, *Cogn. Brain Res.*, 1993, vol. 1, p. 193.

32. Zenkov, L.P. and Ronkin, M.A., *Funktsional'naya diagnostika nervnykh boleznei* (Functional Diagnostics of Neural Diseases), Moscow, 2004.

33. Taghavy, A. and Kugler, F.A., Das Visuelle *P*300 (PFP300) im Physiologischen Alterungsprocess, *Z. EEG EMG*, 1988, vol. 19, p. 100.

34. Polich, J., Howard, L., and Starr, A., Effects of Age on the *P*300 Component of the Event-Related Potential from Auditory Stimuli: Peak Definition, Variation, and Measurement, *J. Gerontol.*, 1985, vol. 40, p. 721.

35. Hegerl, U., Klotz, S., and Ulrich, G., Spate Akustisch Evozierte Potentiale. Einfluss von Alter, Geschlecht und Unterschidichen Untersuchungsbedingungen, *Z. EEG EMG*, 1985, vol. 16, p. 171.

36. Verleger, R., Neukater, W., Kompf, D., et al., On the Reasons for the Delay of P3 Latency in Healthy Elderly Subjects, *EEF Clin. Neurophysiol.*, 1991, vol. 79, p. 488.

37. Pineds, J.A., Swick, D., and Foote, S.L., The Role of Noradrenergic and Cholinergic Systems in the Generation of *P*300-Like Potentials, *EPIC9: Int. Conf. Event-Related Potentials. Brain*, Noorwijk, 1989, p. 39.

38. Yingling, C.D. and Hosobuchi, Y., A Subcortical Correlate of *P*300 in Man, *EEG Clin. Neurophysiol.*, 1984, vol. 594, p. 72.

39. Looren de Jong, H., Kok, A., and Van Rooy J.C.G.M., Stimulus Probability and Motor Response in Young and Old Adults: An ERP Study, *Biol. Psychol.*, 1989, vol. 29, p. 125.

40. Polich, J., On the Correlation between *P*300 Amplitude and Latency, *Bull. Psychonom. Soc.*, 1992, vol. 30, p. 5.

41. Karlin, L., Martz, M.J., Brauth, S.E., and Mordkoff, A.M., Auditory Evoked Potentials, Motor Potentials Band Reaction Time, *EEG Clin. Neurophysiol.*, 1971, vol. 31, p. 129.

42. Gro B., Metz, A.M., and Ullspreger, P., Die *P*300-Komponente des Ereigniskorrelierten Himpotentials in einem Kurzzeitgedahtnisparadigma, *Z. Exp. Angew. Psychol.*, 1992, vol. 39, p. 56.

43. Sommer, W., Schweinberger, S.R., and Matt, J., Human Brain Potential Correlates of Face Encoding into Memory, *EEG Clin. Neurophysiol.*, 1991, vol. 79, no. 6, p. 457.

44. Zenkov, L.P., The Unconscious and Consciousness in Interhemispheric Interaction, *Bessoznatel'noe. Mnogoobrazie videniya* (The Unconscious. A variety of Vision), vol. 1, Novocherkassk, 1994, p. 201.

45. Goodin, D.S. and Martin, S., *P*300, Cognitive Capability, and Personality: A Correlational Study of University Undergraduates, *Pers. Ind. Diff.*, 1992, vol. 21, p. 533.

46. Polich, J. and Kok, A., Cognitive and Biological Determinants of *P*300: An Integrative Review, *Biol. Psychol.*, 1995, vol. 41, no. 2, p. 103.

47. Polich, J., Meta-Analysis of *P*300 Normative Aging Studies, *Psychophysiol.*, 1996, vol. 33, p. 1.

48. Revenok E.V. Cortical- and Subcortical-Type Cognitive Impairments in Cerebral Vascular Diseases (Neuropsychological and Electrophysiological Examinations), *Cand. Sci. (Med.) Dissertation*, Moscow, 1999.

49. Green, J., Woodard, J.L., Sirockman, B.E., et al., Event-Related Potential P3 Change in Mild Parkinson's Disease, *Mov. Disord.*, 1996, vol. 11, no. 1, p. 32.

50. Ivan, A.B. and Polich, J., *P*300 and Response Time from a Manual Stroop Task, *Clin. Neurophysiol.*, 1999, vol. 110, p. 367.

51. Brandeis, D. and Lehmann, D., Event-Related Potentials of the Brain and Cognitive Process: Approaches and Applications, *Neurophysiologia*, 1986, vol. 24, no. 1, p. 151.

52. Frodl–Bauch, T., Bottlender, R., and Hegerl, U., Neurochemical Substrates and Neuroanatomical Generators of the Event-Related *P*300, *Neuropsychobiology*, 1999, vol. 40, no. 2, p. 86.

53. Halgren, E., Squires, N.K., Wilson, C.L., et al., Endogenous Potentials Generated in the Human Hippocampal Formation and Amygdala by Infrequent Events, *Science*, 1980, vol. 210, p. 803.

54. Kropotov, J.D. and Ponomarev, V.A., Subcortical Neuronal Correlates of Component *P*300 in Man, *EEF Clin. Neurophysiol.*, 1991, vol. 78, p. 40.

55. Polich, J. and Squire, L.R., *P*300 from Amnesic Patients with Bilateral Hippocampal Lesion, *EEF Clin. Neurophysiol.*, 1993, vol. 86, no. 6, p. 408.

56. Rogers, R.L., Baumann, S.B., Papanicolaou, A.C., et al., Localization of P3 Sources Using Magnetoencephalography and Magnetic Resonance Imaging, *EEF Clin. Neurophysiol.*, 1991, vol. 79, p. 308.

57. Rudiger, S. and Bolsche, F., Neurophysiologische Methoden in Biologischen Psychiatrie, *Med. Aktuell.*, 1991, vol. 17, p. 68.

58. Gnezditskii, V.V. and Shamshinova, A.M., *Opyt primeneniya vyzvannykh potentsialov v klinicheskoi praktike* (Experience of Application of Evoked Potentials in Clinical Practice), Moscow, 2001.

59. Gnezditskii, V.V., *Obratnaya zadacha EEG i klinicheskaya elektroentsefavografiya* (The Inverse Task of EEG and Clinical Electroencephalography), Taganrog, 2000.

60. Monfort, V., Pouthas, V., and Ragot, R., Role of Frontal Cortex in Memory for Duration: An Event-Related Potential Study in Humans, *Neurosci. Lett.*, 2000, vol. 286, no. 2, p. 91.

61. Tarkka, I.M., Stokie, D.S., Basile, L.F., et al., Electric Source Localization of the Auditory *P*300 Agrees with Magnetic Source Localization, *EEG Clin. Neurophysiol.*, 1995, vol. 95, p. 538.

62. Goodin, D.S. and Squires, K.S., Long Latency Event-Related Components of the Auditory Evoked Potential in Dementia, *Brain*, 1978, vol. 101, p. 635.

63. Pfefferbaum, A., Ford, J.M., Wenegrat, B., et al., Electrophysiological Approach to the Study of Aging and Dementia. Alzheimer's Disease: A Report of Progress, *Aging*, New York: Raven Press, 1982, p. 85.

64. Goodin, D.S. and Aminoff, M.J., Electrophysiological Differences between Subtypes of Dementia, *Brain*, 1986, vol. 109, p. 1103.

65. Polich, J., Ehlers, C.L., Otis, S., et al., *P*300 Latency Reflects the Degree of Cognitive Decline in Dementing Ilness, *EEG Clin. Neurophysiol.*, 1986, vol. 63, p. 138.

66. Picton, T.W., The *P*300 Wave of Human Event-Related Potential, *Clin. Neurophysiol.*, 1992, vol. 9, no. 4, p. 456.

67. Polich, J., Alexander, J.E., and Bauer, L.O., *P*300 Topography of Amplitude/Latency Correlations, *Brain Topogr.*, 1997, vol. 9, no. 4, p. 275.

68. Golob, E.J., Auditory Event-Related Potentials during Target Detection are Abnormal in Mild Cognitive Impairment, *Clin. Neurophysiol.*, 2002, vol. 113, no. 1, p. 151.

69. Molares–Rodriguez, M., Fernande-Lastra, A., and Penzol–Dia, J., Neurophysiological Study and use of *P*300 Evoked Potentials for Investigation in the Diagnosis and Follow-up of Patients with Alzheimer's Disease, *Rev. Neurologia*, 2001, vol. 32, no. 6, p. 525.

70. Syndulko, K., Hansch, E.C., Cohen, S.N., et al., Long-Latency Event-Related Potentials in Normal Aging and Dementia, *Adv. Neurol.*, 1982, vol. 32, p. 279.

71. Marsh, H.T., Schubarth, G., Brown, W.S., et al., PET and *P*300 Relationships in Early Alzheimer's Disease, *Neurobiol. Aging*, 1990, vol. 11, no. 4, p. 471.

72. Blackburn, I.M., Roxborough, H.M., Muir, W.J., et al., Perceptual and Physiological Dysfunction in Depression, *Psychol. Med.*, 1990, vol. 20, p. 95.

73. Polich, J., Ladish, C., and Bloom, F.E., *P*300 Assessment of Early Alzheimer's Disease, *EEG Clin. Neurophysiol.*, 1990, vol. 77, p. 179.

74. Kigler, C.F., Vlajic, P., Funk, P., et al., The Event-Related *P*300 Potential Approach to Cognitive Functions of Nondemented Patients with Cerebral and Peripheral Arteriosclerosis, *J. Am. Geriatr. Soc.*, 1995, vol. 43, p. 1228.

75. Ozden, S., Evoked Potentials in Parkinson's Disease—Correlation with Clinical Involvement, *Clin. Neurol. Neurosurg.*, 2001, vol. 103, no. 3, p. 147.

76. Prabhakar, S., *P*300 in Newly Diagnosed Non-Dementing Parkinson's Disease: Effect of Dopaminergic drugs, *Neurol. India*, 2000, vol. 8, no. 3, p. 239.

77. Stanzione, P., Semprini, R., Tagilati, M., et al., Age and Stage Dependency of *P*300 Latency Alterations in Non-Dementing Parkinson's Disease Patients without Therapy, *EEG Clin. Neurophysiol.*, 1998, vol. 108, p. 80.

78. Elwan, O.H., Baradah, O.H., Madkour, O., et al., Parkinson's Disease, Cognition and Aging. Clinical, Neuropsychological, Electrophysiological and Cranial Computerized Tomographic Assessment, *J. Neurosci.*, 1996, vol. 13, no. 1–2, p. 64.

79. Lagopoulos, J., Clouston, P., Barhamali, H., et al., Late Components of the Event-Related Potentials and Their Topography in Parkinson's Disease, *Mov. Disord.*, 1998, vol. 13, no. 2, p. 262.

80. O'Donnell, B.F., Squires, N.K., Martz, M.J., et al., Evoked Potential Changes and Neuropsychological Performance in Parkinson's Disease, *Biol. Psychol.*, 1987, vol. 2, p. 23.

81. Newton, M.R., Callanan, M.M., and Towell, A.D., Cognitive Event-Related Potentials in Multiple Sclerosis, *Brain*, 1989, vol. 112, p. 1637.

82. Churkina, I.G., Cognitive Potential of *P*300 in Patients with Disseminated Sclerosis, *Annaly FPNPK. Sechenov Mosc. Med. Acad.*, 2001, vol. 3, p. 36.

83. Hammond, E.J., Rangel, R.J., and Wilder, B.J., Cognitive Evoked Potentials in Epileptic Patients: Increased Variability, *EEG Clin. Neurophysiol.*, 1989, vol. 72, p. 16.

84. Ruzicka, E., Tesar, V., Jelinkova, E., et al., Event-Related Potentials in Evaluation of Metabolic Encephalopathies, *Schweiz. Arch. Neurol. Psychiatr.*, 1993, vol. 14, p. 378.

85. Kugler, C.F.A., Fetter, J., Taghavy, A., et al., Dynamics of Cognitive Brain Dysfunction in Patients with Cirrotic Liver Disease: An Event-Related *P*300 Potential Perspective, *EEG Clin. Neurophysiol.*, 1994, vol. 91, p. 33.

86. Korepina, O.S., Spatiotemporal Analysis of Sensory and Cognitive Components of Auditory and Visual Evoked Potential in the Normal and Damaged Brain, *Extended Abstract of Cand. Sci. Dissertation*, Moscow, 1999.

87. Polich, J., *P*300 from a Passive Auditory Paradigm, *EEG Clin. Neurophysiol.*, 1989, vol. 74, p. 312.

88. Schreiber, H.G., Stolz-Bon, G., Rothmeier, J., et al., Endogenous Event-Related Brain Potentials and Psychometric Performance in Children at Risk for Schizophrenia, *Biol. Psychiat.*, 1991, vol. 30, p. 177.

89. Roth, W.T., Pfefferbaum, A., Horvath, T.B., et al., P3 Reduction in Auditory Evoked Potentials of Schizophrenics, *EEG Clin. Neurophysiol.*, 1980, vol. 49, p. 497.

90. Munti, T.F. and Kunkel, H., Ereigniskorrelierte Potentiale in der Psychiatrie–Methodische Grundlagen, *Psychiatr. Neurol. Med. Psychol.*, 1990, vol. 42, p. 69.

91. McCarley, R.W., Faux, S.F., Shenton, M.E., et al., *P*300 Asymmetries in Schizophrenia: Robustness of Topography under Linked-Ears or Nose References and Application of Clinical Correlates, *EPIC9: Int. Conf. Event-Related Potentials. Brain*, Noordwijk, 1989, p. 4.

92. Courchesne, E., Kilman, B.A., Galambos, R., et al., Autism: Processing of Novel Suditory Information Assessed by Event-Related Brain Potentials, *EEG Clin. Neurophysiol.*, 1984, vol. 59, p. 238.

93. Schreiber, H.G., Stolz–Born, G., Born, J., et al., Patterns of Cognitive Evoked Brain Potentials in High-Risk Children for Schizophrenia, *EPIC9: Int. Conf. Event-Related Potentials. Brain*, Noordwijk, 1989, p. 99.

94. Holzman, Ph.S., Recent Studies of Psychophysiology in Schizophrenia, *Schizophr. Bull.*, 1987, vol. 13, no. 1, p. 49.

95. Ford, J.M., White, P., Lim, K.O., et al., Schizophrenics Have Fewer and Smaller *P*300s: A Single-Trial Analysis, *Biol. Psychiatry*, 1994, vol. 35, no. 2, p. 96.

96. Isreal, J.B., Chesney, G.L., Wickens, C.D., et al., *P*300 and Tracking Difficulty: Evidence for Multiple Resources in Dual-Task Performance, *Psychophysiology*, 1980, vol. 17, no. 3, p. 259.

97. Omura, F., Ogura, C., Kishimoto, A., et al., The Abnormalities of Event-Related Potentials in Depression, *EPIC9: Int. Conf. Event-Related Potentials. Brain*, Noordwijk, 1989, p. 86.

98. Saitoh, T., Event-Related Potentials (ERPs) in Depressive Patients. Clinical Application of the *P*300 Component, *J. Iwate Med. Ass.*, 1989, vol. 4, p. 315.
99. Iwanami, A., Isono, H., Okajima, Y., and Kamijima, K., Auditory Event-Related Potentials in Panic Disorder, *Eur. Arch. Psychiat. Clin. Neurosci.*, 1997, vol. 27, no. 2, p. 107.
100. Pauli, P., Dengler, W., Wiedemann, G., et al., Behavioral and Neurophysiological Evidence for Altered Processing of Anxiety-Related Words in Panic Disorder, *J. Abnorm. Psychol.*, 1997, vol. 106, no. 2, p. 213.
101. Dengler, W., Wiedemann, G., and Pauli, P., Associations between Cortical Slow Potentials and Clinical Rating Scales in Panic Disorders: A 1.5-Year Follow-up Study, *Eur. Psychiatry*, 1999, vol. 1, no. 7, p. 399.
102. Voznesenskaya, T.G. and Sinyachkin, M.S., Comparative Psychophysiological Analysis of Permanent and Paroxysmal Anxiety Disorders, *Zh. Nevrol. Psikhiatr.,* 1997, vol. 11, p. 8.
103. Beech, H.R., Ciesielski, K.T., and Gordon, P.K., Further Observations of Evoked Potentials in Obsessional Patients, *Brit. J. Psychiatry*, 1983, vol. 142, p. 605.
104. Morault, P.M., Bourgeois, M., Laville, J., et al., Psychophysiological and Clinical Value of Event-Related Potentials in Obsessive-Compulsive Disorder, *Biol. Psychiatry,* 1997, vol. 2, no. 1, p. 46.
105. Towey, J.P., Tenke, C.E., and Bruder, G.E., Brain Event-Related Potential Correlates of Overfocused Attention in Obsessive-Compulsive Disorder, *Psychophysiology*, 1994, vol. 31, no. 6, p. 535.
106. Russo, F., Zaccara, G., Ragazzoni, A., et al., Abnormal Visual Event-Related Potentials in Obsessive-Compulsive Disorder without Panic Disorder or Depression Comorbidity, *J. Psychiatr. Res.*, 2000, vol. 3, p. 75.
107. Purcell, R., Maruff, P., Kyrios, M., et al., Cognitive Deficits in Obsessive-Compulsive Disorder on Tests of Frontal-Striatal Function, *Biol. Psychiatry*, 1998, vol. 43, p. 348.
108. Metzger, L.J., Orr, S.P., Lasko, N.B., et al., Auditory Event-Related Potential to Tone Stimuli in Combat-Related Posttraumatic Stress Disorder, *Biol. Psychiatry*, 1997, vol. 42, no. 11, p. 1006.
109. Demirci, S. and Savas, S., The Auditory Event-Related Potentials in Episodic and Chronic Pain Sufferers, *Eur. J. Pain*, 2002, vol. 6, no. 3, p. 239.
110. Mazzotta, G., Alberti, A., Santucci, A., et al., The Event-Related Potential *P*300 during Headache-Free Period and Spontaneous Attack in Adult Headache Sufferers, *Headache*, 1995, vol. 35, no. 4, p. 210.
111. Evers, S., Bauer, B., Suhr, B., et al., Cognitive Processing in Primary Headache: A Study on Event-Related Potentials, *Neurology*, 1997, vol. 48, no. 1, p. 108.
112. Evers, S., Bauer, B., Grotemeyer, K.H., et al., Event-Related Potentials (*P*300) in Primary Headache in Children and Adolescence, *J. Child. Neurol.*, 1998, vol. 13, no. 7, p. 322.
113. Hayashi, R., Correlation between Coefficient of Variation of Choice Reaction Time and Components of Event-Related Potentials (*P*300): Effect of Benzodiazepine, *J. Neurol. Sci.*, 2000, vol. 178, no. 1, p. 52.