Neurophysiological Measures of Treatment Efficacy in Late-Onset Depression

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Neurophysiological correlates of treatment efficacy in late-onset depression were identified by analyzing EEG spectral parameters, the peak latencies of the “late” components of cognitive auditory evoked potentials, and sensorimotor reaction times during antidepressant treatment in two groups of older patients (53–72 years) with long-lasting psychogenic depressive reactions (ICD-10 F43.21) and endogenous depression (ICD-10 F33.1 and F31.3). The initial severity of depression was associated with EEG signs of decreases in the functional status of the anterior parts of the left hemisphere and increased activation of the right hemisphere (particularly the temporal areas). Improvements in patients’ mental status in response to antidepressant medication were accompanied by decreases in the peak latencies of the “late” components (P2, N2, and P3) of cognitive auditory evoked potentials and acceleration of sensorimotor reactions, and were linked with improvements in EEG measures of the functional status of the posterior areas of the cerebral cortex and increases in inhibitory processes in the right hemisphere (particularly its frontal-central-temporal areas). These data are consistent with views of the systems nature of impairments to brain activity in depression and the predominant involvement of the left hemisphere in regulating positive emotions and of the right hemisphere in regulating negative emotions, including the pathogenesis of depression.

Keywords: depression, older age, antidepressant therapy, electroencephalography, cognitive evoked potentials, sensorimotor reaction time, interhemisphere relationships.

Introduction

The problem of treatment efficacy in depression is one of the leading questions in contemporary clinical and biological psychiatry. This task is even more important in the case of late-onset depression, as the incidence of incomplete remission at this age period increases by a factor of 2–3 to reach 54% at the involutional age and 72% in patients aged over 70 years [15, 22, 29], partial recovery from depressive episodes laying the grounds for chronicization of illness. Thus, there is potential for studies not only of clinical, but also preclinical biological measures of treatment efficacy based on assessments of the dynamics of therapeutic responses to antidepressant treatment.

One appropriate method of studying the cerebral mechanisms of the pathogenesis and treatment of depressive disorders involves using neuropsychological measures [2, 4, 7, 12–14, 21]. The functional state of the brain in active waking was assessed by analysis of cognitive evoked potentials and measurement of the latent periods of sensorimotor reactions.

Analysis of the parameters of cognitive evoked potentials is an appropriate and highly informative method for objective evaluation of the dynamics of the functional state of the brain during treatment [2, 7, 16]. This approach is included in the list of instrumented neuropsychological methods recommended for clinical use by the International and American Association of Clinical Neurophysiologists [16]. In contrast to standard EEG recordings, evoked potentials methods assess brain function not only at rest, but also in the active state using a simplified model of activity. In the situations of selective attention and a two-alternative selec-
tion reaction (the oddball paradigm), the long-latency positive component of cognitive evoked potentials (the P3 wave, or P300) is seen predominantly in averaged responses to rarely presented target stimuli. Patients with various mental disorders (schizophrenia, different types of dementia, cerebrovascular disorders, sequelae of craniocerebral trauma, etc.), show decreases in the functional state of the brain, particularly affecting the neuronal mechanisms of higher mental functions such as attention, memory, and decision-taking, which are associated with increases in the peak latent period of the P300 wave [2, 7, 8, 17, 24, 28].

The dynamic characteristics of motor disorders and the cerebral mechanisms of decision-taking, as well as the state of attention, can be evaluated objectively using a relatively simple, noninvasive, instrumented psychophysiological method – analysis of the latent periods of sensorimotor reactions [7, 8].

Because of the high level of variability of EEG patterns in patients with depression [6, 10, 12, 13, 21], the clearest assessments of the parameters of the cerebral electrical activity typically associated with this condition are obtained by analysis of changes in the EEG and cognitive evoked potentials during adequate treatment.

The aim of the present work was to identify neurophysiological correlates of treatment efficacy in various types of depressive disorder in older patients.

Materials and Methods

Studies were performed in compliance with generally accepted current biomedical ethical norms.

Two groups of older patients were studied – those with prolonged (more than six months) psychogenically provoked depressive reactions (severe bereavement reactions to the death of a close relative, ICD-10, F43.21 [1]), endogenous depressive states within the framework of recurrent depression (ICD-10 F33.1), or the depressive phase of bipolar disorder (ICD-10 F31.3). There were no significant differences between groups in terms of age, gender, and initial severity of depression.

Clinical assessment of patients included the HAM-D-21, HAM-D-17, CGI-S, and CGI-I scales.

The group of patients with depressive reactions (group 1) included 25 patients (19 women, six men) aged 53–72 (mean 66.0 ± 5.6) years. Clinical assessment and investigations of patients were performed by V. V. Kornilov, Department for Studies of Problems in Geriatric Psychiatry, Scientific Center for Mental Health, Russian Academy of Medical Sciences. These included single-channel recording of baseline EEG, averaging of auditory cognitive evoked potentials in the situation of two-alternative attention (the oddball paradigm), and measurement of the latent periods (LP) of a simple sensorimotor reaction and a sensorimotor two-alternative selection reaction to auditory stimuli.

Baseline recordings of the EEG (2–3 min) and auditory cognitive evoked potentials were made using a programmable Neiro-KM system (Statokin, Russia) and the BrainSys program (by A. A. Mitrofanov) [11]. The patient sat in a comfortable chair with the eyes closed. Brain bioelectrical activity was recorded using the international 10–20 systems in leads F7, F3, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2 relative to ipsilateral reference electrode A1 and A2, with a bandpass of 35 Hz, a time constant of 0.3 sec, and a sampling (digitization) frequency of 500 Hz.

Sound stimulation parameters for averaged cognitive evoked potentials complied with international recommendations [2, 16, 28]. Target and nontarget stimuli (a total of 140–150 stimuli) were presented binaurally in random order. The mean interstimulus interval was 2 sec and, to avoid patients acquiring a conditioned motor response to time, was varied over the range ±15% (from 1700 to 2300 msec).

Target auditory stimuli consisted of tones (duration 50 msec, frequency 2000 Hz, loudness 70 dB) and were presented with a probability of 30%. Nontarget stimuli (tones of duration 50 msec, frequency 1000 Hz, and loudness 70 dB) were presented with a probability of 70%. Patients were instructed to respond as quickly as possible by pressing a computer mouse key with the right index finger in response to target stimuli and not to respond to non-target stimuli.

The latent periods (LP) of two-alternative selection sensorimotor reactions (pressing a mouse key in response to presentation of the target stimulus) were measured automatically during this procedure. The LP of simple sensorimotor reactions was measured after repetition of the sound stimulation session, though new instructions to the patients were given to press the mouse key as quickly as possible in response to both sound stimuli (with frequencies of 1000 and 2000 Hz).