Correlation between the Parameters of Contingent Negative Variation and Characteristics of Variational Pulsometry in Parkinsonian Patients

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In patients suffering from Parkinson’s disease (PD), we analyzed correlations between the parameters of contingent negative variation (CNV) and data of variational pulsometry (according to the measurements of R-R ECG intervals). Studies were carried out on 35 patients (group PD), 49 to 74 years old, with the stage of disease of 1.5 to 3.0 according to the Hoehn-Yahr international classification.

In the course of CNV recording (i.e., in the state of a certain functional loading), we observed significant negative correlations between the integral magnitude (area) of this potential and indices of variational pulsometry (RMSSD, SDNN, C. var, and HF) that characterize the intensity of parasympathetic (respiratory) influences on the cardiovascular system. In the control group, such correlations were absent. We found significant correlations between the autonomic balance, CNV magnitude, and stage of PD reflecting the level of generalization of the pathological process. In the subgroup of patients with the PD stage 1.5 to 2.0, significant changes in the mean values of indices of parasympathetic influences during recording of the CNV were not observed, while in another subgroup (the PD stage 2.5 to 3.0), these values increased significantly ($P < 0.05$ and $P < 0.01$). If the estimates of the PD stage were low, the CNV area demonstrated greater values ($P < 0.01$). The disturbance of coordination of muscle-to-muscle interactions in the PD group is, probably, an important factor responsible for parasympathetic dysregulation and suppression of the CNV generation. We found positive correlation between the intensity of parasympathetic influences in the course of CNV recording and the level of postural disorders ($r = 0.37$, $P < 0.05$). On the contrary, the CNV magnitude demonstrated a negative correlation with the intensity of these disorders ($r = -0.36$, $P < 0.05$), as well as with the level of postural instability ($r = -0.55$, $P < 0.001$). We hypothesize that alterations of the autonomic balance and the activity of those cerebral structures, which are responsible for the motor readiness, result, to a significant extent, from weakening of the activity of the noradrenergic system due to degenerative processes developing in cells of the locus coeruleus. The impairment of the latter structure, together with degeneration of neurons of the substantia nigra and a decrease in the level of nigro-striatal dopamine, underlies the pathomorphological pattern of PD.

Keywords: motor EEG potentials, contingent negative variation, variational pulsometry, parasympathetic and sympathetic control, Parkinson’s disease.

INTRODUCTION

When studying central mechanisms responsible for organization of motor functions, recording of endogenous movement-related (motor) EEG potentials, including the contingent negative variation (CNV), is widely used in modern neurophysiology. The CNV has also been sometimes designated as the “expectation wave,” E wave, or conditioned negative inclination (in English-language publications, the standard term “contingent negative variation, CNV” is used). The CNV is a slow negative inclination preceding the initiation of a signal-related movement; it is to a certain extent similar to another movement-related EEG phenomenon, the readiness potential [1]. Both cortical and subcortical structures are involved in generation of motor EEG potentials [2, 3]. From this aspect, the cerebellar efferent system and basal ganglia play crucial roles [4, 5]. As was demonstrated, EEG motor potentials decrease in diseases that are accompanied by motor disorders (e.g., parkinsonism and muscular dystonias of different types) [5-7].

It was also found that there is a dependence between
the parameters of endogenous motor potentials and the state of both the mechanisms of direct motor control and the mechanisms responsible for higher integral nerve processes, levels of attention and motivation, and voluntary efforts [8-10]. Information on the effects of the autonomic nervous system on motor EEG potentials remains rather limited. There are only single reports where the existence of correlations between the parameters of CNV and the level of autonomic activity (which was estimated using a cardiointervalometric approach) was mentioned [11].

The clinical pattern of Parkinson’s disease (PD) is characterized by a great polymorphism. In addition to the crucial motor disorders (bradykinesia, rigidity, and tremor), significant psychoemotional, cognitive, and autonomic dysfunctions are, as a rule, manifested in the above disease. Among autonomic symptoms, disorders of the cardiovascular control (a combined sympathetic/parasympathetic insufficiency with a relative sympathicotonia) are frequently observed in PD [12-15]. Thus, questions of whether PD-related cardiovascular dysfunction is capable of influencing the characteristics of such a motor potential as the CNV, and if so, what is the significance of such changes, are of special interest.

In this study, we analyzed correlations between the parameters of CNV and data of variational pulsometry in patients suffering from PD.

METHODS

We examined 35 patients with clinically diagnosed PD (group PD, 13 men and 22 women) at the age of 49 to 74 years (mean age 61.1 ± 1.2 years). The estimate of the stage of disease varied from 1.5 to 3.0 (according to the international classification [16]), and the mean duration of the disease was 4.5 ± 0.5 years. To estimate the intensity of motor symptoms, we used a unified international scale (Unified Parkinson’s Disease Rating Scale, UPDRS). Estimates corresponding to point I (aphonia and mood variations), point II (decrease in day activity and breach of hygienic habits), and point III (clear disorders of motor functions, including bradykinesia, rigidity, and tremor) were calculated according to a four-point gradation of each symptom. In patients examined in our study, total estimates by the UPDRS scale varied from 21 to 87, and the mean value was 51.0 ± 3.1 points.

The CNV was recorded unipolarly using a central midline electrode (Cz). A reference electrode was positioned on the earlobe, and a ground electrode was on the left forearm. In the course of examination, the subject was in a relaxed calm state with his/her eyes closed. The EEG signals were amplified with a bandpass of 0.08 to 15 Hz and were saved to the computer hard disk. To record the CNV, we used a testing paradigm with two short acoustic stimuli (clicks of different intensities) divided by a 1-sec-long interval, warning and imperative signals (50 and 80 dB above the hearing threshold for humans). Upon receipt of the imperative signal, the subject should press a button. The sampling rate of EEG signals was 200 sec⁻¹, and the duration of the analyzed epoch was 3.1 sec. Within the first 400 msec, initial (background) EEG was recorded; the mean level of such preceding EEG activity was taken as the zero line. The interval between realizations was equal to 6 sec. For the analysis, we visually selected EEG artifact-free segments. After averaging of 30 samplings, the integral magnitude of the CNV (area between the zero line and the trace of negative deviation) was calculated by the formula $S = \sum Ai \cdot \Delta t$ (mV-msec), where $Ai$ are the values of current amplitudes of negativity with respect to the zero line, and $\Delta t$ is the time interval of digitization (5 msec). The software used allowed us to measure the latency of a simple sensorimotor reaction (mean value of the latency of pressing the button with respect to the imperative signal). Reactions with latencies of 100 msec or less were considered erroneous and ignored.

To compare the characteristics of CNV, we also recorded this potential in the control group in 18 reasonably healthy persons (nine men and nine women, 48 to 68 years old, mean age 58.4 ± 1.6 years).

The state of cardiovascular control in patients with PD was qualified by the data of variational pulsometry obtained using specialized software [17]. The electrocardiogram (ECG) was recorded for 5 min at a standard lead II; using these data, the durations of R-R intervals and their variability were measured. Based on statistical and spectral characteristics of the cardiac rhythm, we determined the tones of sympathetic and parasympathetic divisions of the autonomic nervous system. For the analysis, we used standard indices of pulsometry [13, 14, 18, 19]. These were parameters reflecting the relative intensity of parasympathetic influences (RMSSD, SDNN, C. var., pNN 50, and HF), on the one hand, and those characterizing the intensity of sympathetic influences (index of tension in the regulatory systems, IT, and index of the autonomic balance, IAB, by Baevskii), as well as AMo and LF, on the other hand (see Footnotes to Table 2).