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Mechanisms of Cervico-Vestibular-Oculomotor Disorders at the Early Stages of Parkinson's Disease

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We studied the interaction of the oculomotor, cervical, and vestibular systems using a specially developed technique. A series of two tests were performed on 26 healthy subjects and 42 patients with stages I-II Parkinson's disease receiving and not receiving treatment. In coordinated tests, all amplitude-time characteristics of patients significantly differed from those in healthy subjects. Possible mechanisms of cervico-vestibular-oculomotor disorders are discussed.

Key Words: *coordinated movements of the eyes and head; oculomotor system; vestibular system; regulation of head movements; Parkinson's disease*

For elucidation of the mechanisms of cervico-vestibular-oculomotor disorders (CVOD), it is necessary to investigate the diseases following the known local damage to individual brain structures. These diseases include idiopathic Parkinson's disease (PD). The initial lesion of dopaminergic neurons of the compact part of substantia nigra, which is indirectly involved in the functioning of the cervical, vestibular, and oculomotor systems, allows using the disease as an adequate natural "biological model".

The clinical picture of CVOD at early manifestations of PD (Hoehn and Yahr stages I-II) is not detected; it manifests itself at stage III in the form of postural disorders, balance disturbances, vertigo, *etc*. It is natural to suggest that these violations develop not immediately, but in the course of the disease. The dynamics of these disorders is almost unknown.

Here we studied the mechanisms of coordinated cervico-vestibular-oculomotor relationships in patients in early PD stages (with or without drug therapy) and healthy individuals of the appropriate age (the age norm).

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MATERIALS AND METHODS

The study included 68 subjects. Three groups were formed: healthy individuals (n=26, 11 males and 15 females at the age of 43-67 years, mean age 57 years); patients with stage I-II PD receiving standard therapy (n=23, 13 men and 10 women at the age of 45-68 years, mean age 56 years); patients with stage I-II PD not receiving treatment (n=19, 11 males and 8 females, at the age of 42-58 years, mean age 52 years). All subjects previously passed complex clinical diagnostic tests at the Research Center of Neurology. The diagnosis was verified according to published criteria [3]. Patients with atypical clinical course or doubtful diagnosis were not included in the trial.

Two tests were performed using a hardware-software complex for human locomotion testing (B. Kh. Baziyan, patent No. 2146494) created by the

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method described previously [1]. The examinee was asked to keep his eyes on a stationary target during smooth comfortable horizontal head movements (from shoulder to shoulder) under conditions of light adaptation (test 1) or to keep his eyes on a target moving synchronously with head movements (test 2). In each test, the number of attempts ranged from 20 to 25. The data were processed statistically by nonparametric Mann–Whitney using Statistica 6.0 software.

RESULTS

The main recorded and analyzed parameters were: amplitude and frequency of head movement and coefficient of temporal asymmetry of head trajectory (C_{TA}), which was conventionally determined as the ratio of the time of the head turning to the right to the time of turning to the left; mismatch between the left eye (MLE)/right eye (MRE) and the head (Table 1).

In patients at the early stages of PD, gaze fixation on a stationary target was disturbed (Table 1), while the therapy improved the corresponding parameters. C_{TA} in healthy individuals and patients with PD is 0.94-1.26 and is not an informative indicator for assessing the differences between the normal and early PD. At the same time, movements of the left and right eyes are not synchronous with head movements, which results in loss of gaze fixation. The differences between the mismatch of left and right eyes in groups "with therapy" and "no treatment" group and "normal" are significant ($p<0.05$). Consider typical results of the test. The parameters of movements are different in different form of the disease. Thus, the frequency and amplitude of movement in patients with akinetic form in "no treatment" group (Fig. 1, *b*) considerably differed from normal (Fig. 1, *a*) and rigid-tremulous form (Fig. 1, *c*).

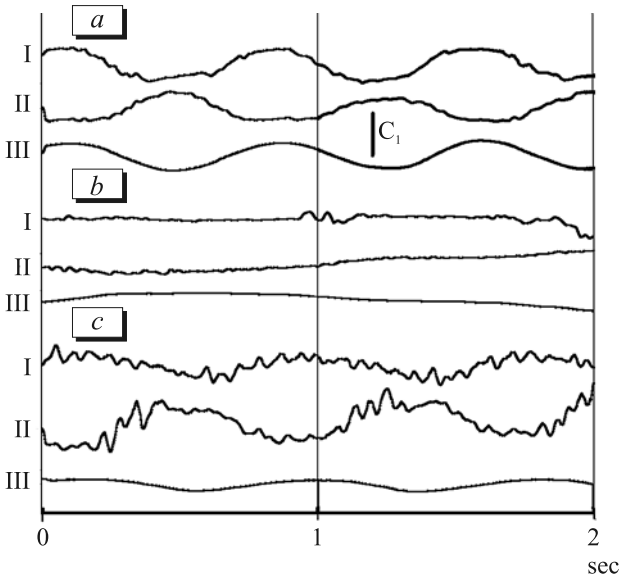

Fig. 1. Test of gaze-holding during fixation of a stationary target during horizontal movements of the head from shoulder to shoulder. Here and in Fig. 2: normal (*a*), akinetic (*b*) and rigid-trembling (*c*) forms of PD (stages I-II). Trajectories: I: left eye; II: right eye; III: head movement. C_1: calibration of head and eye movements (100°).

TABLE 1. Indicators of Head and Eye Movement in the Test of Gaze-Holding During Fixation of a Stationary Target (Me, 25%; 75%)

Group	HMA, degrees	HMF, Hz	C_{TA}	MLE, msec	MRE, msec
Normal	77.7 (75; 83,5)	1.35 (1.21; 1.49)	0.98 (0.94; 1.05)	16 (11; 24)	14.5 (9; 20)
No treatment	61 (58; 63.5)	0.83 (0.78; 0.95)	1.1 (0.95; 1.2)	99 (80; 113)	120 (99; 131)
With therapy	69 (64.5; 71)	0.99 (0.93; 1.15)	1.08 (0.94; 1.26)	64 (50; 78)	72 (58; 87)

Note. HMA, head movement amplitude; HMF, head movement frequency; MLE, mismatch between the left eye and the head; MRE, mismatch between the right eye and the head.

TABLE 2. Indicators of Head and Eye Movement in the Test of Gaze Fixation and Tracing the Target Moving Synchronously with Head Movements (Me, 25%; 75%)

Group	HMA, degrees	HMF, Hz	C_{TA}	DLE, degrees	DRE, degrees
Norm	100.9 (88; 108.5)	1.43 (1.25; 1.61)	0.98 (0.95;1.05)	9 (7; 11)	7.5 (6.6; 9)
No treatment	80.1 (69; 91.3)	0.87 (0.8; 0.95)	1.1 (0.95; 1.2)	37 (33; 41)	42 (38; 45)
With therapy	81.4 (70.5; 94.8)	0.99 (0.94; 1.14)	1.02 (0.99; 1.09)	25.4 (21; 31)	24 (19; 28)

Note. DLE, deviation of the left eye; DRE, deviation of the right eye.

In test 2, we analyzed head movement amplitude, head movement frequency, C_{TA}, and the deviation of the left and right eyes from straight gaze fixation on the target (Table 2).

In PD patients with and without treatment, head movement amplitude is reduced by 20% even at the early stages of the disease (Table 2). The amplitude and frequency of head movements differ between PD patients at I-II stages and depend on the form of the disease (Fig. 2). The therapy improves the corresponding parameters. CTA in the normal and in patients with PD lies within 0.95-1.2 and the differences are insignificant. In contrast to normal minor natural drift, electrooculogram recorded in patients was characterized by the presence of high-frequency bursts exceeding by their frequency the first phase of the tremor in PD and were close to physiological tremor. Temporary deviations of eye movements from the head were observed. Eye movements were faster or slower than head movements (Fig. 2, *b, c*).

Thus, we have revealed the disorders associated with gaze fixation and tracing the target at the early stages of PD. This process involves the cervical, vestibular, and visual-motor systems. Enhancement of these CVOD with the progression PD (II-III stage) is known to lead to postural disorders, balance disturbances, vertigo, *etc*.

In contrast to the known disturbances of the vestibular-ocular reflex in PD described previously [4], our work is related to evaluation of voluntary targeted and coordinated movements of the eyes and head, therefore the role of the vestibular-ocular reflex is minimum under these conditions.

At the early stages of PD, there is mainly one zone of organic brain damage, namely the deficiency of dopamine cells in the compact part of the substantia nigra. Other structures that control and perform movements remain almost intact. It is therefore logical to assume that CVOD are most likely caused by indirect influence of the nigro-striato-nigral relationships on colliculo-reticular and reticulo-colliculo-spinal pathways.

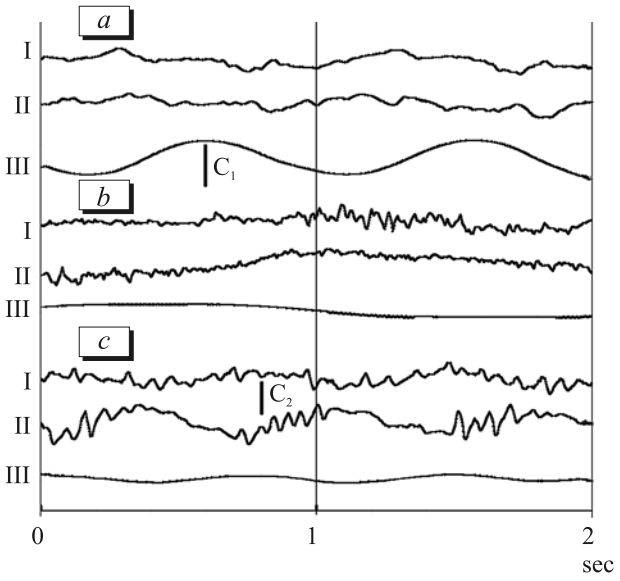

Fig. 2. Test of gaze fixation on a stationary target during horizontal movements of the head from shoulder to shoulder. Trajectories: I: left eye; II: right eye; III: head movement. C_1, calibration of head movements (100°); C_2, calibration of eye movements (25°).

Thus, monitoring of cervico-vestibular-oculomotor relationships allows us to estimate CVOD at the early stages of PD and their dynamics as the disease progresses. When examining close relatives of PD patients, CVOD can be used as a marker, along with others [2], for identification of risk groups and preclinical diagnosis of PD.

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