EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Disturbances in Cervico-Vestibulo-Oculomotor Interaction in Patients with Late Stages of Parkinson Disease

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 152, No. 10, pp. 466-469, October, 2011
Original article submitted March 29, 2010

Cervico-vestibulo-oculomotor interactions in patients with Parkinson disease stages III-IV and healthy subjects were studied in horizontal head movement and gaze fixation on immobile and mobile targets. Significant changes in the amplitude, head movement frequency and asymmetry, eye movement amplitude, and phase mismatch between head and eye movements were revealed in patients in comparison to the normal.

Key Words: *cervical vestibular oculomotor interaction, coordinated eye and head movements; Parkinson disease; gaze fixation and retention*

Parkinson disease (PD) is a chronic disease associated with progressive degeneration of dopaminergic neurons in the substantia nigra leading to dopamine deficiency and increase in functional activity of cholinergic systems. This leads to basal ganglia dysfunction and development of typical motor disturbances: hypokinesis, stiffness, and resting tremor [3] and postural instability, which becomes apparent only at stage III. The main function of postural system is the maintenance of stable vertical posture during various hand, leg, and trunk movements. Afferent part of the postural system is provided by information exchange between the muscular, articular, vestibular, and visual systems. Afferent nerve fibers from the labyrinth, cervical proprioceptors, and proprioceptors of oculomotor muscles are anatomically interconnected, which provides the basis of cervico-vestibulo-ocular reflexes. Biological role of reflexes resides in assurance of stable image on the retina during trunk and head movements, what allows sufficiently clear vision of the environment even during walking and running. Disturbances in the interactions between muscular, visual and vestibular systems developing in PD substantially reduce adaptive capacities, whereas the mechanism of development and dynamics of cervico-vestibulo-oculomotor dissociations in PD require more detailed investigation.

Here we studied parameters of cervico-vestibulo-oculomotor dissociation in patients with stages III-IV PD.

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MATERIALS AND METHODS

Fifty subject participated in the study: 26 healthy subjects (11 males and 15 females; 43-67 years, mean age 57 years) and 24 patients (15 males and 9 females, 52-70 years, mean age 59 years) with late stages of PD (Hoehn-Yahr stages III-IV). The patients enrolled in this study were fully examined at Neurology Research Center, Russian Academy of Medical Sciences. Subjects were selected on the basis of case history analysis, additional examination to assess motor system and neuropsychological state (UPDRS and Hoehn-Yahr scales), and functional and laboratory diagnostic

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methods. Patients with doubtful diagnosis and atypical course of the disease were excluded.

Hardware-software complex was used to examine motor activity of the subjects [1]. Movement parameters obtained in two tests were analyzed. In the first test, the examinee was asked to turn his head in the horizontal plane from one shoulder to another and to fix and retain gaze on immobile target located 70 cm from the nose bridge. In the second test, the examinee was asked to fix and retain gaze on the target that moved with the same speed and direction as the head movement. The examinees had to move head smoothly, quickly, and comfortably in both tests. The analysis epoch lasted 2-4 sec. The examinee made 20-25 trials in each test. Electrooculogram and head movements were recorded.

Comparative analysis of obtained head movement parameters were compared between the groups of healthy subjects and patients with PD stages III-IV using nonparametric Mann–Whitney test.

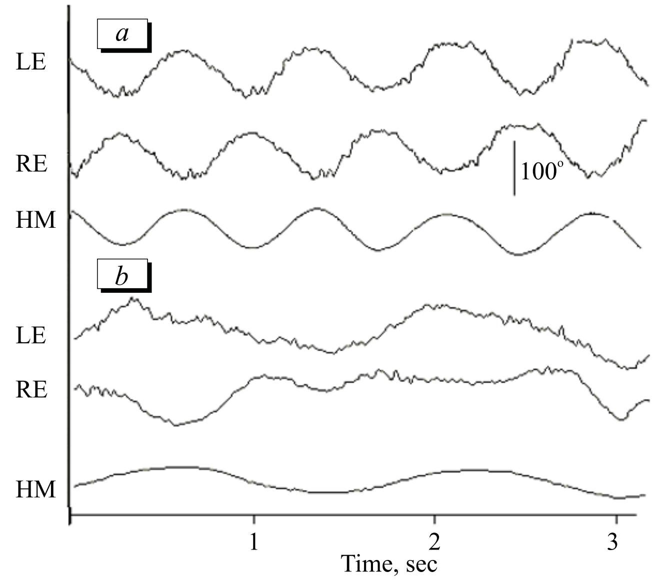

Fig. 1. Test with gaze fixation and retention on immobile target with horizontal HM (from one shoulder to another). *a*) normal; *b*) PD, stages III-IV.

RESULTS

Analysis of the parameters obtained in test 1 revealed significant changes in patients with stage III-IV PD in comparison with healthy subjects (Table 1; Fig. 1). Head movement (HM) amplitude, right eye (RE) movement amplitude and left eye (LE) movement amplitude were significantly below normal values in severe PD. HD deceleration averagely 2.5 fold was also established. Asymmetry in absolute magnitude of LE and RE movements also significantly differed from the normal values. Time desynchronization of eyes and head exceeded normal values approximately 7-fold (Table 1). Eye motion trajectory was showed to be more impaired than HM trajectory. In particular, changes in HM trajectory in patients with stage III-IV PD primarily manifested in reduction of HM frequency and by the presence of local sites of HM deceleration. At the same time, eye movement trajectory could be so altered that assessment of some quantitative parameters was impossible.

When HM and eye movements were performed synchronously with the target, the mean HM amplitude in healthy subjects was 100.9° (Table 2) and their eyes followed the target and remained immobile relatively to the head, therefore their trajectory is close to a straight line (Fig. 2, *a*), deviations recorded on the oculogramm were negligible. At late stages of PD, a

TABLE 1. Parameters of HM and Eye Movement in the Test of Gaze Fixation and Retention on Immobile Target (median; upper quartile; lower quartile)

Parameter		Normal	PD, stages III-IV
Amplitude, degrees HM		77.7 (75; 83.5)	58.7 (42.2; 75.2)
	LE	70.5 (60; 82.1)	43.5 (38.8; 53.3)
	RE	60.1 (53.4; 70.1)	47.9 (41.2; 50.7)
HM frequency, Hz		1.35 (1.21; 1.49)	0.58 (0.44; 0.71)
Asymmetry, msec HM		10 (0; 30)	152 (100; 429)
	LE	10 (0; 29)	153 (30; 210)
	RE	10 (0; 24)	131 (30; 184)
Movement desynchronization, msec	LE	16 (11; 24)	95 (36; 247)
	RE	14.5 (9; 20)	110 (25; 199)

Note. Here and in Table 2: for all PD patients $p<0.05$ in comparison with normal values.

TABLE 2. Parameters of HM and Eye Movement in the Test of Gaze Fixation and Retention on a Target Moving Synchronously with HM (median; upper quartile; lower quartile)

Parameter		Normal	PD, stages III-IV
HM amplitude, degrees		100.9 (88; 108.5)	49.7 (39.9; 69.6)
HM frequency, Hz		1.43 (1.25; 1.61)	0.63 (0.41; 0.84)
HM asymmetry, msec		12 (0; 28)	160 (112; 262)
Deviations from direct gaze fixation, degrees	LE	9 (7; 11)	94.9 (58.8; 203)
	RE	7.5 (6.6; 9)	113.6 (68.8; 264.2)

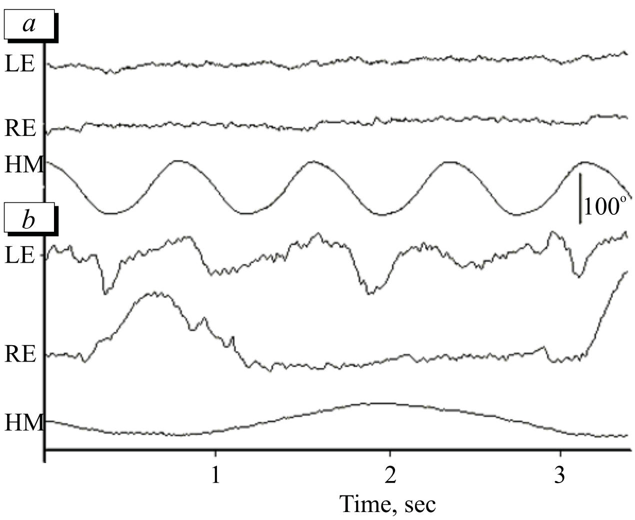

Fig. 2. Test with gaze fixation and retention on the target moving synchronously with HM (from one shoulder to another). *a*) normal; *b*) PD, stages III-IV.

significant decrease in HM amplitude (by 2 times) was revealed similar to that observed in test 1 (Table 2). Deviations of eye movements from target movement were much more substantial. In addition, HM frequency decreased to 0.63 Hz (*vs*. 1.43 Hz in normal).

These findings suggest that stage III-IV PD is associated with significant disturbances in the interactions of the neck muscles and vestibular and visual systems resulting in inability to fix and retain gaze on immobile target, as well as on the target moving synchronously with the head, to disalignment and asynchrony in eye movements and HM, what manifests in clinics as postural disturbances, balance disorder and dizziness. With respect to neurophysiological mechanisms, that result in mentioned disturbances, we have following assumption. PD is characterized by inner imbalance in the basal ganglia [5]. Degeneration of dopamine neurons in the substantia nigra leads to inner imbalance in the basal ganglia, particularly, to depletion in caudate nucleus; these changes through a number of closed circuits involving globus pallidus and subthalamic nuclei result in dysregulation of the anterior quadrigeminal bodies. Latter are responsible for integration and processing of information, coming from retina, cortex and subcortical structures of visual and other systems, as well as participate in planning of eye movements [4]. When central inhibitory mechanisms are disordered, control of globus pallidus system declines, impulse transmission in reticulospinal tract, which provides tonus and coordination of muscle responses, suffers. Impulses from proprioceptors of muscle and joint system of the neck are also altered, which results in deterioration of the information processing at the level of brain stem structures and paramedical reticular formation of the pons. At stage III-IV PD, the pathological process gradually involves the whole brain areas (frontal, occipital and temporal). As a result, symptoms consistently progress.

Our results extend our knowledge on the role of some subcortical and brainstem structures and their interconnection in the functional organization of cervico-vestibulo-oculomotor interaction. Disturbances developing at the late stages of PD were evaluated quantitatively. We believe that comparison of these data with analogous data obtained in patients with early stages of PD [2] will open new the ways for controlling the development of these disturbances and timely prevention of deterioration of patient's state.

REFERENCES

1. B. Kh. Baziyan and I. E. Dmitriev, *Zh. Vyssch. Nervn. Deyat.*, **46**, No 2, 396-399 (1996).
2. B. Kh. Baziyan, A. Yu. Shvetsov, E. A. Ivanova, and G. A. Yakovlev, *Structure Functional and Neurochemical Regularities of Brain Asymmetry and Plasticity* [in Russian], Moscow (2007), pp. 62-66.
3. V. L. Golubev, Ya. I. Levin, and A. M. Vein, *Parkinson Disease and Parkinsonism* [in Russian], Moscow (2000).
4. O. Hikosaka, Y. Takikawa, and R. Kawagoe, *Physiol Rev.*, **80**, No. 3, 953-978 (2000).
5. J. A. Obeso, M. C. Rodríguez-Oroz, B. Benitez-Temino, *et al.*,