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The Effect of Sleep and Wakefulness Disorders on Cognitive Function in Parkinson's Disease

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Abstract

Objective: To clarify clinical features of sleep disorders in patients with Parkinson's disease (PD) and their effect on cognitive function and emotional-personal sphere.

Material and methods: The study involved 62 patients with PD (33 men and 29 women) mean age 47.8±7.1 years. The control group consisted of 20 patients without Parkinsonism matching by age and sex. The diagnosis of PD was established by criteria A.Hughes. Patients underwent an extended neuropsychological study with qualitative and quantitative analysis. To determine cognitive disorders, we used neuropsychological tests.

Results: 49 patients (79,3%) had sleep disorders. In the structure of sleep disorders: 29 (59.2%) patients had insomnia and 11 (22.4%) patients – parasomnia and 9 (18.4%) - hypersomnia. In a control group, numbers were 4.5 times less. The analysis showed that the structure of sleep disorders correlates with the form of PD. So, insomnia is more rapidly met in akinetic-rigid form (55.5%), whereas hypersomnia is presented in mixed form. Patients with insomnia present 35% of predement cognitive impairment and 34% of dementia (66.7% of mild degree dementia and 33.3% moderate dementia severity). Whereas, in patients with hypersomnia 35% of predement cognitive impairment, 60% of dementia (54.6% and 45.4%) were observed. Among patients with permanent drowsiness 32.4% of predement cognitive impairment and 58.4% of dementia (44.8% and 55.2%) were diagnosed. Dementia (65.4%) was observed more in patients with sudden sleep (42,8% and 57.2%).

Conclusion: sleep and wakefulness disorders depend not only on the severity of motor symptoms, but also depend on the emotional and cognitive state.

Keywords: Parkinson's disease; Cognitive disorders; sleep disturbances.

Introduction

The actual problem of modern neuroscience is to explore the early diagnosis and progression factors of extrapyramidal hyperkinesia, including Parkinson's disease (PD). PD is characterized by a steady progression that inevitably leads to significant morbidity and socio-economic losses. PD frequency among neurodegenerative diseases ranked second after Alzheimer's disease [1, 2].

PD – degenerative, multifocal and multisystem disease of the central nervous system, manifested by motor, mental and autonomic disorders [3]. At present, the study of the relationship of PD and non-motor manifestations as sleep and cognitive function disturbances is one of the priority areas of research in clinical neurology and attached great importance to the pre-clinical diagnosis. Timely correction of sleep and cognitive function infringement slows the progression of PD and reduces invalidation [4, 5].

Advances in symptomatic antiparkinsonic treatment, an increase in life expectancy of patients with this disease makes it clear that with progression of PD, more attention is drawn to the so-called non-motor symptoms [6]. These include cognitive disorders, sleep infringement, hallucinations, depression, fatigue, constipation, and others. The most disabling non-motor manifestations in PD is dementia which occurs in 40-70% of patients [7, 8].

Sleep disorders in PD occur in 1.5-3.5 times higher than in the elderly population or in other chronic diseases [7]. They affect the entire sleep-wake cycle and can be represented by the fragmentation of sleep, excessive daytime sleepiness, and behavioral disturbances in REM sleep [9, 10, 11].

It is believed that to formation of cognitive impairment in PD affects the damage of: dopaminergic neurons of the medial part of the substance (C.Da Cunha et al., 2002) and the ventral tegmentum (K.Ito et al., 2002), which form mesocortical pathway; noradrenergic neurons in locus coeruleus (C. Zarow et al., 2003), as well as cholinergic neurons in nucleus basalis of Meynert, and cerebral cortex (N.T.Bohnen et al., 2002). A certain role in cognitive impairment presentation is assigned to deficiency of dopamine in the caudate nucleus (A. Bruck et al., 2001). In recent years, data on the role of glutamatergic mechanisms in the development of dementia are accumulated (J.H Krystal, 2001) and glutamatergic neurotransmission pathology is seen as the main component of the pathogenesis of neurodegenerative diseases (AY Bespalov, 2000).

The progression of cognitive impairment in PD depends not only on the patient's age, the age of onset of the disease, the patient's emotional state, and the opening stage of the disease, a genetic condition, but also depends on the state of sleep disorders [12, 13].

The aim of our study is to clarify the clinical features of sleep disorders in patients with PD and their effect on cognitive function and emotional-personal sphere.

Material and methods

The study was performed on the basis of 1-Republican Clinical Hospital and Department of Nervous Diseases of the Tashkent Medical Academy. The study involved 62 patients with PD (33 men and 29 women) aged 30 to 65 years (mean age 47.8±7.1 years). The control group consisted of 20 patients without Parkinsonism matching main groups by age and sex. The diagnosis of PD was established in accordance with the criteria A. Hughes et al. UK bank and brain [14]. All patients underwent clinical neurological examination, including a detailed assessment of movement disorders using the unified Parkinson's disease Rating Scale (UPDRS).

Assessment of the stage of disease was performed using scale - Hoehn and Yahr [15]. All patients underwent an extended neuropsychological study with qualitative and quantitative evaluation of the results. To determine cognitive disorders, we used the following neuropsychological tests: Mini-mental state examination (MMSE) [16], a battery of tests to evaluate the frontal dysfunction (Frontal assessment battery-FAB) [17], the clock drawing test (CDT) [Lezak MD, 1983]. According to the degree of cognitive impairment, we have identified mild, moderate and severe cognitive impairment according to the classification and ICD-10 diagnostic criteria modified by R. Petersen [18]. To determine the sleep disorders special questionnaire was used.

Statistical processing of the results was carried out using the methods of variation statistics recommended for biomedical researches. The results were processed using the software package Microsoft Excel, version 7.0 for Windows 98. The indicators are presented as the arithmetic average of a number of variations and standard error of the arithmetic mean ($M \pm m$). The significance of differences of mean values was assessed using the Student t-test. Differences were considered significant at $p < 0.05$.

All studies were conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Results

The results of our research show that 49 patients (79.03%) met sleep disorders. On the structure of sleep disorders 29 (59.2%) patients had insomnia and 11 (22.4%) patients had parasomnia and 9 (18.4%) met hypersomnia. Whereas, in control group, these figures were 4.5 times less than in the main group. Fig. 1.

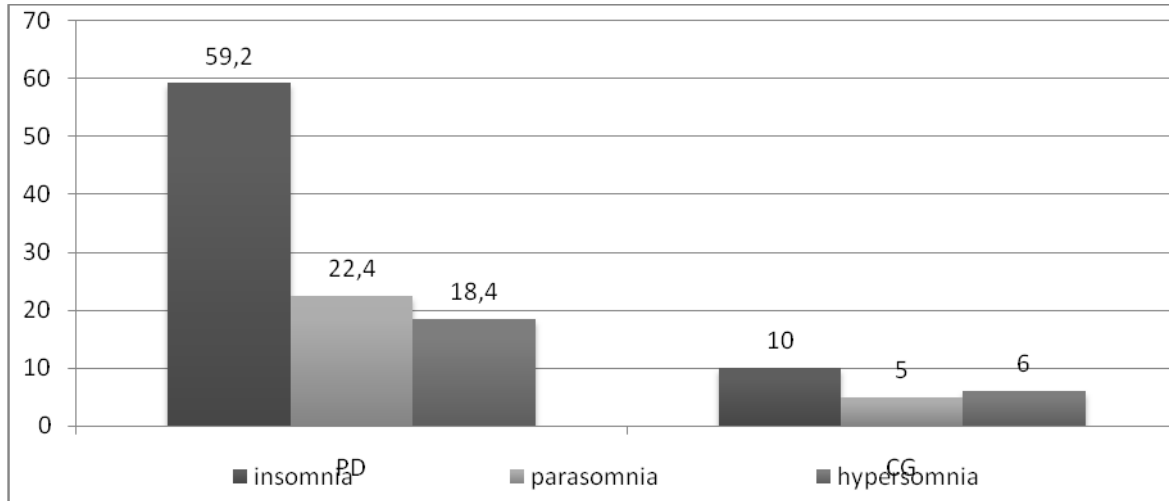


Fig. 1. Sleep disorders in PD and control group

Our 4 year scientific research show that cognitive impairment in PD depends on the form and stage of disease [19, 20]. It was found that Parkinson's disease is characterized by cognitive impairment and has progressive course, mainly due to the growth of severity of disregulatory and neurodynamic disorders, visual-spatial function abnormalities. The degree of cognitive impairment in PD depends on the form and stage of the disease, so in a row akinetic-rigid -tremor-mixed progression of cognitive impairment is observed that leads to the development of dementia disorders in the advanced stages of the disease. The analysis of our study show that the structure of sleep disorders depends on the form of PD. So, insomnia more frequently is met in akinetic-rigid form (55.5%), whereas in mixed form hypersomnia is detected more than in akinetic-rigid and tremor forms. (65.5%). Fig. 2.

The next stage of our study was the comparison of the level of violations with cognitive dysfunction in PD. We conducted a correlation analysis between the structural parameters of sleep disorders and neuropsychological test performance. To do this, we first studied the structure of cognitive function in PD. Neuropsychological test (MMSE) score of 8 patients with PD was ranged 28-30 points on average $28,5 \pm 2,5$, which indicates the absence of cognitive impairment. These patients did not have sleep disturbances. 22 patients of 24 to 27 points, on average of $25,8 \pm 3,6$ points. This indicates a moderate (predement) cognitive impairment, which met the criteria for mild cognitive disorders in ICD-10 and modified diagnostic criteria. In 32 patients with PD MMSE total score ranged from 23-11, with an average of $18,6 \pm 2,6$, indicating the presence of dementia, according to the diagnostic criteria of ICD-10. In this case, in 17 patients mild dementia severity (MMSE total score at 20-23 on average $22,4 \pm 2,7$) was revealed, 15-moderate severity of dementia (MMSE total score at 11-19 on average $14,8 \pm 2,6$).

BTLD technique was proposed for the screening of dementia, mainly affecting the frontal lobes and subcortical cerebral structures, i.e. when the sensitivity of the MMSE may be insufficient. With this method you can determine the level of conceptualization, dynamic movement, a simple choice reaction, the reaction of complicated choice, fluency, and study the grasping reflexes. The result of this test showed that in 8 patients, MMSE performance ranged from 28 to 30 points, BTLD was $17,8 \pm 1,3$ points, in 22 patients (MMSE 24-27) $15,4 \pm 0,6$ points. In 32 patients (MMSE 23-11) BTLD was $11,00 \pm 1,03$, of which 17 patients (MMSE 20-23) $11,2 \pm 0,8$ and 15 patients (MMSE 11-19) $10,8 \pm 1,2$ points.

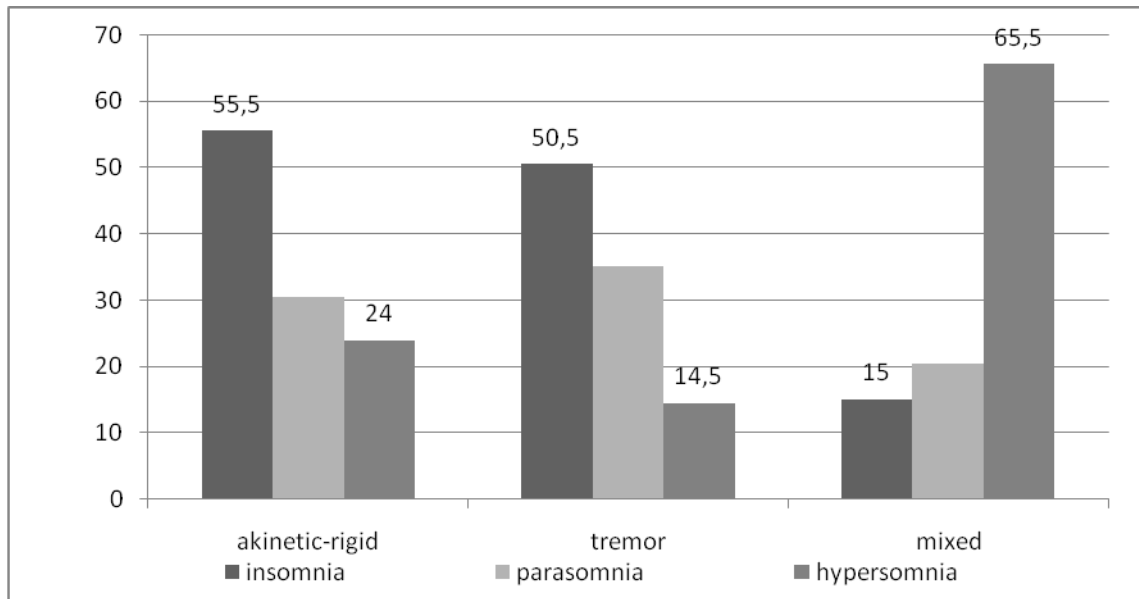


Fig. 2. Sleep disorders depending on the form

Another typical kind of cognitive impairment in PD is visuo-spatial disorder. They appear both in perception sphere and in the study of spatial praxis. This type of cognitive impairment was assessed by clock drawing test. According to the results of neuropsychological tests in 8 patients (MMSE 28-30) who found no cognitive impairment assessment by CDT was $9,7 \pm 0,6$ points; 22 patients (MMSE 24-27) $8,2 \pm 0,8$ points; 32 patients (MMSE 23-11) $6,95 \pm 0,6$ points, of which 17 patients (MMSE 20-23) $7,4 \pm 0,4$ and 15 patients (MMSE 11-19) $6,5 \pm 0,7$ points.

The structure of sleep disorders, suggest that patients with insomnia met 35% predement cognitive impairment and dementia, 34% (66.7% of dementia mild degree and 33.3% moderate dementia severity). Whereas, in patients with hypersomnia 35% predement cognitive impairment was observed, 60% dementia (54.6% mild dementia severity and 45.4% moderate dementia severity). Patients with permanent drowsiness met 32.4% predement cognitive impairment and 58.4% dementia (44.8% mild dementia severity and 55.2% moderate dementia severity). Dementia is more (65.4%) observed in patients with sudden sleep (42,8% moderate dementia severity and 57.2% mild dementia severity). Fig. 3.

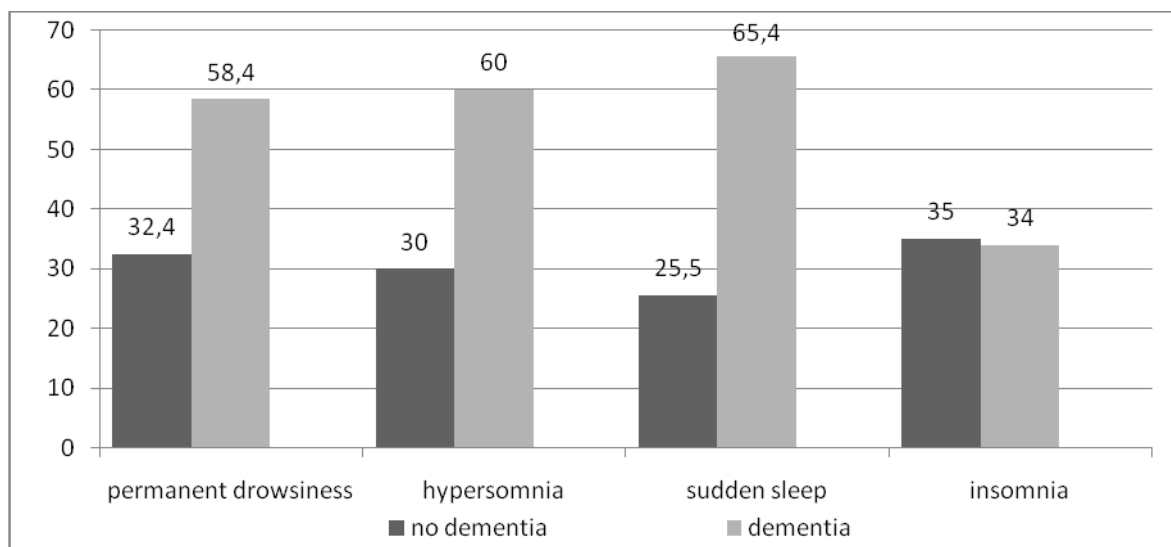


Fig. 3. Types of sleep disorders and cognitive impairment

In the next step we analyzed the changes in the emotional sphere of patient depending on the structure of cognitive impairment and sleep disorders. According to the results of neuropsychological tests by Spielberg-Hanin and Tsung, depending on the form of PD. Anxiety and depression were more presented in mixed form. Thus, in akinetic-rigid form level of RA was -30.3, PA, 33.7, 53.2 depression – points, and in tremor form: 30.6, 35.5 and 55.8 points, respectively, and in mixed form: 30.8, LT-37, 57.2 points. The analysis of indicators of anxiety (reactive and personal) and depression in PD patients depending on the form led to the following conclusions: the state of emotional and personal sphere in PD depends on the form of the disease, and deep disorders occur in patients with mixed form, personal reactivity and depression in a row akinetic-rigid-tremor-mixed forms rises, and reactive anxiety in all forms was almost the same. Correlative analysis of emotional personal sphere with the level of cognitive impairment and sleep disorders shows direct correlation of the level of sleep disorders with depression, and virtually no connection with this level of anxiety. This result suggests the influence of the level of depression on the progression of cognitive impairment and sleep disturbance in PD.

The leading causes of sleep disorders in PD are motor symptoms, as well as sensory, emotional disturbances, and nocturia [21]. Violations of falling asleep to a greater extent are associated with symptoms of PD (hypokinesia, rigidity, tremor), dystonia, sensory disorders, depression. Thus, the research confirms the dependence of sleep disorders in PD with severity of motor, sensory symptoms, emotional disorders. Identified linkage of sleep disorders and depression confirms the importance of depression in insomnia. Although classical sign of depression are early awakening, our study suggests the possibility of development of sleep disorders on the background of emotional distress. However, the coexistence of depression and insomnia in PD may be due to common neurotransmitter disorders underlying neuropsychiatric symptoms of PD.

So, we can conclude that sleep disorders is characteristic for PD and the findings suggest the heterogeneity of nature of multifactorial pathogenesis of these disorders. Clinical evaluation of sleep disorders showed their dependence on the clinical forms and stages of Parkinson's disease. A disturbance of sleep and wakefulness depend not only on the severity of motor symptoms, but also depends on the emotional and cognitive symptoms. Patients with hypersomnia, parasomnia and sudden sleep more commonly had dimension cognitive impairment. Timely determination of the severity of sleep disorders and cognitive functions and their correction allows you to improve the quality of life of patients with PD.

Conflict of interests

The authors have no conflicts of interest or competing financial interest to declare.

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