

COGNITIVE DISORDERS IN PATIENTS WITH PARKINSON'S DISEASE**Khubetova IV**

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КОГНІТИВНІ РОЗЛАДИ У ХВОРИХ НА ХВОРОБУ ПАРКІНСОНА**Хубетова І.В.**

Одеська обласна клінічна лікарня, м. Одеса, Україна

Abstract. The aim of the study was to identify cognitive disorders in patients with Parkinson's disease

Material and methods. The study was performed on the basis of the neurological department of the Regional Clinical Hospital (Odesa) during 2011-2021. There were diagnosed 364 patients with Parkinson's disease (PD) on the basis of diagnostic criteria of the British Brain Bank. Clinical and demographic data were studied: age, sex, severity according to the UPDRS scale, stage of the disease according to the Hoehn-Yahr scale, the presence of cognitive impairment and their nature. MMSE (Mini-Mental State Examination;) and PD-CRS (Parkinson's Disease-Cognitive Rating Scale) were used to study cognitive functions. Statistical processing was performed by analysis of variance, correlation and factor analysis using Statistica 13.0 software (TIBCO, USA).

Results. At the onset of the disease, left-side lesions were noted in 126 of 364 patients, i.e., 34.6%, right-side – in 127 (34.9%), the remaining 111 (30.5%) patients had bilateral lesions. The structure of the disease was dominated by mixed forms. Akinetic-rigid form was observed in 92 (25.3%) cases, tremor-dominant – in 27 (7.4%), mixed rigid-tremor in 157 (43.1%) cases, tremor-rigid in 92 (7.4%). Patients with stage 2 and 3 of PD were most often registered in 28.6% and 28.0% of cases, respectively. 31 (8.5%) patients had more severe motor disorders (stages 3.5 and 4). Cognitive impairment was detected in a significant number of patients (238 or 45.2%), the mean score on the MMSE scale was 25.3 ± 0.3 . Accordingly, on the PD-CRS scale, the average score was 91.2 ± 3.4 points. Subdemential changes were present in 82 (15.6%) patients. Accordingly, mild dementia was found in 15 (2.8%) patients, moderate dementia – in 18 (3.4%).

Conclusions:

1. The frequency of detection of cognitive impairment in patients with PD was 45.2% with a mean score on the MMSE scale of 25.3 ± 0.3 , and on the PD-CRS scale – 91.2 ± 3.4 points
2. Dementia changes were in 82 (15.6%) patients, mild dementia was found in 15 (2.8%) patients, moderate dementia – in 18 (3.4%) patients
3. There is a direct correlation between the age and severity of intellectual disabilities ($r = 0.50$).
4. Self-care disorders are determined by the severity of both motor and cognitive disorders by 72% ($R = 0.851$; $R^2 = 0.723$; Adjusted $R^2 = 0.721$; $F(2,2) = 309$; $p < 10^{-4}$; $SE = 4.6$).

Key words: Parkinson's disease, cognitive impairment, quality of life

Резюме. Метою дослідження було визначення когнітивних розладів у хворих на хворобу Паркінсона

Матеріал та методи. Дослідження проведене на базі неврологічного відділення обласної клінічної лікарні (м. Одеса) впродовж 2011-2021 рр. Обстежено 364 пацієнта, яким виставлено діагноз ХП на підставі критеріїв діагностики Британського банку мозку. Вивчалися клінічні і демографічні дані: вік, стать, ступінь тяжкості за шкалою UPDRS, стадія захворювання за шкалою Хен-Яр, наявність когнітивних порушень та їх характер. Для дослідження когнітивних функцій використовували шкали MMSE (Mini-Mental State Examination;) та PD-CRS (Parkinson's Disease-Cognitive Rating Scale). Статистична обробка проведена методом дисперсійного, кореляційного та факторного аналізу за допомогою програмного забезпечення Statistica 13.0 (TIBCO, США).

Результати. При дебюті захворювання лівобічне ураження констатували у 126 з 364 хворих, тобто 34,6%, правобічне – 127 (34,9%), в решті 111 (30,5%) – білатеральне ураження. В структурі захворювання переважали змішані форми. Акінетико-ригідна форма спостерігалася у 92 (25,3%) випадках, тремтлива – у 27 (7,4%), змішана ригідно-тремтлива у 157 (43,1%) випадках, тремтливо-ригідна у 92 (7,4%). Найбільш часто у пацієнтів реєструвалися 2 та 3 стадії ХП, відповідно у 28,6% та 28,0% випадків. 31 (8,5%) пацієнтів мали більш виражені моторні порушення (3,5 та 4 стадії). У значної кількості хворих (238 або 45,2%) були виявлені когнітивні порушення, середній бал за шкалою MMSE склав $25,3 \pm 0,3$. Відповідно, за шкалою PD-CRS середня оцінка склала $91,2 \pm 3,4$ балів. Преддементні зміни були у 82 (15,6%) пацієнтів. Відповідно, деменція легкого ступеня була констатована у 15 (2,8%) хворих, помірна деменція – у 18 (3,4%).

Висновки:

1. Частота виявлення когнітивних порушень у хворих на ХП склала 45,2% при середньому балі за шкалою MMSE $25,3 \pm 0,3$, а за шкалою PD-CRS - $91,2 \pm 3,4$ балів
2. Преддементні зміни були у 82 (15,6%) пацієнтів, деменція легкого ступеня була констатована у 15 (2,8%) хворих, помірна деменція – у 18 (3,4%)

3. Між показниками віку та вираженості порушень інтелекту існує прямий кореляційний зв'язок середньої сили ($r=0,50$).

4. Порушення самообслуговування детермінуються вираженістю як моторних, так й когнітивних порушень на 72% ($R=0,851$; $R^2=0,723$; Adjusted $R^2=0,721$; $F(2,2)=309$; $p<10^{-4}$; $SE= 4,6$).

Ключові слова: хвороба Паркінсона, когнітивні порушення, якість життя

Problem statement and analysis of recent research.

Parkinson's disease (PD) is the most common movement disorder, and at the same time the second most common neurodegenerative disease after Alzheimer's disease [1, 2]. Histopathological signs of PD are the loss of dopaminergic neurons in the substantia nigra and the accumulation of α -synuclein in intraneuronal inclusions [1, 3]. The pathogenesis of PD is complex, it involves mechanisms such as oxidative stress, mitochondrial dysfunction, impaired cellular calcium metabolism, activation of neuroinflammation and deficiency of other neurotransmitters [1, 2, 4]

In addition to cardinal motor manifestations such as bradykinesia, rigidity and rest tremor, PD is associated with a heterogeneous spectrum of non-motor symptoms that significantly aggravate the disease and impair quality of life (QOL) [1, 5]. It is known that cognitive impairment is six times more common in people with PD than in healthy people of the same age [5-7], and is thus one of the most important non-motor manifestations of PD.

Cognitive impairment has serious economic consequences, both due to direct costs of treatment and indirect losses associated with the need for constant care and diversion of society resources [6, 8].

The range of cognitive impairment in PD is very wide: from mild cognitive dysfunction to severe dementia [6, 7]. But even with minimal cognitive impairment, including changes in performance, attention, vision, and memory, the impact on daily functioning can be significant. The most vulnerable are executive functions (mental flexibility, changing settings, switching, effective planning of future actions and problem solving) [7]. Despite the fact that decompensation in the cognitive sphere in PD is developing slowly, it is this disorder that researchers have been paying the most attention to in recent years [6, 7, 9, 10].

The aim of the study was to identify cognitive disorders in patients with Parkinson's disease

Material and methods

The study was conducted on the basis of the Neurological Department of the Regional Clinical Hospital (Odesa) during 2011-2021. There were diagnosed 364 patients with PD on the basis of diagnostic criteria of the British Brain Bank. Clinical and demographic data were studied: age, sex, severity according to the UPDRS scale, stage of the disease according to the Hoehn-Yahr scale, the presence of cognitive impairment and their nature [11]. MMSE (Mini-Mental State Examination);

and PD-CRS (Parkinson's Disease-Cognitive Rating Scale) were used to study cognitive functions [13, 14].

The study was performed in compliance with modern bioethical requirements. All patients or their full representatives signed an informed consent. The study was in line with the provisions of the Helsinki Declaration on Medical Ethics, the Universal Declaration on Bioethics and Human Rights (2005); Convention on Human Rights and Biomedicine "(1997), the Principles of Good Clinical Practice (ICH GCP), the Code of Ethics for Physicians (2006), and the Guidelines for Medicinal Products. Good Clinical Practice "(2009) and was conducted with respect for the rights, interests and personal dignity of participants.

Statistical processing was performed by analysis of variance, correlation and factor analysis using Statistica 13.0 software (TIBCO, USA) [15]

Results and discussion.

At the onset of the disease, left-side lesions were noted in 126 of 364 patients, i.e. 34.6%, right-side – in 127 (34.9%), the remaining 111 (30.5%) patients had bilateral lesions.

The structure of the disease was dominated by mixed forms. Akinetic-rigid subtype of PD was observed in 92 (25.3%) cases, tremor-dominant forms subtype – in 27 (7.4%), mixed rigid-tremor subtype – in 157 (43.1%) cases, tremor-rigid – in 92 (7.4%) cases.

The distribution of patients according to the degree of severity on the modified Hoehn-Yahr scale is shown in Fig. 1.

As can be seen from the figure, the most common patients with PD were diagnosed stage 2 and 3, respectively, in 28.6% and 28.0% of cases. 31 (8.5%) patients had more severe motor disorders (stages 3.5 and 4). There were no patients with diagnosed stage 5 at all (tab. 1).

Table 1. Distribution of patients by severity of the disease

Stage	Absolute number	%
1	33	9.1
1.5	58	15.9
2	104	28.6
2.5	36	9.9
3	102	28.0
3.5	6	1.6
4	25	6.9
5	-	-

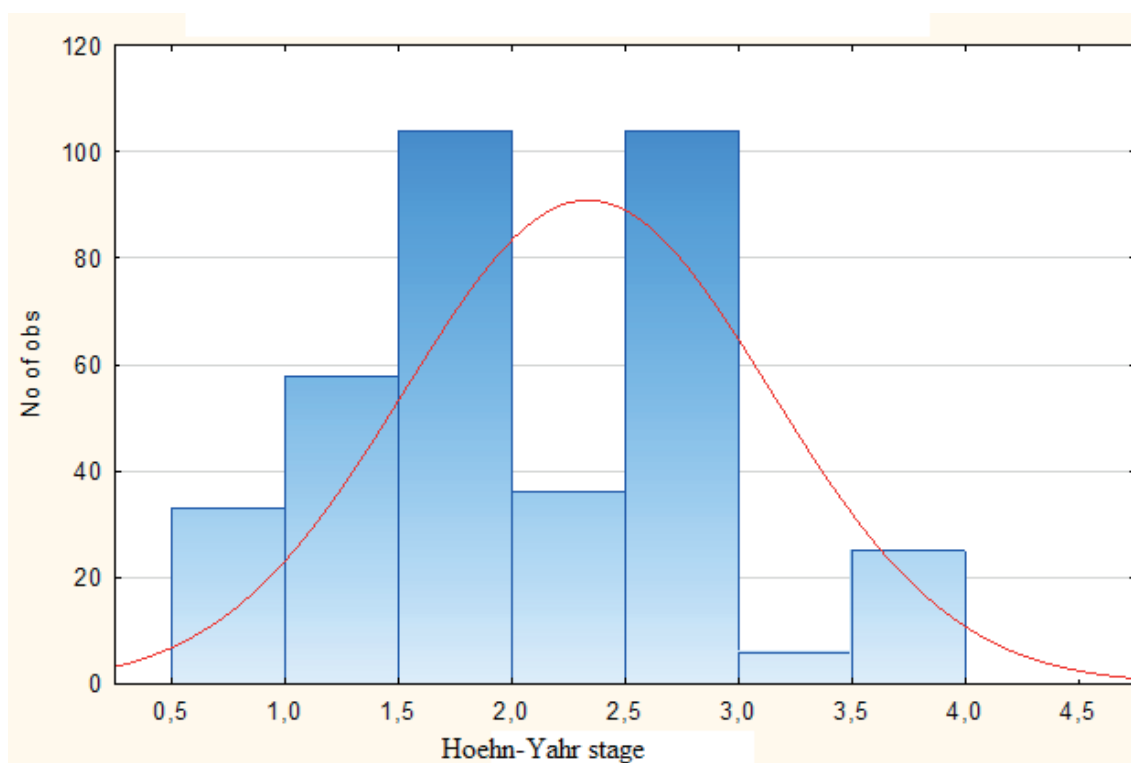


Figure 1. Distribution of patients by severity of the disease

Cognitive impairment was detected in a significant number of patients (238 or 45.2%), the mean score on the MMSE scale was 25.3 ± 0.3 . Accordingly, on the PD-CRS scale, the average score was 91.2 ± 3.4 points.

A more detailed analysis of the distribution of patients according to age of onset of the disease (Fig. 1) shows that pre-dementia changes were in 82 (15.6%) patients. Accordingly, mild dementia was found in 15 (2.8%) patients, moderate dementia – in 18 (3.4%).

Cognitive impairment in PD, including both dementia and non-dementia disorders, is an increasingly recognized non-motor complication of Parkinson's disease with significant clinical impact. They cause the need for constant third-party care, require the establishment of specialized clinics and hospices, have a negative impact on mortality [8]. PD with dementia occurs in approximately 30% of patients [6, 9]. Aarsland et al. (2021) recently reported that 19% of their untreated patients with PD had some form of cognitive impairment at the time of diagnosis [10].

As can be seen from Figure 3 below, there is a direct correlation between age and severity of intellectual disabilities ($r = 0.50$).

If we take motor and intellectual disorders as factor traits, and self-care disorders as a performance trait, we can state that the latter is determined by the first two by 72%: $R = 0.851$; $R^2 = 0.723$; Adjusted $R^2 = 0.721$; $F(2,2) = 309$; $p < 10^{-4}$; $SE = 4.6$.

Thus, it is advisable to perform a regular thorough

examination of the cognitive sphere of patients with PD and other extrapyramidal disorders. Even with minimal changes in the cognitive sphere, it becomes difficult for a patient with PD to perform professional duties and maintain social contacts.

We believe it is important to emphasize that even in the absence of severe dementia, screening for mild to moderate cognitive impairment in patients with PD is important to assess prognosis. This coincides with the views of other experts [5, 6, 10]. The combination of executive dysfunction with concomitant disorders of other cognitive areas, such as speech dysfunction, visual spatial abilities and memory impairment, has the greatest prognostic significance [5, 7]. The cumulative prevalence of dementia in PD within 10 years reaches 80% [10], another 40% of patients even at an early stage have concomitant mild cognitive impairment. Semiotic cognitive dysfunction in PD can be divided into two main clinical variants. The first is related to planning difficulties, lack of working memory and executive dysfunction. Anatomical substrate may be damage to the frontal ligaments in combination with low dopamine levels. The second type of cognitive impairment is represented by predominant attention disorders, semantic verbal disorders, changes in visual and spatial abilities involving the temporal lobe and posterior cortical dysfunction [9, 10]. Our data suggest that the predominance of one or another clinical variant of cognitive dysfunction may be age-dependent in PD.

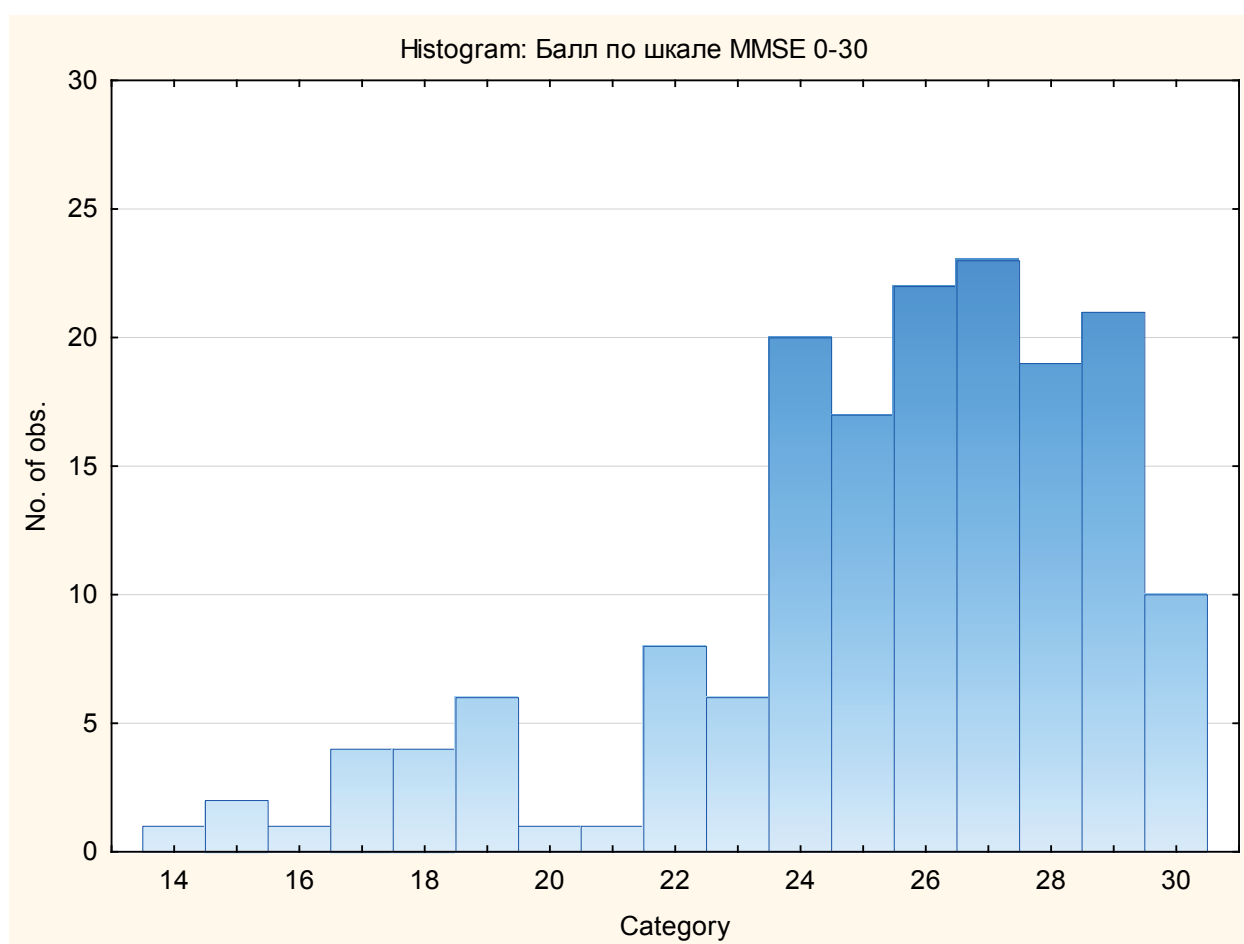


Figure 2. The severity of cognitive impairment in patients with PD

Conclusions:

1. The frequency of detection of cognitive impairment in patients with PD was 45.2% with a mean score on the MMSE scale of 25.3 ± 0.3 , and on the PD-CRS scale – 91.2 ± 3.4 points

2. Dementia changes were in 82 (15.6%) patients, mild dementia was found in 15 (2.8%) patients, moderate dementia – in 18 (3.4%)

3. There is a direct correlation between the age and severity of intellectual disabilities ($r = 0.50$).

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Conflict of interest: no conflict

Financial Disclosure: nothing to declare

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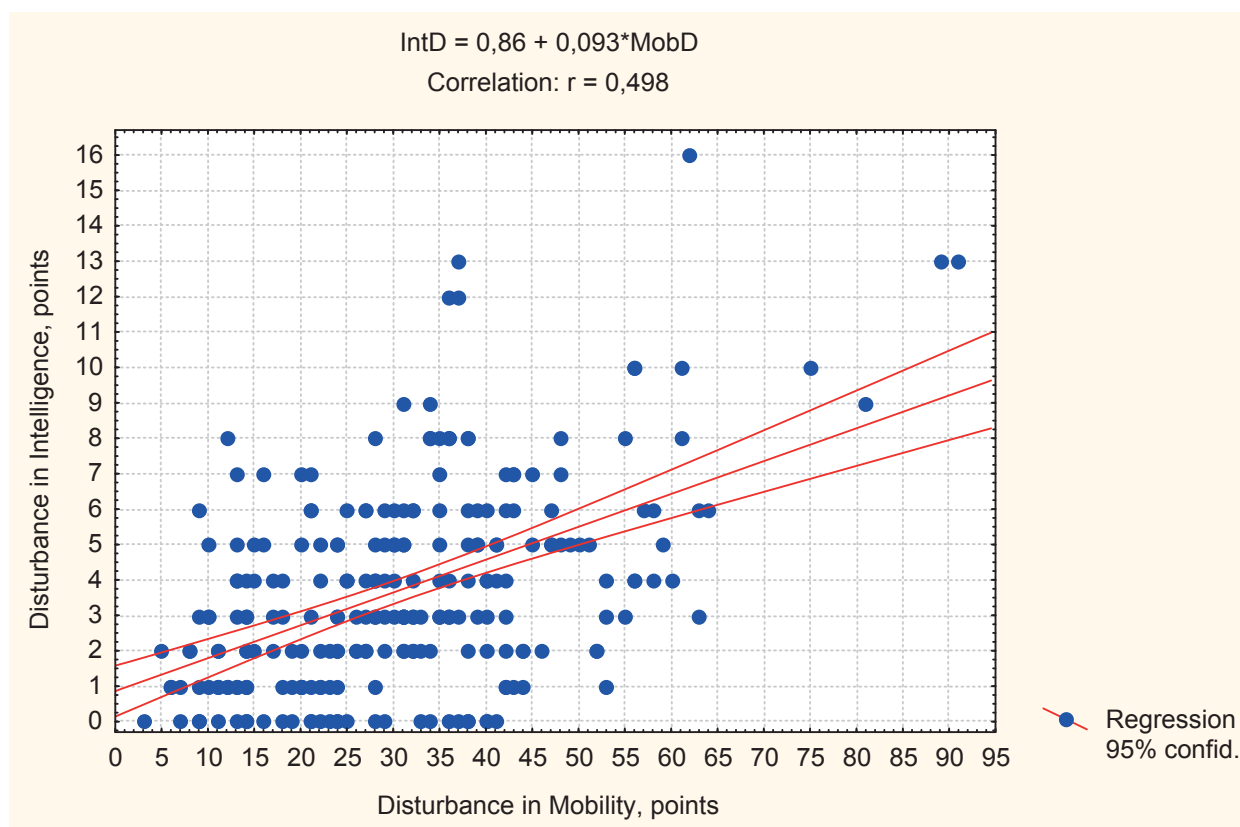


Figure 3. Correlation between the severity of movement disorders (X-axis) and intelligence (Y-axis)

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