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THE USAGE OF ELECTRONEUROMYOGRAPHY FOR OPTIMIZATION DIAGNOSTIC APPROACHES TO PARKINSON'S DISEASE

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Motor and sensory symptoms in patients with Parkinson's disease are usually measured by clinical scales with subjective assessments. That is why the development of new techniques and improvement of objective methodology is necessary for clinical practice. We conducted an analytical cross-sectional study based on the Parkinson's disease and other neurodegenerative diseases centre based on Poltava State Medical University in the period 2020–2021. We performed a factor analysis of features of electroneuromyography. We determined indicators and their relationships that characterize the tremor and the severity of the cubital syndrome on the dominant side, as well as the severity of the carpal syndrome on the non-dominant side in patients with Parkinson`s disease. Thus, the usage of factor loads determined by the results of our study allows optimizing the diagnostic approach to peripheral lesions in Parkinson`s disease by calculating the severity of tremor and tunnel neuropathies in these patients.

Key words: Parkinson's disease, tremor, carpal tunnel syndrome, cubital tunnel syndrome, electromyography, factor analysis.

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ВИКОРИСТАННЯ ЕЛЕКТРОНЕЙРОМІОГРАФІЇ ДЛЯ ОПТИМІЗАЦІЇ ДІАГНОСТИЧНИХ ПІДХОДІВ ПРИ ХВОРОБІ ПАРКІНСОНА

Хвороба Паркінсона характеризується розвитком моторних симптомів, зокрема брадикінезії, м'язової ригідності та тремору, а також немоторних симптомів, зокрема порушень сну, настрою, серцево-судинної та травної системи і сенсорні розлади. Моторні та сенсорні симптоми зазвичай при хворобі Паркінсона аналізуються за клінічними шкалами з суб'єктивними оцінками. Тому необхідний розвиток нових технік та оптимізація об'єктивних методик у клінічній практиці. Нами проведено крос-секційне аналітичне дослідження на базі центру хвороби Паркінсона та інших нейродегенеративних захворювань при Полтавському державному медичному університеті у період 2020–2021 рр. Нами виконано факторний аналіз електронейроміографічних показників. Було визначено показники, які характеризують тремор та тяжкість карпального і кубітального тунельних синдромів у пацієнтів з хворобою Паркінсона. Так використання факторних навантажень, встановлених за результатами нашого дослідження, дозволяють оптимізувати діагностичні підходи до периферичних уражень при хворобі Паркінсона та розрахувати тяжкість тунельних нейропатій і вираженість тремору.

Ключові слова: хвороба Паркінсона, тремор, карпальний тунельний синдром, кубітальний тунельний синдром, електроміографія, факторний аналіз.

The study is a fragment of the research project "Clinical, molecular genetics and neurophysiologic features of the course of the various forms of Parkinson's disease", state registration No. 0119U102848.

Parkinson's disease (PD) is a common neurodegenerative disease of the nervous system, characterized by steady progression, which inevitably leads to disability [10]. PD is a chronic, progressive age-related disorder characterized by motor (bradykinesia, muscle rigidity, tremor) and non-motor symptoms, including neuropsychiatric, sensory, autonomic, and olfactory disorders [13].

Neurophysiological methods play an important role in diagnosing PD and comorbid disturbances. One of them is electroneuromyography (ENMG) which assesses the function of peripheral nerves and

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muscles of the extremities [4]. Peripheral neuropathy is a common neurological problem involving motor, sensory, and autonomic nerve dysfunction. The presence of peripheral neuropathies has recently been observed in PD. This concomitant disorder is striking because it increases the burden on patients whose motor functions have been previously impaired [8].

In PD populations, peripheral neuropathies are predominantly distal, symmetrical, axonal, and in most cases sensitive. The latest meta-analysis shows that although many studies of nerve conduction in PD patients have been performed, most have focused on the lower extremities and limited nerves. There is little evidence to support a direct link between levodopa treatment and the development of peripheral neuropathies in PD, so the authors have emphasized the necessity for further clinical and neurophysiological studies in this area [15].

In addition, ENMG is used to assess the frequency and type of tremor in PD. It is known that patients with PD may experience rest, postural and kinetic tremor. The most common symptom is rest tremor, which is associated with a contralateral decreasing in dopamine binding in the striatum [5]. Two tremor phenotypes were identified in patients with PD: re-emergent tremor and pure postural tremor. Re-emergent tremor had a higher frequency than rest tremor, a distant onset, and a clear dopamine response, while pure postural tremor also had a higher frequency, but occurred immediately after posture. It is believed that different types of tremor have different central origins and require different approaches to treatment [3]. Despite the fact that kinetic tremor is not considered a crucial feature, it significantly affects quality of life. Its frequency ranges from 4–9 Hz and reaches a resting tremor frequency of 4–6 Hz [11].

Motor symptoms in PD are usually assessed on a clinical scale, so it is necessary to develop instrumental methods and optimize the methods of their use in the examination of PD patients to increase the objectivity of assessment and further treatment.

The purpose of the study was to investigate the indices of neurophysiological study that can be used to diagnose motor symptoms and peripheral nerve neuropathy in PD and evaluate their relationship with various motor forms.

Materials and methods. We performed an analytical cross-sectional study based on the Parkinson's disease and other neurodegenerative diseases centre on the basis of Poltava State Medical University in the period 2020–2021. All studied patients gave informed consent to participate in the study. The research protocol was approved by the Bioethics Committee of Poltava State Medical University.

The study included 64 patients with PD and 30 healthy subjects in the control group. The inclusion criteria were clinically confirmed PD according to the United Kingdom PD Society Brain Bank Clinical Diagnosis Criteria, Hoen and Yar stage less than 4, disease duration more than 1 year, age 18 to 89 years, levodopa therapy. Exclusion criteria: severe comorbid psychiatric or somatic pathology, age over 90 years, secondary parkinsonism, neuroimaging and clinical signs of atypical parkinsonism characteristic of dementia with Lewy bodies, progressive supranuclear palsy, corticobasal degeneration, or multisystem atrophy, treatment with B1, B2, B12 vitamins or glucocorticosteroids.

In all patients with PD, a motor subtype was identified according to the Unified PD Rating Scale: akinetic-rigid form (AR) (n=26) or mixed (akinetic-rigid-tremor form) (ART) (n=38). All patients received the following therapy: levodopa/carbidopa 250/25 mg 4 times a day, 1/4 tablet, levodopa/carbidopa retard 200/50 mg, 1/2 tablet at night, pramipexole with prolonged action 0.75 mg after meals in the morning.

To assess the neurophysiological characteristics of all patients, electromyography of agonist and antagonist muscles of the upper extremities was performed on both sides. For patients with PD, they were designated as the dominant or non-dominant side according to the hemitype of the disease, and for healthy individuals, the dominant or non-dominant side was determined according to the dominant arm.

We determined the characteristics of tremor at rest when performing postural and coordination tests by interference electromyography. The state of conductivity of motor and sensory fibres was assessed by stimulation electromyography at different levels using the short-distance method.

Median and ulnar nerve conduction studies were performed bilaterally in all subjects at the level of the wrist, elbow, lower third of the shoulder was assessed, as well as using the method of short distances. Orthodromic sensory responses from peripheral nerves were measured. Assessment of the severity of tremor was carried out at the beginning and at the end of the study period.

Data processing. Statistical analysis of the obtained data was performed using IBM SPSS Statistic v. 26.0 (IBM inc., USA). Qualitative features were presented in the form of absolute values (n) and percentages (%). Factor analysis was performed by the principal components' method using varimax rotation, calculating the adequacy of the Kaiser-Mayer-Olkin sample and the Bartlett sphericity criterion. The critical value of the correlation coefficient for its inclusion was chosen to be 0.75. The value of each factor was calculated using the obtained factor loads. The obtained values of factors for all patients were ranked into 4 subgroups of

percentiles, which corresponded to the severity of the sign. To compare qualitative features, χ^2-Pearson with Yates correction was used. P-values less than 0.05 were considered critical.

Results of the study and their discussion. To create integrated indicators of neuromuscular conduction of the upper extremities in patients with different motor subtypes of Parkinson's disease, a factor analysis of 40 studied parameters was performed. The admissibility of factor analysis was calculated by calculating the adequacy of the Kaiser-Mayer-Olkin sample (KMO=0.696) and the Bartlett sphericity criterion ($p<0.001$), which indicate the adequacy of the chosen method of reducing the dimension. The required number of factors that best describe the study sample was determined using the Kettel test on the schedule of eigenvalues. As shown in figure 1, after the third point, the steepness of the slope decreases, which indicates a number of factors that determine the variability of numerical data.

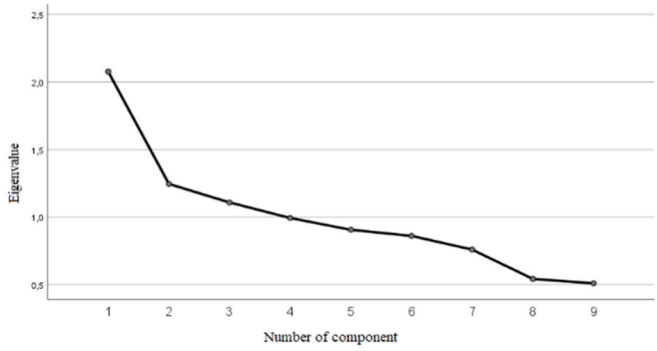

Fig. 1. Graph of eigenvalues of the factor analysis protocol

By factor analysis using varimax rotation, we formed 3 factor features characterized by electromyographic indices. Each of the selected factors was a linear combination of indices that had a factor load above 0.75, which had a strong correlation with the value of the factor and allowed its clinical interpretation. During the factor analysis, an inverse matrix of principal components with factor loads was obtained, which is shown in Table 1. The total amount of variance due to selected factors was 79.3 %, of which 42.8 % was explained by factor 1, 23.8 % by factor 2, and 12.7 % by factor 3.

Table 1

Inverse matrix of factor loads of components

Nerve	Index	Factor load		
		Factor 1	Factor 2	Factor 3
n.radialis	Rest tremor frequency in m. extensor carpi, D	0.762		
n.ulnaris	M-answer (wrist), D			0.762
	M-answer (below elbow), D			-0.931
	M-answer (above elbow), D			-0.814
	Motor conduction velocity, D			-0.776
n.medianus	M-answer (wrist), N		-0.894	
	M-answer (below wrist), N		-0.803	
	M-answer (above wrist), N		-0.811	
	Motor conduction velocity, N		-0.782	
	Sensory conduction velocity, N		-0.751	
	Distal motor latency, N		0.816	
	Rest tremor frequency in m. flexor carpi, D	0.907		
	Postural tremor frequency in m. flexor carpi, D	-0.845		
	Kinetic tremor frequency in m. flexor carpi, D	0.738		

Note. D – dominant side, N – non-dominant side

The model is built in 6 iterations. Thus, factor 1 showed a direct relationship with rest and kinetic tremor frequency in m. flexor carpi, rest tremor frequency in m. extensor carpi, and reverse with postural tremor frequency in m. flexor carpi on the dominant side, which describe the severity of parkinsonic tremor in the upper limb of the dominant side. Factor 2 has a positive correlation with the distal motor latency of the non-dominant side and a negative correlation with M-answer (wrist), M-answer (below wrist), M-answer (above wrist), motor conduction velocity and sensory conduction velocity, which can to characterize the severity of carpal tunnel syndrome in the limb of the non-dominant side. Factor 3 correlates positively with M-answer (wrist) of the dominant side and negatively with the following indicators of the dominant side: M-answer (below elbow), M-answer (above elbow) and motor conduction velocity, and may describe cubital canal syndrome at the dominant side.

The obtained factor values for each case were ranked on the 4th percentile with marks of severity, where 1 is no sign, 2 – mild, 3 – moderate, 4 – severe.

We analysed the conjugation of these factor traits with motor subtypes of PD. The severity of tremor in different motor forms is shown in figure 2. Absence of tremor was found in 12 of 26 patients (46 %) with AR form and in 26 of 30 people (87 %) of the control group. Mild tremor was detected in 11

of 26 people (42 %) with AR form, in 9 of 38 people (24 %) with ART form and in 1 of 30 (3 %) persons of the control group, moderate tremor in 3 of 26 12 %), 22 out of 38 (58 %), and 3 out of 30 (10 %), respectively. Severe tremor was found in 7 of 38 people (18 %) with ART form.

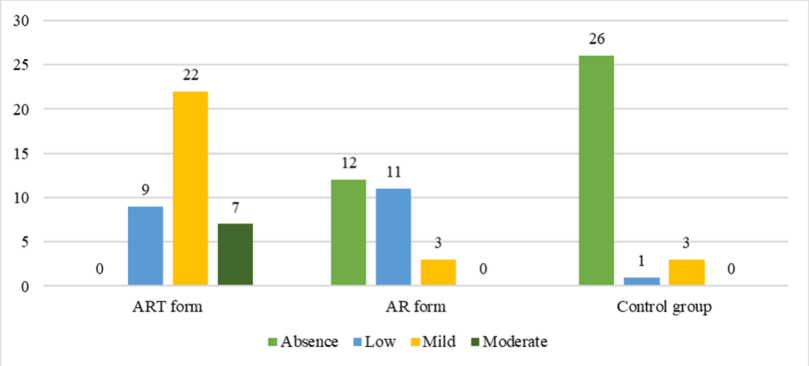

Fig. 2. Distribution of the severity of factor 1 "tremor of the dominant side" in different motor subtypes of Parkinson's disease

It is established that in PD tremor of the upper extremities is more pronounced (χ^2=68.21, df=6, p<0.001). In the ART subtype significantly more pronounced tremor of the dominant side (χ^2=32.53, df=3, p<0.001), however, its presence in patients with AR is also noteworthy.

Carpal tunnel syndrome of varying degrees was found in patients of all groups, as shown in figure 3. Absence of carpal tunnel syndrome was found in 12 of 38 patients (32 %) with ART form, in 16 of 26 people (62 %) with AR form and in 23 of 30 people (77 %) of the control group. Mild carpal tunnel syndrome was found in 16 of 38 people (42 %) with ART, 9 of 26 (35 %) with AR and 5 of 30 (17 %) in the control group, moderate in 7 of 38 (18 %), 1 out of 26 (4 %), and 2 out of 30 (7 %), respectively. Severe carpal tunnel syndrome was found in 3 of 38 people (8 %) with ART form.

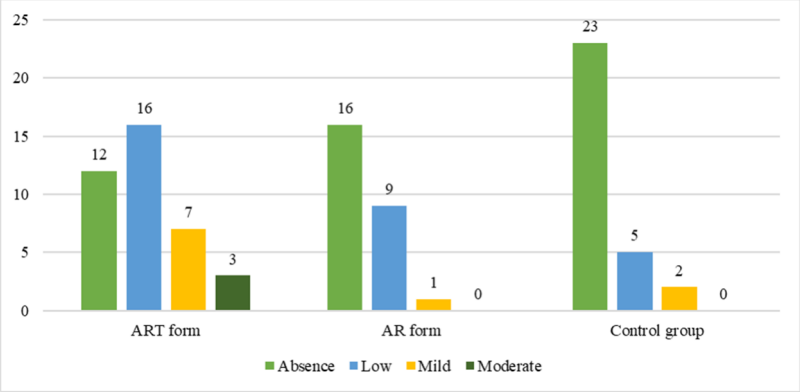

Fig. 3. Distribution of the severity of factor 2 "carpal tunnel syndrome" of the non-dominant side in different motor subtypes of Parkinson's disease

For patients with PD was more typical detection of signs of carpal tunnel syndrome in the non-dominant side (χ^2=18.27, df=6, p<0.001). In patients with ART form, its severity was statistically significantly higher (χ^2=8.07, df=3, p=0.045).

Cubital canal syndrome was the least pronounced feature in all groups, as shown in figure 4. Mild degree of cubital syndrome was determined in 3 of 38 people (8 %) with ART form, in 4 of 26 people (15 %) with AR form and in 2 of 30 (7 %) people of the control group, moderate in 7 of 38 (18 %), 2 of 26 (8 %), and 0 of 30 (0 %), respectively. Severe cubital syndrome was detected in 1 of 38 people (3 %) with ART form. Absence of cubital syndrome was found in 27 of 38 patients (71 %) with ART form, in 20 of 26 people (77 %) with AR form and in 28 of 30 people (93 %) of the control group.

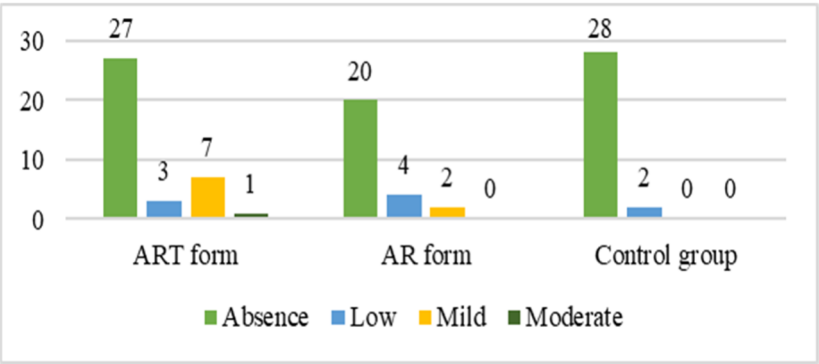

Fig. 4. Distribution of the severity of factor 3 “cubital tunnel syndrome” of the dominant side in different motor subtypes of Parkinson's disease

There were no statistically significant differences in the severity of the cubital canal between patients with PD and the control group (χ^2=9.92, df=6, p=0.428).

Thus, ENMG can be a reliable diagnostic method that allows you to evaluate several different components during one study. On the one hand, ENMG makes it possible to assess the type of tremor, which is essential for the diagnosis of PD [1].

We identified 3 factors that characterize different motor forms of PD and the indicators that characterize them. Factor 1 was called “dominant tremor” and was described by the increase in rest and kinetic tremor frequency in m. flexor carpi, Rest tremor frequency in m. extensor carpi, and a decrease in postural tremor frequency in m. flexor carpi on the dominant side, factor 2 “carpal tunnel syndrome on non-dominant side” was associated with an increase in distal motor latency of the non-dominant side and

a decrease in M-answers from all 3 points, motor conduction velocity and sensory conduction velocity, and factor 3 "cubital tunnel syndrome on dominant side", which was characterized by an increase in M-answer from wrist of the dominant side and a decrease in M-answers below and above elbow, and motor conduction velocity of the dominant side.

The results obtained as a result of factor analysis also allow us to assess the severity of tremor, which, as demonstrated above, can occur in both motor forms and differs in severity.

Tunnel neuropathy in PD may be associated with motor symptoms [7, 12]. According to our study, to reduce tunnel syndromes in PD, you can use an abbreviated list of parameters that allow you to assess their severity. Thus, we determined that patients with PD are characterized by the appearance of carpal tunnel syndrome on the non-dominant side. It is noteworthy that it is more pronounced in the ART form, which may be due to the higher frequency of use of the non-dominant hand due to tremor [2]. Similar data were obtained for patients with tremor-dominant form in other researchers. It is believed that more frequent use of the non-dominant hand can cause excessive mechanical stress, which leads to the development of carpal tunnel syndrome. Therefore, it is important to teach such patients early treatment of the upper extremities in everyday life [6].

One of the highlighted factors according to the results of our study was the cubital canal syndrome. Although its severity has not been established among the examined patients, its assessment is of important diagnostic value. It is believed that this syndrome is the second most common among tunnel neuropathies [9]. Its occurrence in PD can be caused by forced posture due to muscle rigidity, which leads to prolonged flexion of the upper limb and damage to the ulnar nerve [14].

Conclusion

We determined the indicators and their relationships that characterize the tremor and the severity of the cubital syndrome of the dominant side, as well as the severity of the carpal syndrome of the non-dominant side in patients with PD. It is established that although tremor is more characteristic of the mixed motor subtype, it can occur in akinetic-rigid form, but with a low degree of severity (χ^2=68.21, df=6, p<0.001). Patients with PD are more likely to develop carpal tunnel syndrome (χ^2=15.18, df=6, p=0.028), while differences in the frequency of different degrees of the cubital channel were not detected (χ^2=9.92, df=6, p=0.428). Thus, the use of factor loads determined by the results of our study allows to optimize the diagnostic approach to peripheral lesions in PD by calculating the severity of tremor and tunnel neuropathies in these patients.

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