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POSSIBILITIES OF ELECTRONEYROMIOGRAPHIC RESEARCH IN DIAGNOSIS AND EVALUATION OF DYNAMICS OF THE TREATMENT OF PATIENTS WITH PARKINSON'S DISEASE

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Assessment of tremor in Parkinson's disease is crucial to clarify the correct diagnosis and treatment. To date, there is no generally accepted method for assessing or measuring tremor. The aim of the work was to study the possibilities of using the method of electroneuromyography in the diagnosis and evaluation of treatment outcomes in patients with Parkinson's disease. To confirm the nature of tremor, its evaluation, the method of electroneuromyography has become widely used, which allows using surface electrodes to assess changes in agonist-antagonist muscles in Parkinson's disease at rest and in trials, to evaluate the effectiveness of treatment. The hypothesis of a link between tremor and the development of tunnel neuropathies in Parkinson's disease, disease progression and prognosis is discussed. It has been established that the manifestations of tunnel neuropathies are more characteristic of tremor-dominant forms of the disease and dominate on the side of the onset of the disease. Against the background of treatment there is a positive dynamics – a decrease in the frequency and amplitude of oscillations on both the dominant and opposite sides with the data of electroneuromyographic examination, increased motor activity.

Key words: Parkinson's disease, electroneuromyography, EMG-tremography, diagnosis, treatment.

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МОЖЛИВОСТІ ЕЛЕКТРОНЕЙРОМІОГРАФІЧНОГО ДОСЛІДЖЕННЯ В ДІАГНОСТИЦІ ТА ОЦІНЦІ ДИНАМІКИ ЛІКУВАННЯ ПАЦІЄНТІВ ІЗ ХВОРОБОЮ ПАРКІНСОНА

Оцінка тремору при хворобі Паркінсона має вирішальне значення для уточнення правильного діагнозу та лікування. На сьогодні, не існує загальновизнаного методу оцінки або вимірювання тремору. Метою роботи було вивчення можливостей використання методу електронейроміографії в діагностиці та оцінці результатів лікування хворих на хворобу Паркінсона. Для підтвердження характеру тремору, його оцінки, широку популярність набув метод електронейроміографії, який дозволяє за допомогою поверхневих електродів оцінити зміни, що відбуваються в м'язах агоністах-антагоністах при хворобі Паркінсона у спокої та при пробах, оцінити ефективність лікування. Обговорюється гіпотеза про зв'язок між тремором і розвитком тунельних нейропатій при хворобі Паркінсона, прогресуванням і прогнозом захворювання. Встановлено що прояви тунельних нейропатій більш характерні для тремор-домінантних форм захворювання та домінують на стороні початку захворювання. На фоні лікування спостерігається позитивна динаміка – зменшення частоти та амплітуди коливань як на домінантній, так і на протилежній стороні з даними електронейроміографічного дослідження, підвищення рухової активності.

Ключові слова: хвороба Паркінсона, електронейроміографія, ЕМГ-треморографія, діагностика, лікування.

The work 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 progressive neurodegenerative disease associated with degeneration of dopaminergic neurons and mainly among the old with increasing incidence with age [8, 12]. The main symptoms of PD are rigidity, rest tremor, bradykinesia, and postural instability [1]. PD is divided into two types according to the predominant clinical signs, which are the akinetic- rigid syndrome (ARS) and tremor dominant (TD). A clear clinical proof shows that different subtypes of PD have different clinical progressions and prognoses [14]. Majority of patients with PD experience rest tremor during their course of disease, that can be present either in the beginning or a latter phase of the disease, or the whole time. PD tremor is unilateral in onset and increases with rest [7].

Given the severity of symptoms, incorrect posture, gait, lifestyle changes, compression neuropathy (CN) is quite common in patients, it negatively affects the workforce and impairs quality of life. CN mainly covers the upper extremities, manifested in the form of carpal tunnel syndrome, cubital tunnel [7, 13]. Carpal tunnel syndrome (CTS) is the most commonly observed neuropathy in the general population, and it result from compression of the median nerve at the carpal tunnel level. Today, the hypothesis is being discussed that tremor in Parkinson's disease may be the cause of tunnel neuropathies, mainly carpal tunnel syndrome [2].

Methods of tremor assessment include simple clinical observation, standardized rating scales, objective clinical assessment of drawn figures, and computerized tremor analysis. As there are different kinds of tremor with numerous underlying causes, the process of tremor classification and evaluation is of critical importance to establish a correct diagnosis and initiate the most appropriate treatment [10].

Though tremor may be the most quantifiable of all movement disorders, there is currently no universally accepted method of rating or measuring tremor [4].

Clinically, to optimize comparability between patient populations, the Fana-Tolosa-Marina Tremor Rating Scale (TRS) was used in each part of the body [11].

Tremors are sinusoidal movements; they are amenable to quantitative mathematical analysis and modeling with a high degree of fidelity to the clinical picture. To record tremor activity, accelerometry, electromyography (EMG), and other signals are acquired, digitized through an analog-to-digital board and analyzed. With modern computers, tremors can be analyzed in real time at a high sampling rate or processed off-line [7]. Two of the most important characteristics of tremor assessed by tremor analysis are frequency and amplitude. In spite of tremors are typically described by frequency (such as parkinsonian rest tremor ranging from 3 to 6 Hz), patients are usually not greatly bothered by tremor frequency, but rather by the amplitude of their tremor [3].

The EMG tremorography provides complete information about the activity of the muscles involved in the generation of tremors. Method can provide information on the recruitment and synchronization of motor units, as well as draw parallels between the muscles involved and tremor movements, revealing whether the antagonist muscles are working simultaneously or alternately, causing tremors [11].

The purpose of the research was to study the possibilities of using the electroneuromyography method in the diagnosis and assessment of treatment results in patients with Parkinson's disease.

Materials and methods. We examined 84 patients with PD who were treated at Poltava Regional Clinical Hospital. The diagnosis was put according to the United Kingdom PD Society Brain Bank Clinical Diagnosis Criteria. The Hoehn and Yahr (H&Y) scale was used to determine PD severity and disability.

Patients were divided into 2 groups according to the motor subtype: group 1 – patients with akinetic-rigidity-tremor subtype (n=48), group 2 – with an akinetic-rigidity subtype (n=36). Control group consists of 26 patients without signs of neurodegenerative disease. Each group collected demographic data and the overall score of Unified Parkinson's Disease Rating Scale (UPDRS) – III part, for estimation tremor [9, 15]. The criteria of inclusion are: availability of PD stage by H&Y scale 2–3, age younger than 80 years, the main method of treatment of levodopa and agonist dopamine therapy. Criteria of exclusion: secondary parkinsonism, “parkinsonism-plus”, stage of PD by H&Y scale more than 3, cerebrovascular diseases, age 80 years and older, presence in patients of 1) clinical or electrophysiological evidence of concomitant conditions that can mimic tunnel syndromes of the upper extremities; 2) treatment with vitamin B1, B2 or B12, or with steroid hormones; 3) systemic diseases.

To assess the severity of the tremor and to study the conduction along the peripheral nerves, all patients underwent surface interference EMG of agonist-antagonists of the forearms from both sides at rest, with a postural and a coordinator test at 23°C to 25°C. Conduction along the motor fibers of the upper extremities was assessed using stimulation EMG at different levels using the method of short distances. 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. 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.

Statistical analysis of the obtained data was performed using IBM SPSS Statistic v. 26.0 (IBM inc., USA) and EZR Statistics 1.53 (Jichi Medical University, Japan). Normality of distribution of quantitative data have assessed according to the Shapiro-Wilk test. The obtained data were processed by the methods of descriptive statistics, according to which the arithmetic mean and standard error (M±σ) for normal distribution and medians (Me) with interquartile (25-75 %) range (Q1-Q3) were calculated. Qualitative features were presented in the form of absolute values (n) and percentages (%). Comparisons of qualitative indicators were performed using the Fisher's exact test for 2×2 tables. Comparison of data in 2 groups with non-normal distribution was performed by the Mann-Whitney test and with normal ones by T-test for independent groups. One-way analysis of variance (ANOVA) with Bonferroni correction test was used to comparison in 3 independent groups. Kruskall-Wallis criterium was used for analysis ENMG features. For post hoc analysis, we have used Steel-Dwass test. The critical p-value was considered 0.05.

Results of the study and their discussion. According to the data obtained, the patients were divided into groups. All patients were matched for age, sex and duration diseases. Mean age in group 1 was 59.94±7.97, in group 2 – 62.13±10.39, in control group – 58.63±6.16. In group 2 age was significantly higher (p=0.047). In the group 1 male/female ratio was 28/20, in group 2 – 19/17 and in control – 14/12. Male portion in group was larger (p=0.032). In group 2 was higher (p=0.014) duration of the disease than in a group 1 (9.13±1.87 vs. 6.42±2.13 years). Body mass index in group 1 was 27.13±3.59 kg/m^2, in group 2 – 25.4±3.93 kg/m^2, in control group – 22.41±3.37 kg/m^2. It was significantly higher (p=0.021) in the group 2.

H&Y stage was 2.7 (0.3-2.9) in group 1 and 2.8 (0.8-3.0) in group 2 (p=0.351). At the same time UPDRS tremor score was 2.3 (0.3–3.5) in group 1 and 1.0 (0.0–3.0) in group 2 (p=0.117). We had not find significant differences between groups by these features. In group 1 was 26 (54.2 %) patients with right-sided symptoms onset and 22 (48.8 %) with left-sided and in group 2 – 12 (33.3 %) and 24 (66.7 %) accordingly without significant difference of portions (p=0.094).

According to the data obtained, the first group included patients with akinetic-rigid tremor form, where the dominant symptom was tremor, the second group of patients – with akinetic-rigid form of the disease. Medians of the severity of the disease according to the H&Y scale was 2.7 stage of Parkinson's disease in group 1 and 2.8 stage – in group 2. According to the data obtained in 26 patients of the first group and 12 patients from group 2 the disease started on the right side, in 22 patients from group 1 and 24 patients from group 2 on the left side.

Assessment of tremor in groups of patients was performed using interference surface ENMG-tremography using superficial skin electrodes with a fixed distance. The technique was performed at room temperature, in a sitting position, at rest, during postural and kinetic tests of agonist muscles and antagonists of the forearms on both sides, as shown in table 1.

Table 1

ENMG characteristics of tremor in the study groups

Indices	Side	Groups		
		Group 1 (n=48)	Group 2 (n=36)	Control group (n=26)
Forearm agonist muscles				
At rest: amplitude, мV	R	23.4±3.3 ^/^^	0	0
	L	19.9±3.1^/^^	0	0
frequency Hz	R	3.8±0.78^/^^	0	0
	L	3.4±0.75^/^^	0	0
Postural test: amplitude, мV	R	46.4±16.1*/^/^^	9.1±0.21*/^	0
	L	40.8±12.5*^/^^	13.1±1.1*/^	0
frequency Hz	R	4.6±1.3*^/^^	0.72±0,31	0,1±0.07
	L	3.1±0.93^/^^	0.93±0,28	0,4±0.11
Kinetic test: amplitude, мV	R	34.2±14.1**/^/^^	6.1±0.011^	0
	L	32.2±11.3**/^/^^	10.2±1.3^	0
frequency Hz	R	3.5±0.97^/^^	0	0
	L	2.7±0.65^/^^	0	0
Antagonist muscles of the forearms				
At rest: amplitude, мV	R	22.3±4.4^/^^	0	0
	L	24.3±2.6^/^^	0	0
frequency Hz	R	4.2±0.92^/^^	0	0
	L	3.9±0.69^/^^	0,12±0,031	0
Postural test: amplitude, мV	R	42.9±7.6*/^/^^	9.1±0.13^	0
	L	46.2±4.5*/^/^^	13.5±3.5*/^	0
frequency Hz	R	6.8±1.3*/^/^^	0.91±0.26	0
	L	6.6±1.5*/^	0.76±0.18	0
Kinetic test: amplitude, мV	R	31.8±6.4**/^/^^	7.2±0.53*/^	4.4±0.22**
	L	38.2±3.3**/^/^^	9.8±2.2^	2.6±1.7**
frequency Hz	R	5.1±0.23**/^/^^	0	0
	L	4.8±0.46**/^/^^	0.13±0.024	0

Note. * – between rest and postural test (p<0.05), ** – between postural and kinetic tests (p<0.05), ^ – compared to control group (p<0.05), ^^ – between the patients of Group I and Group II (p<0.05).

EMG reflection of tremor is burst activity. An EMG profile of PD rest tremor typically shows alternating (less commonly synchronous) contraction of agonist and antagonist muscles at a frequency of less than 6 Hz with relatively sinusoidal displacement.

In the group of patients with akinetic-rigid form of the disease, the presence of subclinical low-frequency and low-amplitude tremor in the form of bursts of oscillations with an accent in the dominant side was revealed. This indicates that in Parkinson's disease there cannot be some form of isolation. Each patient has manifestations of both rigidity and tremors, so the forms are mixed with a predominance of some kind of syndrome. Terminal latency by ENMG measurement was 4.3±0.9 ms in group 1, 3.16±0.7 ms in group 2 and 3.23±0.9 in control group for cubital channel and 4.76±0.9 ms in group 1, 3.23±0.6 ms in group 2 and 3.1±0.9 ms in control group for carpal channel without significant differences (p=0.533 and p=0.482 accordingly). The amplitude of the motor response at the distal point of stimulation was within normal limits, but there was a sharp decrease in amplitude during stimulation at the level of the cubital

channel, namely: the maximum drop in the first group of patients at the elbow flexion and lower third of the shoulder 2.3±0.7 μV and 2.8±0.5 μV (p=0.014 and p=0.011 respectively) compared to group 2 and control group (fig.1).

There is also a decrease in the rate of excitation at the level of the elbow flexion – the lower third of the shoulder to 23.12±5.3 m/s (p=0.026) compared with group 2 – 45.1±10.3 m/s and the control group 44.3±9.8 m/s (fig.2).

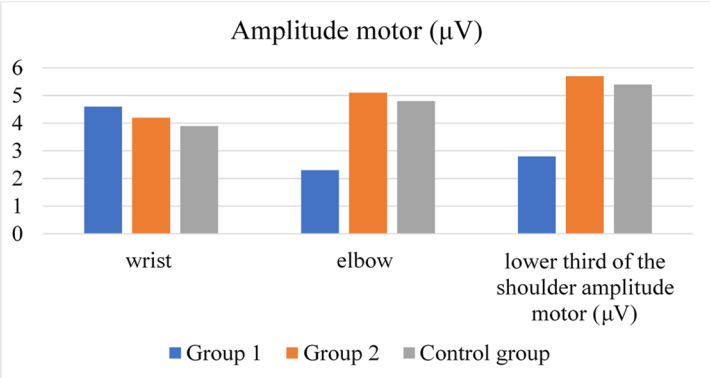

Fig.1. Amplitude motor in cubital channel

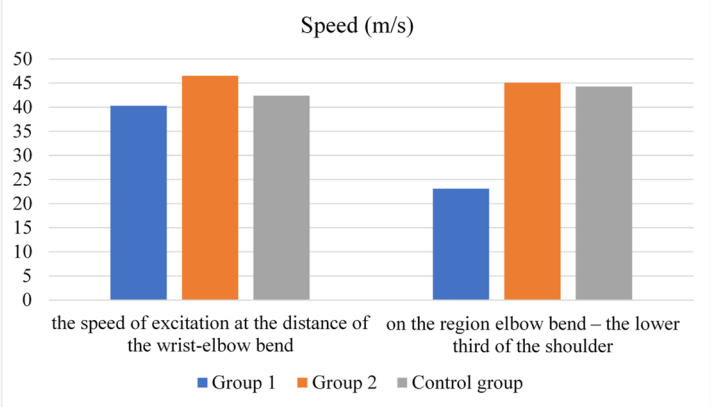

Fig.2. ENMG measurement of speeds in cubital channel

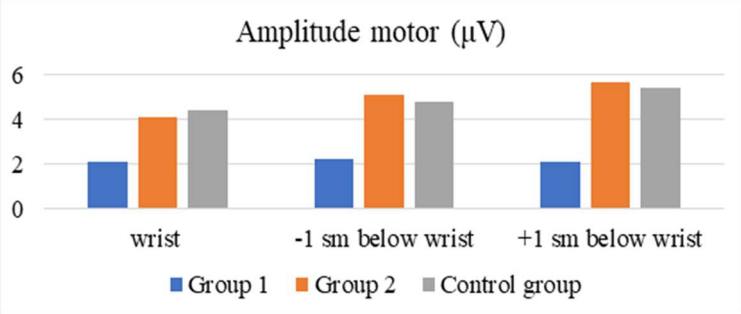

Fig.3. Amplitude motor in carpal channel

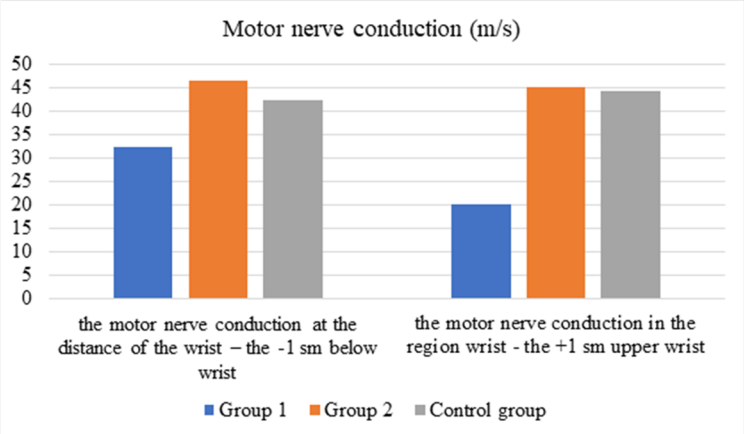

Fig.4. Motor nerve conduction in carpal channel

ENMG criteria in the diagnosis of median tunnel neuropathy (carpal tunnel syndrome) were as follows: increased terminal latency in the median nerve ≥4.2 m/s, decreased conduction in the motor and sensory fibers ≤40 m/s for the segment -wrist – distance + 1 cm above and below the wrist and a decrease in amplitude at the second point of stimulation of more than 30 %.

For carpal tunnel neuropathies in groups of patients terminal latency by ENMG measurement was 4.76±0.9ms in the 1 group 3.23±0.63 ms – in the group 2 and 3.1±0.9 ms in control group (p=0.482). There was also a decrease in the amplitude of the muscular response at the level of the wrist, 1 cm below and above the wrist 2.1±1.1 μV – 2.2±0.4 μV and 2.1± 0.5 μV, respectively (p=0.012, p=0.007, p=0.006, respectively) (fig.3).

From the speed of excitation along the motor fibers of the ulnar nerve, there was a decrease in velocity at a distance of -1 cm below the wrist and +1 cm above the wrist 32.3±9.4 m/s and 20.21±5.7 m/s (p=0.004) in comparison with the control group 42.4±10.3 and 44.3±9.8 m/s and the group of patients 2: 46.5±12.1 m/s and 45.1±10.3 m/s (fig.4).

ENMG criteria for the diagnosis of ulnar tunnel neuropathy (cubital channel) were as follows: decrease in the amplitude of the motor response at the level of the second point of stimulation (elbow), decrease in the speed of excitation along the motor nerve to 40 m/s from the wrist to the next points of stimulation (-1 or +1 cm) above or below the elbow).

It can be noted that the manifestations of tunnel neuropathy, carpal or cubital canal syndrome, are more typical for tremor-dominant forms of the disease. Manifestations of neuropathy dominate on the side of pronounced motor symptoms, on the side of the onset of the disease.

After treatment with levodopa drugs (levodopa/carbidopa 250/25 mg ½ tablet 2 times a day and ¼ tablet 2 times a day one hour before or an hour after a meal, prolonged-release pramipexole at a dose of 0.75 mg 1 time per day in the morning for 1 month), patients noted a decrease in tremor, increased motor activity. In the study with the help of ENMG agonists-antagonists of the forearms from two sides, it was revealed: a decrease in the frequency and a decrease in the amplitude of oscillations both on the dominant side and on the opposite side (Table 2).

Table 2

ENMG- characteristics of tremor in the study groups after treatment

Indices	Side	Groups		
		Group 1 (n=48)	Group 2 (n=36)	Control group (n=26)
Forearm agonist muscles				
At rest: amplitude, мV	R	19.1±2.2*	0	0
	L	13.9±1.2*	0	0
frequency Hz	R	2.8±0.25*	0	0
	L	2.9±0.34*	0	0
Postural test: amplitude, мV	R	22.1±16.1*	6.1±0.11*	0
	L	29.8±8.7*	7.1±0.92*	0
frequency Hz	R	3.1±0.94*	0.42±0.13	0.19±0.071
	L	2.2±0.23*	0.61±0.12	0.43±0.11
Kinetic test: amplitude, мV	R	28.3±1.1*	3.1±0.012*	0
	L	18.5±7.2*	5.1±0.11*	0
frequency Hz	R	3.0±0.97*	0	0
	L	2.7±0.65*	0	0
Antagonist muscles of the forearms				
At rest: amplitude, мV	R	18.8±3.7*	0	0
	L	19.1±1.8*	0	0
frequency Hz	R	2.8±0.37*	0	0
	L	2.2±0.32*	0.11±0.053	0
Postural test: amplitude, мV	R	26.7±3.8*	6.1±0.82	0
	L	21.09±3.5*	10.1±1.3	0
frequency Hz	R	4.2±1.3*	0.36±0.18	0
	L	4.1±1.4*	0.27±0.11	0
Kinetic test: amplitude, мV	R	22.8±6.4*	7.1±0.5	4.4±0.23
	L	19.2±3.2*	9.9±2.3	2.6±1.7
frequency Hz	R	3.2±0.13*	0	0
	L	2.7±0.32*	0.1±0.02	0

Note: * – compare to data before treatment in Table 2 ($p<0.05$).

As a result of our research, we found that the prevalence of tremor is characteristic of a group of patients with a dominant tremor form of Parkinson's disease. Despite the fact that it is known from the literature that the disease is characterized by rest tremor, an increase in the amplitude and frequency of tremor in the postural test in both groups of patients with Parkinson's disease with an emphasis on the dominant side. In group 1 of patients with the tremor-dominant form of the disease, the maximum increase in the frequency of tremor is observed in the antagonists of the forearms on the dominant side. Kinetic test (finger-nose test) leads to a decrease in the frequency and probable decrease in the amplitude of tremor, which is confirmed in the literature and allows to distinguish this tremor from other types [1].

Manifestations of tunnel neuropathies, namely, carpal and cubital canal syndrome, are more characteristic of akinetic-rigid-trembling forms of the disease and dominate on the side of the disease, on the side of motor deficit, which can be explained by increased muscle tone, forced position of the extremities against the background diseases [5, 6].

The use of ENMG-tremography in practical medicine is well-founded, valuable in the diagnosis of the disease in the early stages, as a method of diagnosing disease predictors and as a diagnostic criterion for inserting the type of tremor, diagnosis of neuropathies, assessment of treatment dynamics in Parkinson's disease.

Conclusion

Thus, the study found that electromyography can be used to objectify the prevalence of trembling Parkinson's disease, to establish the exact characteristics of tremor at rest and during functional tests (postural and finger-nose tests). This technique, performed using interference electroneuromyography, the method of short intervals, is indicated in the diagnosis of tunnel neuropathies, namely carpal tunnel and cubital channel syndrome, which is more common in akinetic-rigid-tremor-dominant form of the disease. The technique makes it possible to determine conduction disorders in the motor and hay fibers of peripheral nerves at different levels of the spinal cord.

It has been proved that tunnel neuropathies predominate on the side of the onset of symptoms and are associated with forced limb position, increased limb tone (outside the flexor – the petitioner). The appearance of subclinical tremor on the non-dominant side of the disease can be considered as a predictor of neurodegenerative disease, namely Parkinson's disease.

The ENMG study revealed an improvement in tremor (decreased frequency and amplitude) in the treatment of Parkinson's disease with levodopa and dopamine agonists.

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