

What determines spontaneous physical activity in patients with Parkinson's disease?

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Abstract: Physical activity (PA) is a factor that may have an influence on the symptoms of Parkinson's disease (PD). The aim of this study was to identify the potential determinants of spontaneous PA in the PD patient group. 134 PD patients aged 65.2±9.2 years, Hoehn-Yahr scale ≤ 4, Mini Mental State Examination (MMSE) ≥ 24 were examined. For the study purposes, the authors analyzed: age, sex, education, history of PD, dopaminergic treatment, the severity of PD symptoms using Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn-Yahr scale. Additionally all participants were evaluated through a set of scales for specific neuropsychiatric symptoms including: depression, anxiety, apathy, fatigue and sleep disorders. An analysis of linear regression was used with backward elimination. In the total explanatory model, 12% of the variability in activity ($R^2=0.125$; $F(16.133)=2.185$; $p<0.01$), the significant predictor was starting therapy with the dopamine agonist (DA) ($\beta=0.420$; $t=4.068$; $p=0.000$), which was associated with a longer duration of moderate PA. In the total explanatory model, for more than 13% of the variance in time spent sitting ($R^2=0.135$; $F(16.130)=2.267$; $p<0.01$), the significant predictors were secondary education and the results of the UPDRS. The patients with secondary and vocational education, those starting treatment with DA and those with a less severe degree of Parkinson's symptoms (UPDRS) spent less time sitting in a day. It is possible to identify determinants of spontaneous PA. It may elucidate consequences in terms of influence on modifiable conditions of PA and the proper approach to patients with unmodifiable PA factors.

Keywords: Parkinson's disease; physical activity; sedentary way; non-motor symptoms; apathy; dopaminergic therapy

Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative diseases and the most common form of parkinsonian syndrome. It affects 1% of people older than 60 years of age and 4% of people older than 80 years of age [1]. The main symptoms of PD primarily result from the dopaminergic deficit and include bradykinesia, tremor, rigidity and postural instability, but in the course of PD, there are also numerous non-motor symptoms including neuropsychiatric, autonomic and digestive-intestinal aspects [2].

The evidence collected thus far indicates that one of the important non-pharmacological interventions in the course of PD is the physical activity (PA) of the patients [3,4,5]. Even cortical activity tends to increase with PA like walking and balance tasks in older and PD groups compared to baseline conditions (sitting/standing) or controls [6]. The beneficial effects of PA on the central nervous system (CNS) are associated with many factors, including neurotrophic factors and, above all, the cerebral nerve growth factor and attributable neuroplasticity [7,8]. Which is promising while

current PD treatments are aimed at addressing motor symptoms but there is no therapy focused on modifying the course of the disease [9].

So far, the literature has not elucidated the determinants of physical activity or inactivity in patients with PD. The present study analyses the impact of sociodemographic factors, clinical features of the disease and treatment on the time patients spend participating in spontaneous PA.

Material and Methods

Subjects

A total of 134 PD patients aged 65.2 ± 9.2 years (61 women, 73 men), treated at the outpatient Neurology Clinic of the Silesian Medical University in Katowice, were examined. The study was approved by the Bioethics Committee of the Academy of Physical Education in Katowice (12/2013). All participants signed the informed consent form. PD was diagnosed based on the principles of the United Kingdom Parkinson's Disease Society Brain Bank. Patients diagnosed with Parkinson's syndromes other than idiopathic PD and patients with diagnosed PD whose mobility disorders may have resulted from other previous or concomitant diseases, e.g., stroke and circulatory insufficiency with reduced exercise tolerance, were not eligible for the study. All other diseases in stable patients were under medical supervision. In the examined group, the basic treatment was levodopa followed, in the frequency of use, by a DA. The levodopa equivalent daily dose (LED) was calculated on the basis of the conversion ratios accepted based on the literature review [10]. The participants were patients with Hoehn-Yahr stage [11] ≤ 4 with a Mini-Mental State Examination (MMSE) score [12] ≥ 24 points, and the with a duration of symptoms and dopamine replacement therapy (DRT) ≥ 0.5 year.

Table 1. Characteristics of the subjects.

Variable	M [SD]
Sex: women/men [n]	61 / 73
Age [years]	65.2 [9.2]
Place of residence [%]	A city with over 100 thousand inhabitants.
	A city with fewer than 100 thousand inhabitants.
Marital status [%]	Married
	Single
	Basic
Education [%]	Professional
	Medium
	High
Accompanying conditions [%]	84.3
The age of the start of symptoms [years]	57.9 [11.1]
EOPD / MOPD / LOPD [%]	21.6 / 66.4 / 12.7
The duration of the disease [years]	7.3 [4.2]
Hoehn-Yahr scale [degrees]	2 [0.6]
Time to start treatment [years]	1.4 [1.5]
Daily levodopa equivalent dose - LED [mg]	755.4 [418.7]
Levodopa / dopaminergic agonist [%]	96 / 52

EOPD, early onset Parkinson's disease; MOPD middle age onset Parkinson's disease; LOPD, late onset Parkinson's disease

Methods

The study used a diagnostic survey with an authorial questionnaire for the purpose of gathering information on demographics, the clinical picture of PD, concomitant diseases and treatment of the PD patient. The questionnaire was verified in terms of accuracy and reliability in the pilot studies preceding the main study.

The severity of PD symptoms was evaluated using the UPDRS scale and the Hoehn-Yahr scale [11]. For mental performance, the MMSE was used [12]. PA was assessed using the International Physical Activity Questionnaire (IPAQ) [13] and the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ) [14]. The questionnaires concerning activity were conducted by the researcher. For the assessment of non-motor symptoms (NMS), the following evaluations were used: depression and anxiety - the Beck Depression Inventory (BDI) [15] and the Hospital Anxiety and Depression Scale (HADS) [16], apathy – the Apathy Scale (AS) [17], fatigue – the Parkinson's Fatigue Scale (PFS-16) [18,19], sleep disturbances – the Pittsburgh Sleep Quality Ratio (PSQI) [20,21], and excessive daytime sleepiness – the Epworth Sleepiness Scale (ESS) [21].

For the analysis of PA, the data coming from IPAQ [13] and MLTPAQ [14] concerning the type of PA undertaken based on the level of difficulty (light, moderate, average), the duration of participation (hours/minutes) and the frequency during the week (number of days) was used.

To assess the results, the following operationalization of data concerning PA was conducted: the index of time of moderate weekly activity was calculated (ITMWA), which was established by the following formula: $ITMWA = (\text{average time of moderate physical activity from the MLTPAQ questionnaire} + \text{average time of moderate weekly activity from the IPAQ questionnaire}) / 2$. On the basis of a percentile empiric division of the results obtained, the patients were divided into two groups: the 33% least active (ITMWA < 45 minutes a week) and the 33% most active (ITMWA > 2,5 hrs a week), which constituted the basis to characterize inactive and active patients.

Results

As potential factors impacting the duration of PA expressed by means of ITMWA, the following factors were taken into account: age, sex, education, type of medication initiating the therapy and the current treatment, LED, stage of disease based on the Hoehn-Yahr scale, severity of movement symptoms in part III of the UPDRS scale, degree of intensification of other Parkinson's symptoms based on the UPDRS scale parts I+II+III, anxiety, depression, apathy, fatigue and sleep disorders. The results of the assessment of all the factors listed using methodology tools are presented in Table 2.

The physically "inactive" PD patient group (PI-G), compared to the physically "active" PD patient group (PA-G), was characterized by a longer duration of the disease (8.2 ± 4.2 vs 6.3 ± 4.0 ; $p < 0.01$) and less frequent treatment initiation with dopaminergic receptor agonist (DA) (1.9% (N=1) vs 21.8% (N=12); $p < 0.01$). In addition, PI-G had greater difficulties performing the activities of daily living (ADLs) assessed by UPDRS II (9.2 ± 5.5 vs 7.0 ± 5.7 ; $p < 0.05$), and the PI-G more often suffered from apathy (15.9 ± 5.6 vs 13.2 ± 5.4 ; 63.5% (N=33) vs 49.1% (N=27); $p < 0.05$). The other analyzed factors did not reveal statistically significant differences between the PA-G and PI-G.

Table 2. Characteristics and results of the physically active and physically inactive subjects.

Variable	PA-G (n=55)	PI-G (n=53)	p value
Age [years]	66.3 ± 8.1	65.5 ± 10.0	0.516 ¹
Sex	W – 45.5% (N=25)	W – 47.2% (N=25)	0.858 ²
[W – women, M – Men]	M – 54.5% (N=30)	M – 52.8% (N=28)	
The duration of the disease [years]	6.3±4.0	8.2±4.2	p<0.01 ¹
Age of onset of [years]	65.4 ±8.1	66.3 ±10.0	0.622 ¹
UPDRS I [points]	1.3±1.9	1.6±1.4	0.405 ¹
UPDRS II [points]	7.0±5.7	9.2±5.5	p<0.05 ¹
UPDRS III [points]	24.9±12.5	27.1±13.0	0.246 ¹
UPDRS IV [points]	1.8±1.7	2.3±2.8	0.381 ¹
Hoehn-Yahra scale [degree]	2.2±0.6	2.4±0.6	0.055 ¹
LED [mg]	730.4±433.4	797.6±414.7	0.177 ¹
Treatment: levodopa / DA [%]	96.4 (N=53)	98.1 (N=52)	0.580 ²
Start of treatment with levodopa [%]	74.5 (N=41)	83.0 (N=44)	0.282 ²
Start of treatment with DA [%]	21.8 (N=12)	1.9 (N=1)	p<0.01 ²
Time to initiate treatment [years]	1.3 ±1.4	1.0 ±1.5	0.212 ¹
Depression BDI [M±SD]	9.5 ±6.4	11.9 ±8.6	0.287 ¹
[% with depression]	23.6 (N=13)	35.8 (N=19)	
Depression HADS [M±SD]	4.9 ±3.7	5.3 ±3.7	0.462 ¹
[% with depression]	20.0 (N=11)	26.4 (N=14)	
Anxiety HADS [M±SD]	5.7 ±3.9	5.1 ±3.4	0.517 ¹
[% with anxiety]	29.1 (N=16)	24.5 (N=13)	
Apathy AS [M±SD]	13.2 ±5.4	15.9 ±5.6	p<0.05 ¹
[% with apathy]	49.1 (N=27)	63.5 (N=33)	
Fatigue PFS-16 [M±SD]	2.8 ±0.9	3.1 ±1.0	0.078 ¹
[% with fatigue]	27.3 (N=15)	45.3 (N=24)	
Sleep disorders PSQI [M±SD]	6.4 ±3.3	6.2 ±3.6	0.634 ¹
[% with sleep disorders]	56.4 (N=31)	52.8 (N=28)	
Excessive daytime sleepiness ESS [M±SD]	6.3 ±4.9	7.7 ±5.3	0.167 ¹
[% with excessive daytime sleepiness]	21.8 (N=12)	39.6 (N=21)	

PA-G - Physically Active Patients, PI-G - Physically Inactive Patients

After analysing the complete model, using an analysis of linear regression with the method of backward elimination for each explained variable, the optimum model of factors affecting PA was created to explain the largest variance of data. Only those models that explained more than 10% of variability are discussed below.

The complete model explained 12% of the variation in PA and was statistically significant ($R^2=0.125$; $F(16.133)=2.185$; $p<0.01$). The only significant predictor was starting therapy with DA ($\beta=0.420$; $t=4.068$; $p=0.000$), which was associated with a longer duration of moderate PA. While performing the analysis to determine the best predictors in accordance with the principle of step-wise approach regression, it was found that 6 predictors, with the 2 most significant being beginning the treatment with DA and the severity of the disease based on the Hoehn-Yahr scale ($R^2=0.171$; $F(6.133)=5.585$; $p<0.001$), were responsible for 17% of the variability of ITMWA (table 3).

Table 3. Analysis of backward regression, which determines % of the variability of ITMWA, conditioned by the group of social-demographic and clinical predictors in the group of patients with Parkinson's disease.

Depended variable	Model	Predictors	R ²	F	p	β	t	p	
ITMWA	Complete model	Sex	R ² =0,125; F(16,133)=2,185; p<0,01			0,007	0,083	0,934	
		Age				0,041	0,452	0,652	
		Professional education				0,141	0,944	0,347	
		Medium education				0,092	0,551	0,582	
		High education				0,206	1,266	0,208	
		Levodopa treatment				0,138	1,493	0,138	
		DA treatment				0,033	0,364	0,717	
		MAOBI treatment				-0,047	-0,547	0,585	
		Amantadine treatment				0,010	0,119	0,905	
		Anticholinergic treatment				0,004	0,044	0,965	
		Start of treatment with levodopa				0,157	1,483	,141	
		Start of treatment with DA				0,420	4,068	0,000	
		LED				-0,087	-0,892	0,374	
		Hoehn-Yahra scale				-0,210	-1,821	0,071	
		UPDRS part III				0,352	1,181	0,240	
	UPDRS part. I+II+III	-0,242	-0,785	0,434					
	Optimal model highest value R ²	Higher Education	R ² =0,171; F(6,133)=5,585; p<0,001				0,105	1,261	0,210
		Levodopa treatment					0,120	1,421	0,158
		Start of treatment with Levodopa					0,153	1,537	0,127
		Start of treatment with DA					0,440	4,595	0,000
		Hoehn-Yahra scale					-0,238	-2,283	0,024
		UPDRS part III					0,144	1,400	0,164

R² – amount of explained variance, F – value of Fisher's statistics, p – statistical significance, β – significance of the predictor in the model, t – result of Student's t test

Another linear regression analysis was carried out to determine the significance of individual factors in the time spent being sedentary during the day. The complete model with the same predictors as in the previous analysis, in which the variable to be explained was the time spent sitting, explained over 13% of the variance and was statistically significant (R²=0.135; F(16,130)=2.267; p<0.01). Significant predictors in this model were secondary education, aggravation of movement disorders in part III of the UPDRS scale and intensification of Parkinson's symptoms in UPDRS scale, parts I+II+III. Assuming the best solution (i.e. model with the highest R²) in accordance with the principle of step-wise approach regression, it was found that 6 predictors, the most significant of which were vocational and secondary education, commencement of treatment with DA and intensification of mobility symptoms in part III on the UPDRS scale (R²=0.193; F(7,130)=5.429; p<0.001), were responsible for over 19% of the variability of daily time spent sitting (in a sedentary way). Less time spent sitting during the day was observed in the patients with vocational and secondary education, whose first medication for the treatment of PD was DA and who had more intensified mobility symptoms.

Table 4. Analysis of backward regression, which determines % of variability of time spent in the sedentary position conditioned by the group of social-demographic and clinical predictors in the group of patients with Parkinson disease.

Depended variable	Model	Predictors	R ²	F	p	β	t	p	
Time spent in the sedentary position	Complete model	Sex	R ² =0,135; F(16,130)=2,267; p<0,01			-0,013	-0,149	0,882	
		Age				0,070	0,768	0,444	
		Professional education				-0,262	-1,787	0,077	
		Medium education				-0,339	-2,026	0,045	
		High education				-0,198	-1,218	0,226	
		Levodopa treatment				0,017	0,178	0,859	
		DA treatment				0,007	0,077	0,939	
		MAOBI treatment				0,126	1,461	0,147	
		Amantadine treatment				0,032	0,376	0,708	
		Anticholinergic treatment				-0,002	-0,025	0,980	
		Start of treatment with levodopa				0,007	0,062	0,951	
		Start of treatment with DA				-0,151	-1,457	0,148	
		LED				-0,029	-0,290	0,772	
		Hoehn-Yahra scale				-0,006	-0,052	0,958	
		UPDRS part III				-0,817	-2,705	0,008	
	UPDRS part. I+II+III	1,047	3,362	0,001					
	Optimal model highest value R ²	Professional education	R ² =0,171; F(6,133)=5,585; p<0,001				-0,289	-2,124	0,036
		Medium education					-0,362	-2,320	0,022
		Higher education					-0,213	-1,388	,168
		Treatment MAOBI					0,125	1,541	0,126
Start of treatment with DA		-0,162					-1,996	0,048	
UPDRS part III		-0,813					-2,849	0,005	

As all the models tested, except those presented above, explained less than 10% of the variance of dependent variables concerning PA, additional analyses of regression (taking into account the predictors that, in particular models, turned out to be significant) were conducted.

When using the ITMWA as a dependent variable in the model, the predictors were education, duration of the disease, starting treatment with DA, severity of the disease on the Hoehn-Yahra scale and the level of depression symptoms (BDI). The analysis using the method of backward elimination showed that the optimal model takes into account only 3 predictors: duration of the disease, starting treatment with DA, and advancement of the disease on the Hoehn-Yahr scale. This model was significant and explained more than 15% of the variance (R²=0.151; F(3,133)=8.85; p<0.001). However, the only significant predictor turned out to be the start of treatment with DA, which was connected with increased duration of PA.

In the model where the variable was time spent sitting during the day, the predictors were education, intensification of mobility symptoms in part III of the UPDRS scale, intensification of parkinsonian symptoms based on the UPDRS scale parts I+II+III, commencement of DA treatment, the results of the PFS-16 fatigue scale and excessive sleepiness (ESS). The analysis conducted with the method of reverse elimination excluded only the results from the PFS-16 scale, causing the obtained optimal model to be significant, which explained over 19% of the variance (R²=0.195; F(7,130)=5.509; p<0.001). It was found that the patients with secondary and vocational education, who started treatment with DA and those who had less intense parkinsonian symptoms (UPDRS scale parts I+II+III), spent less time in a sedentary way during the day.

Table 5. Analysis of backward regression, which determines % of the variability of ITMWA and time spent in the sedentary position in a day in the group of patients with Parkinson disease (solely optimum models with the highest R^2 are presented).

Optimal model	Predictors	R^2	F	p	β	t	p
ITMWA	Duration of the disease	$R^2=0,151$; $F(3,133)=8,85$; $p<0,001$			-0,114	-1,379	0,170
	Start of treatment with DA				0,348	4,306	0,000
	Hoehn-Yahr scale				-0,105	-1,273	0,205
Time spent in the sedentary position	Medium education	$R^2=0,195$; $F(7,130)=5,509$; $p<0,001$			-0,375	-2,407	0,018
	Professional education				-0,294	-2,172	0,032
	Higher education				-0,202	-1,322	0,188
	UPDRS part. III				-0,589	-1,939	0,055
	UPDRS parts I+II+III				0,787	2,535	0,013
	Start of treatment with DA				-0,177	-2,190	0,030
	ESS				0,147	1,677	0,096

The overall level of PA in the examined group of patients with PD was low, which is also indicated by the results of other authors [22]. In terms of NMS, the authors only noted lower apathy in the group of more physically active patients with PD. The other NMS had no influence on the level of PA. Moreover, many authors have reported a clear relationship between lower intensity of these symptoms and PA [23,24,25]. However, this activity was undertaken within a planned rehabilitation context, and it was not likely to be replaced with spontaneous PA as a control of NMS. The level of education turned out to be one of the most important factors affecting participating in PA more often and for a longer duration and shortening the time during the day spent sitting. Thus, in the model explaining over 15% of the variability in the number of days participating in moderate activity, vocational and higher education were the strongest predictors ($p<0.05$). In previous research, the authors related a higher level of education with participating in health-oriented behaviours, including PA [26].

The results obtained in this study may indicate that patients with higher and secondary education have a greater awareness of pro-health behaviours and ways to create a healthy lifestyle. PA in this group may be a continuation of the previously practised healthy behaviours, including various forms of PA. In addition, participating in PA in this group may also be a result of a better understanding of the nature of the disease and non-pharmacological measures to improve health conditions. However, patients with vocational education may treat PA as a continuation of work-related activity more often. Additionally, in the model explaining almost 20% of the variability in lack of time spent participating in PA during the day, secondary and vocational education were strong predictors ($p<0.05$). Other authors also pointed to the importance of education in participating in PA in adult [27] and those diagnosed with PD [28].

One of the observations of the present study is that increased levels of PA were connected with the commencement of dopaminergic therapy with DA. In the model explaining nearly 20% of the variability in time spent sitting during the day, the start of dopaminergic therapy with DA was one of the 4 significant explanations ($p=0.030$). It is possible that the group of patients starting treatment with DA have less initial motor dysfunction and experience motor problems that disrupt their activity to a lesser extent. This may not be associated only with the oligosymptomatic onset of the disease but also with its mild course. At the same time, it can be assumed that with the appropriate treatment, patients who report more severe parkinsonian symptoms with greater negative effects on

daily functioning receive the levodopa drug first to initiate the treatment. LED did not affect the level of PA, which was also reported by other researchers [26]. It should also be taken into account that the reduced risk of motor complications in patients who use DA but not levodopa at the beginning of their treatment makes these patients more physically active. This topic requires further research. It has been reported that DA group drugs (described here as pramipexol) can result in physical exercise dependence, which is a form of impulse control disorder [29]. The authors also observed such disorders in the course of ropinirole therapy. However, it should be noted that this type of disorder may manifest in patients who are currently using the drug and will probably not affect patients who have discontinued DA therapy. A short assessment of the disorders of impulse control is necessary when excessive PA is recorded for a patient treated with DA. It is also one of the important reasons for the assessment of spontaneous PA in patients with PD, with the need to search for ways to best evaluate it and unify the methods of its examination.

Other strong predictors of the number of days with moderate PA in the model described above explained over 15% of the variance in this variable, except for education and commencement of treatment with DA, and included the continuation of treatment with DA in this group. This phenomenon seems to be connected with the analogic mechanisms related to starting therapy with DA. In turn, in the model explaining almost 20% of the variability in time spent sitting during the day, except for education and commencement of treatment with DA, the intensification of Parkinson symptoms assessed by the sum of the points from part I, II and III of the UPDRS scale was the strongest predictor in this case. Therefore, with reference to patients with PD, the time spent participating in PA becomes shorter for the benefit of time spent sitting. The result of the degree of intensification of Parkinson symptoms, both in terms of mobility and non-mobility, and the limitations in everyday functioning are generally related to increased disability in the middle-aged period, which has also been noted by other authors [30].

In the case of average weekly PA time, the model accounting for 17% of the variability included the following significant predictors: starting treatment with DA and lower stage of Hoehn-Yahr disease, which were associated with a longer duration of physical activity. In turn, among all significant factors that explained over 19% of the variance in time spent sitting during the day, the following were notable: vocational and secondary education, lesser total intensification of symptoms from parts I, II and III of the UPDRS scale and, as previously discussed, commencement of treatment with DA. All of the factors mentioned above were predictors of less time spent sitting during the day.

In this paper, the importance of the Hoehn-Yahr scale for scientists was confirmed. The subsequent degrees of the scale reflect the symptoms determining patient mobility. The result of the Hoehn-Yahr scale also depends on the presence of posture disorders, which are usually connected with distinctive motor deterioration. The Hoehn-Yahr scale turned out to be more useful in the analysis of the movement aspects of the disease than Part III of the UPDRS, whose paradoxically lower result is associated with a longer time spent sitting. This result may be related to the fact that with lower intensity of tremor or by slowing down, patients need less time to perform daily activities; hence, they can spend more time sitting, and this effect disappears when assessing the results of parts I and II of the UPDRS.

Conclusions

The results obtained in this study indicate the association between the selected clinical, demographic and therapeutic factors and the PA undertaken by PD patients. It may allow for better identification of the patients threatened by lack of activity and may help increase their activity levels.

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