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Educational level and cognitive impairment in patients with Parkinson disease

Wykształcenie a zaburzenia funkcji poznawczych u osób z chorobą Parkinsona

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Abstract

Background and purpose: Parkinson disease (PD) is a risk factor for dementia. In addition, specific cognitive deficits can occur in PD patients without dementia. A patient's level of education could have an influence on the development of cognitive impairment in PD. The aim of this study was to examine the relationship between the level of education and cognitive performance in non-demented patients with PD.
Material and methods: Thirty-seven consecutive, nondemented PD patients and 40 healthy controls fulfilled the inclusion criteria and were enrolled in the case-control study. Each of the controls and PD patients were classified, for the purpose of this study, into one of three groups (low, intermediate, higher), categorized by the number of years of education. There were no differences in education and age between the controls and PD patients. All of the subjects were evaluated with a battery of neuropsychological tests: Mini-Mental State Examination, Trail Making Tests, Stroop Test, Mental Rotation Test, and Verbal Fluency Test.
Results: Less (low and intermediate) education was correlated with poor results from tests. The comparison of all groups of PD patients and controls demonstrated that PD subjects received lower test scores, especially for the low and intermediate groups. However, no statistically significant difference was reached between educationally advanced PD patients and the appropriate control subjects.
Conclusions: As compared to the controls, most non-demented PD patients presented executive-type cognitive dysfunction. The higher educational level, however, was associated

Streszczenie

Wstęp i cel pracy: Choroba Parkinsona (ChP) jest czynnikiem ryzyka wystąpienia otępienia, pewne zaburzenia poznawcze mogą występować jednakże już u chorych niespełniających kryteriów demencji. Poziom wykształcenia może mieć wpływ na obecność zaburzeń poznawczych. Postuluje się, że niski poziom edukacji może być związany z szybszym pogorszeniem funkcjonowania poznawczego, a wyższe wykształcenie może stanowić czynnik ochronny. Celem badań była próba ustalenia związku pomiędzy obecnością zaburzeń poznawczych a poziomem wykształcenia u chorych na ChP bez otępienia.
Materiał i metody: Przebadano 37 chorych na ChP i 40 osób z grupy kontrolnej. Dla celów pracy badanych podzielono na trzy podgrupy w zależności od poziomu wykształcenia (podstawowe/zawodowe, średnie, wyższe). Poszczególne podgrupy osób badanych i kontrolnych nie różniły się pod względem liczebności i wieku. W obu grupach oceniono funkcjonowanie poznawcze przy zastosowaniu testów psychologicznych (Krótka Skala Oceny Stanu Psychicznego, Test Łączenia Punktów, Test Stroopa, Test Rotacji Figury, Test Fluencji Słownej).
Wyniki: Niższe wykształcenie (podstawowe/zawodowe i średnie) wiązało się z gorszymi wynikami testów psychologicznych. Porównanie grupy chorych i kontrolnej wykazało, iż chorzy osiągają gorsze wyniki testów, w szczególności chorzy z niższym wykształceniem (podstawowym/zawodowym i średnim) w porównaniu z osobami z grupy kontrolnej o tym samym poziomie wykształcenia. Porównując chorych na ChP

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with a lower risk of cognitive deterioration. We conclude that higher education might have protective effects in cognitive decline in PD.

Key words: Parkinson disease, cognitive impairment, educational level.

i grupę kontrolną z wykształceniem wyższym, nie stwierdzono znamiennych statystycznie różnic dla wyników żadnego z testów.

Wnioski: U osób z ChP bez otępienia stwierdzono występowanie niewielkiego stopnia, łagodnych zaburzeń poznawczych. Wyższy poziom wykształcenia związany był z niższym ryzykiem wystąpienia zaburzeń, dlatego może być czynnikiem ochronnym dla zaburzeń poznawczych w ChP.

Słowa kluczowe: choroba Parkinsona, zaburzenia poznawcze, poziom wykształcenia.

Introduction

Cognitive deficits are common in Parkinson disease (PD), even in early stages and in newly diagnosed cases [1-4]. In many patients, these deficits may not be clinically apparent, but they are detectable with specific neuropsychological tests. According to Caviness *et al*., neuropsychological testing for abnormalities in nondemented patients could have predictive value for the potential development of dementia [5]. The most frequent early cognitive abnormalities in PD are executive and visuospatial dysfunction, attention and memory impairment, and bradyphrenia [6-9].

The prevalence of dementia in PD is estimated at a level of 24 to 31% [10,11], and longitudinal studies show a frequency as high as 60% after 12 years of follow-up [12] and even 83% in 20-year survivors [13]. With such high rates of cognitive decline, diagnostic methods and tests that could help in identifying PD patients at higher risk of developing dementia could be useful in planning patient management and treatment.

A number of risk factors for cognitive deterioration and dementia in PD patients have been identified, including the following: older age [11,12,14,15], later age at onset [4,14], longer duration of PD [12], more advanced motor symptoms [15] and bradykinesia-dominant PD with postural instability and gait difficulty [8,15,16].

Recently, the positive role of education has been described in a number of studies; the data suggest that a more advanced educational level seems to be protective against cognitive dysfunction, while poorer education was associated with a faster rate of cognitive decline in nondemented patients with PD [2,6,11,15, 17-19].

The aim of this study was to assess the relationship between the level of education and cognitive performance in nondemented PD patients.

Material and methods

Patients

Thirty-seven consecutive PD patients admitted to the Department of Neurology at Poznan University of Medical Sciences were examined between January 2006 and November 2007. Patients were included in the study on the basis of UK Parkinson's Disease Society Brain Bank criteria for idiopathic PD and evaluated for the severity of symptoms using the Unified Parkinson's Disease Rating Scale (UPDRS). None of the patients fit the American Academy of Neurology (AAN) criteria for having dementia in PD assessed by the Clinical Dementia Rating (CDR) scale and the Mini-Mental State Examination (MMSE) [20,21]. Moreover, the subjects with depression and advanced motor symptoms (UPDRS > 50) that impeded neuropsychological examination were also excluded from the study.

The patients were treated with the following: levodopa plus a peripheral levodopa-decarboxylase inhibitor (37 patients), a dopamine agonist (9 patients), amantadine (11 patients), an anticholinergic drug (7 patients) and an inhibitor of monoamine oxidase B (5 patients).

Neurologic examinations were conducted in all patients to confirm the diagnosis of PD. Additionally, magnetic resonance imaging (MRI) of the brain was performed for all patients. Those with severe ischaemic changes, defined as 3 points (white matter and/or basal ganglia) on the Age-Related White Matter Changes Scale, were excluded from the study [22].

Controls

The control group consisted of 40 volunteers without any known neurological or vascular diseases, including cognitive impairment and depression.

To avoid including any subjects with detectable abnormalities of the nervous system all control persons

underwent the same neuropsychological assessment process as PD patients.

Ethical requirements

Written informed consent was obtained from all subjects after the nature of the study was fully explained. The study was approved by the local Ethics Committee of the University of Medical Sciences in Poznan, Poland.

Neuropsychological assessment

We used the MMSE for the assessment of global cognitive functioning, as well as the Hamilton Depression Rating Scale (HDRS), to avoid any confounding presence of depression in the study [23]. The HDRS is recommended in screening for depression in PD, and, according to Schrag *et al*., the cut-off level was established at 13/14 points [24].

Specific neuropsychological tests were administered for the assessment of executive functions, including attention and executive and visuospatial working memory, as follows:

- Trail Making Test (TMT), part A and B [25], Polish translation [26],
- Stroop Test part A (reading colour names in black) and B (naming the colour of different words; colour-word interference effect) [27], Polish translation [26],
- Mental Rotation Test (MRT) [28],
- Verbal Fluency Test [29], for letters 'k', 'm', 'p' (an adaptation for Polish language according to Daniluk [30]).

Overall, 12 cognitive measures were included in statistical analyses: time and numbers of errors in parts A and B of TMT, time and number of errors in both parts of the Stroop test, number of correct responses in MRT (from 0 to 5), and number of words for the letters 'k', 'm' and 'p' in the Verbal Fluency Test in one minute. Due to the lack of normative data for Polish versions of tests assessing executive functions, the results of neuropsychological tests of PD patients were compared with the results of healthy controls. The groups were matched for age and educational levels.

Table 1. Clinical and demographic characteristics of Parkinson disease (PD) patients and control subjects

	PD patients* $n = 37$	Controls* $n = 40$
Age, years mean ± SD, range	61.03 ± 7.5, 46-76	63.22 ± 6.4, 46-77
Gender, male/female, *n* (%)	15/22 (40.5%/59.5%)	26/14 (65%/35%)
Educational level, *n* (%)		
low	10 (27.1%)	10 (25%)
intermediate	15 (40.5%)	17 (42.5%)
high	12 (32.4%0	13 (32.5%)
Age at disease onset, years mean ± SD	54.7 ± 6.9	–
UPDRS score mean ± SD	28.9 ± 12.4	–
Disease duration, years mean ± SD	6.2 ± 4.4	–
MMSE score mean ± SD	28.7 ± 1.3	29.2 ± 0.8

SD – standard deviation

**PD patients and control groups did not differ significantly in terms of age, time of education and MMSE score*

Education

The level of education of the patients and controls was self-reported during the demographic interview and classified for the purpose of this study by the years of education. Patients and controls were divided into 3 groups: low (primary or vocational education: 7-11 years of education), intermediate (secondary education: 12-13 years) or higher educational level (university education: 14-17 years).

Statistical analysis

The distributions of continuous variables were evaluated using the Kolmogorov and Smirnov method. For each variable with a normal distribution, we calculated the mean value and standard deviation (SD) and applied unpaired *t*-tests.

Data with non-normal distributions are provided as geometric mean and 1 SD range. The Mann-Whitney test and Kruskal-Wallis H-test were used for these variables to assess statistically significant differences between the groups. The pre-established level of significance was two-tailed at $p < 0.05$.

Results

Study population

Thirty-seven subjects with PD and 40 controls were enrolled for the study.

Clinical and demographic characteristics of the examined subjects are shown in Table 1.

The PD and control groups did not differ significantly in terms of age, education and MMSE score. There were some disproportions in gender between groups; however, we did not find any differences between males and females in terms of neuropsychological tests within the education groups.

Results of neuropsychological tests in PD patients

Significant differences were found on the basis of educational level for the majority of tests, with the exception of the number of correct responses for the MRT. In relation to PD patients at the higher educational level, the poorer-educated (low and intermediate level) patients completed the tests more slowly and made more errors (Table 2).

Results of neuropsychological tests in controls

Significant differences were found in terms of educational level (the lowest educational level was correlated with poorer performance on 4 measures), time of TMT A, time of TMT B, time of Stroop A, and numbers of errors in TMT B (Table 3).

Comparisons between PD patients and control subjects

Significant differences were found between PD patients and controls. In comparison to healthy persons, the PD patients without dementia showed worse results on neuropsychological tests that assessed executive functions for 10 evaluated measures. In addition, PD

Table 2. Results of neuropsychological tests in Parkinson disease (PD) patients in different educational groups*

Test	Educational level		
	Low	Intermediate	High
TMT A Mean time, sec. (SD)	**95.80 (32.79)**	**64.26 (27.10)**	**46.50 (16.77)**
TMT A No. of errors, mean (SD)	**2.30 (3.06)**	**0.40 (0.83)**	**0.00 (0.00)**
TMT B Mean time, sec. (SD)	**257.40 (105.16)**	**151.13 (79.37)**	**102.91 (35.52)**
TMT B No. of errors, mean (SD)	**11.40 (7.95)**	**7.73 (6.79)**	**2.75 (4.57)**
Verbal Fluency Test K, *n*, mean (SD)	**8.90 (2.38)**	**11.06 (2.68)**	**14.00 (3.49)**
Verbal Fluency Test M, *n,* mean (SD)	**5.70 (2.67)**	**9.66 (2.99)**	**11.25 (4.02)**
Verbal Fluency Test P, *n*, mean (SD)	**8.10 (3.51)**	**8.80 (3.53)**	**12.41 (4.23)**
MRT, No. of correct responses, mean (SD)	3.10 (1.29)	3.00 (0.65)	3.67 (1.15)
STROOP A Mean time, sec. (SD)	**45.00 (13.81)**	**37.00 (12.28)**	**27.17 (4.95)**
STROOP A No. of errors, mean (SD)	**3.70 (3.37)**	**3.27 (2.31)**	**1.00 (1.04)**
STROOP B Mean time, sec. (SD)	**86.90 (28.44)**	**104.87 (38.42)**	**67.08 (13.30)**
STROOP B No. of errors, mean (SD)	**3.90 (5.13)**	**0.47 (0.92)**	**0.08 (0.29)**

TMT – Trail Making Test, MRT – Mental Rotation Test

**Significant differences ($p < 0.05$) are shown in bold*

Table 3. Results of neuropsychological tests, in controls in different educational groups*

Test	Educational level		
	Low	Intermediate	High
TMT A Mean time, sec. (SD)	**56.70 (19.33)**	**35.06 (8.45)**	**44.85 (17.40)**
TMT A No. of errors, mean (SD)	0.30 (0.67)	0.06 (0.24)	0.15 (0.55)
TMT B Mean time, sec. (SD)	**130.00 (41.28)**	**84.70 (23.42)**	**98.31 (27.12)**
TMT B No. of errors, mean (SD)	**4.20 (5.22)**	**0.47 (1.23)**	**1.69 (2.69)**
Verbal Fluency Test K, *n*, mean (SD)	13.60 (4.15)	14.12` (2.87)	14.23 (3.06)
Verbal Fluency Test M, *n*, mean (SD)	9.70 (3.74)	10.53 (1.94)	11.77 (2.80)
Verbal Fluency Test P, *n*, mean (SD)	10.00 (4.08)	11.88 (1.65)	13.69 (3.64)
MRT, no. of correct responses, mean (SD)	3.60 (1.35)	3.70 (0.77)	4.15 (0.99)
STROOP A Mean time, sec. (SD)	**33.40 (9.29)**	**25.53 (3.41)**	**25.31 (3.97)**
STROOP A No. of errors, mean (SD)	1.10 (1.29)	0.59 (0.94)	0.38 (0.77)
STROOP B Mean time, sec. (SD)	77.20 (22.57)	64.06 (9.29)	62.92 (9.03)
STROOP B No. of errors, mean (SD)	0.40 (0.69)	0.06 (0.24)	0.15 (0.55)

TMT – Trail Making Test, MRT – Mental Rotation Test

**Significant differences ($p < 0.05$) are shown in bold*

Table 4. Comparison of the results of neuropsychological tests between Parkinson disease (PD) patients and control subjects*

Test	PD patients	Controls
TMT A Mean time, sec. (SD)	**67.03 (31.84)**	**43.65 (16.88)**
TMT A No. of errors, mean (SD)	0.78 (1.87)	0.15 (0.48)
TMT B Mean time, sec. (SD)	**164.22 (96.62)**	**100.45 (34.32)**
TMT B No. of errors, mean (SD)	**7.11 (7.19)**	**1.80 (3.38)**
verbal Fluency Test K, *N*, mean, (SD)	**11.43 (3.46)**	**14.03 (3.21)**
verbal Fluency Test M, *N*, mean, (SD)	**9.11 (3.89)**	**10.73 (2.80)**
Verbal Fluency Test P, *n*, mean, (SD)	**9.78 (4.11)**	**12.00 (3.32)**
MRT, no. of correct responses, mean (SD)	**3.24 (1.04)**	**3.83 (1.01)**
STROOP A Mean time, sec. (SD)	**35.97 (12.76)**	**27.43 (6.46)**
STROOP A No. of errors, mean (SD)	**2.65 (2.57)**	**0.65 (1.00)**
STROOP B Mean time, sec. (SD)	**87.76 (33.09)**	**66.98 (14.63)**
STROOP B No. of errors, mean (SD)	1.27 (3.10)	0.18 (0.50)

TMT – Trail Making Test, MRT – Mental Rotation Test
**Significant differences ($p < 0.05$) are shown in bold*

patients' responses were slower and exhibited more errors (Table 4). The less-educated (low and intermediate level) PD patients, compared with less-educated controls, displayed worse results for most of the psychological tests. In contrast to the lower education groups, there were no significant differences between test results of higher-educated PD patients and higher-educated controls (Table 5).

Discussion

Our study shows that PD patients who did not fulfil standard criteria for dementia had specific cognitive deficits in terms of visuospatial working memory, attention and verbal fluency when compared to age- and education-matched controls without PD. Similar results were obtained by other authors who compared patients at earlier stages of PD with healthy subjects, in terms of the onset of cognitive disorders [1,4,7,9]. However, these studies found no significant differences between groups with respect to education. In our study, the analysis of the effect of education on cognitive performance for the PD group demonstrated that higher-educated subjects performed best on most tests, and those with shorter education periods performed worse. Similar effects were also noticeable in subjects without PD. According to Spreen *et al.* [29], the poor education of the general, healthy population may particularly account for the results of the TMT and Stroop tests. In our study, the time taken to complete the tests differed significantly, not only in PD patients but also in control groups. However, in the group of PD patients, the negative influence of poorer education was clearly stronger. Significant differences between education groups are apparent for the results of most tests (11 of 12 measures) performed by PD patients. In the controls, significance was achieved between education groups in only 4 out of 12 measures (time TMT A, time TMT B, time Stroop A, numbers of errors in TMT B) (Table 2).

Lower-educated PD patients (low and intermediate educational level) performed worse on psychological tests compared with lower-educated controls (respectively, for 7 and 9 measures). The finding that there were no significant differences in terms of test results between higher-educated PD persons and higher-educated controls, however, suggests that more advanced education may foster a protective effect against early cognitive decline in PD. The positive effect of a higher educational level has also been described by Cohen *et al.* [17], who compared PD patients based on education level and reported better cognitive performance among higher-educated patients, especially for tests assessing executive functions. A similar relationship was also affirmed by Kandiah *et al.* [2] in a de novo PD group, as well as by Green *et al.* [6] in patients with advanced PD. In another study targeting the lower educational level, more severe disease states (as assessed by UPDRS total score) and older age at disease onset were the prominent risk factors for dementia [18]. Additionally, in a meta-analysis that included 13 longitudinal studies, lower educational levels have been found to be associated with a greater rate of cognitive decline in PD patients [19]. From a theoretical point of view, better-educated persons may have greater cognitive reserves, which could be a protective factor against cognitive decline, especially in the early phases of the disease.

Table 5. Comparison of educational level for matched groups of Parkinson disease (PD) patients and controls*

Test	Low educational level		Intermediate educational level		High educational level	
	PD *n* = 10	Controls *n* = 10	PD *n* = 15	Controls *n* = 17	PD *n* = 12	Controls *n* = 13
TMT A Mean time, sec. (SD)	**95.80 (32.79)**	**56.70 (19.33)**	**64.27 (27.10)**	**35.06 (8.45)**	46.50 (16.77)	44.85 (17.40)
TMT A, No. of errors, mean (SD)	**2.30 (3.06)**	**0.30 (0.67)**	0.40 (0.83)	0.06 (0.24)	0.00 (0.00)	0.15 (0.55)
TMT B Mean time, sec. (SD)	**257.40 (105.16)**	**130.00 (41.23)**	**151.13 (79.37)**	**84.71 (23.42)**	102.92 (35.53)	98.31 (27.12)
TMT B No. of errors, mean (SD)	**11.40 (7.95)**	**4.20 (5.22)**	**7.73 (6.79)**	**0.47 (1.23)**	2.75 (4.58)	1.69 (2.69)
Verbal Fluency Test K, *n*, mean (SD)	**8.90 (2.38)**	**13.60 (4.14)**	**11.07 (2.69)**	**14.12 (2.87)**	14.00 (3.49)	14.23 (3.06)
Verbal Fluency Test M, *n*, mean (SD)	**5.70 (2.67)**	**9.70 (3.74)**	9.67 (2.99)	10.53 (1.94)	11.25 (4.03)	11.77 (2.80)
Verbal Fluency Test P, *n*, mean (SD)	8.10 (3.51)	10.00 (4.08)	**8.80 (3.53)**	**11.88 (1.65)**	12.42 (4.23)	13.69 (3.64)
MRT, no. of correct responses, mean (SD)	3.10 (1.29)	3.60 (1.35)	**3.00 (0.65)**	**3.71 (0.77)**	3.67 (1.15)	4.15 (0.99)
STROOP A Mean time, sec. (SD)	**45.00 (13.82)**	**33.40 (9.30)**	**37.00 (12.28)**	**25.53 (3.41)**	27.17 (4.95)	25.31 (3.97)
STROOP A, No. of errors, mean (SD)	3.70 (3.37)	1.10 (1.29)	**3.27 (2.31)**	**0.59 (0.94)**	1.00 (1.04)	0.38 (0.77)
STROOP B Mean time, sec. (SD)	86.90 (28.44)	77.20 (22.57)	**104.87 (38.42)**	**64.06 (9.29)**	67.08 (13.30)	62.92 (9.03)
STROOP B No. of errors, mean (SD)	3.90 (5.13)	0.40 (0.70)	0.47 (0.94)	0.06 (0.24)	0.08 (0.29)	0.15 (0.55)

TMT – Trail Making Test, MRT – Mental Rotation Test

**Significant differences ($p < 0.05$) are shown in bold*

Cognitive and brain reserves are hypothetical constructs that are suggested to occur in patients with Alzheimer disease [31,32]. However, the cognitive reserve theory may, to some extent, help to explain the results of our study. According to Stern [31], cognitive reserve could be defined as 'individual differences in how people process tasks, allowing some to cope better than others with brain pathology'. According to the same hypothesis, such a reserve theory focuses on the process that allows individuals to sustain brain damage and maintain function. In the cognitive reserve construct, the are two main components: (a) neural reserve: assuming that brain networks are more efficient and have greater capacity or are more flexible in persons with greater reserve, greater neural reserve would equate to a larger capacity to cope with the disruption imposed by brain pathology; and (b) neural compensation, which Stern defined as 'inter-individual variability in the ability to compensate for the pathological disruption of standard processing networks by using brain structures or networks not normally used by individuals with an intact brain' [31]. Whether one, or both, of these mechanisms is involved in the protective effect of education, and whether the mechanism is influenced by working in more intellectually demanding professions, are still open questions.

Recently, it was shown that vascular risk factors, along with white matter abnormalities, probably do not contribute significantly to cognitive impairment in PD patients, with the exception of PD patients with severe cerebral ischaemic lesions [33,34]. Therefore, it is possible that pathomechanisms of cognitive decline in PD could be different than in vascular dementia or Alzheimer disease [34,35].

Conclusions

1. It seems probable that educational achievements may positively affect the cognitive performance after the onset of PD.
2. Hypothetically, protective effects of higher levels of education, independent of dementia aetiology, may be due to greater functional brain reserves.

Disclosure

Authors report no conflict of interest.

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