Special Issue - Neuroscience
PROVISIONAL PDF

Cognitive Profiles in Parkinson's Disease and their Correlation with Dementia, Anxiety and Depression: A Preliminary Study

Wan Nor Azlen Wan Mohamad[1], Normah Che Din[2], Norlinah Ibrahim[3]

Submitted: 10 Nov 2014
Accepted: 5 Nov 2015

[1] *Department of Neurosciences, Universiti Sains Malaysia, School of Medical Sciences , Health Campus USM Kubang Kerian, 16150 Kelantan, Malaysia*

[2] *Health Psychology Programme, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia*

[3] *Universiti Kebangansaan Malaysia Medical Centre, Neurology Unit, Pusat Perubatan UKM, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia*

Abstract

A cross-sectional study was carried out at a medical centre to determine the cognitive profiles of 30 Parkinson's disease patients with age of 69.76 ± 7.39 years. Thirty-seven percent of the patients were found to be at risk for dementia. The scores on subscales of working memory and alternating verbal fluency were significantly lower in Parkinson's disease patients who were older than 77 years old. The scores on a subtest of working memory on the Parkinson's Disease Cognitive Rating Scale (PDCRS) were significantly lower in Parkinson's disease patients with a duration of illness of more than 10 years. In cognitive measurement, the subtests of verbal memory, delayed free recall and verbal fluency on the PD¬CRS were significantly lower in patients with less than six years of education. The patients who had difficulty with sustained attention, working memory and movement had significant anxiety and depression symptoms. In conclusion, multiple patterns in cognitive profiles influence the quality of life of patients with Parkinson's disease in multi-dimensional ways.

Keywords: *cognitive Parkinson's disease, dementia, anxiety, depression*

Introduction

Parkinson's disease (PD) is commonly linked with limited physical movements among the elderly. Researchers may want to investigate further how PD affects other modalities in cognition, behaviour and emotion. Non-motor complications may worsen the prognosis of the disease and further increase the psychosocial impact on patients and their family members (1).

Cognitive impairment and dementia in PD are still largely not officially reported in the Malaysian population. Some patients develop dementia a few years after the onset of PD while others remain free of dementia during the course of the disease. The time from onset of PD to the onset of dementia is related to the type and extent of brain pathology and other risk factors that are still being investigated (2).

The researchers in earlier research (3) has described the Cognitive Reserve (CR) Theory in their research. They found that lower education levels were associated with an increased risk of dementia, suggesting that higher education may have a protective effect on the cognitive modalities in PD. The CR hypothesis proposes that the degree of cognitive impairment could be affected by both innate biological factors and lifelong mental stimulation.

PD also has a significant impact on patients' quality of life (QoL). Some patients isolate themselves from society, and this worsens their emotional pain. Thus, measurement of QoL in PD patients would facilitate better management of PD. However, the findings may not be very conclusive because the ethnic or cultural differences in health belief and attitudes towards PD also need to be considered. Some researchers believe that it is necessary to study the effects of various socio¬demographic factors on the

QoL of patients with PD from different cultural settings (4). The objective of the present study is to describe cognitive decline in patients with PD in local settings according to sociodemographic profiles incorporating age, years of education and duration of illness. We aim to determine the relationship between cognitive profiles and dementia, anxiety, depression and QoL.

Methods

This study was conducted during 2012. A cross-sectional study design was chosen as appropriate for achieving the research objectives. Thirty patients who had been diagnosed with PD were chosen randomly from the database in the Neurology Clinic at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Patients who had other diseases, such as schizophrenia, cerebrovascular accident (CVA) or other neurodegenerative disease, were excluded from this study as they have different courses of disease. The age range was from 50 to 90 years old. Patients who agreed to participate in the study were interviewed using cognitive assessment with the PD Cognitive Rating Scale, the Dementia Rating Scale (DRS) and the Hospital Anxiety and Depression Scale (HADS). Patients were evaluated at the Neurology Clinic in a quiet room or at home using a Chinese translator. Statistical analysis was carried out using the paired *tt*-test and the Pearson Correlation. Cronbach alpha was 0.7950 for PD-CRS, 0.8008 for PDQ-39, 0.7766 for DRS and 0.7524 for HADS, reflecting the internal consistency of the questionnaire and showing that each questionnaire item assesses a single underlying construct of interest.

The PD-CRS is a practical tool for cognitive assessment and a new PD-specific cognitive scale that aims to capture the whole spectrum of cognitive functions impaired over the course of PD. The information provided by the assessment of fronto-subcortical and cortical cognitive functions may help to increase the sensitivity and specificity of PD diagnosis, to separate subgroups of patients according to their pattern of cognitive impairment at early stages of the disease and to identify those patients at higher risk of eventually developing dementia. The intraclass correlation coefficient (ICC) of total scores on the initial version of the PD-CRS showed a strong concurrent validity with the total score on the Mattis Dementia Rating Scale (ICC 0.86). Strong concurrent validity was also obtained for immediate (0.86) and delayed memory (0.85), alternating verbal fluency (VF) (0.80), action VF (0.86), phonemic VF (0.87), semantic VF (0.85), attention (0.80), naming (0.71), and both drawing (0.71) and copying (0.73) a clock. Scores on working memory showed a moderate concurrent validity with digit span backward scores (0.64).

The PDQ-39 includes 39 items in 8 domains: mobility (10 items); activities of daily living (ADL) (6 items); emotional well-being (6 items); stigma (4 items); social support (3 items); cognition (4 items); communication (3 items); and bodily pain (3 items). Questions refer to the preceding month. Scores for each item range from 0 (no problem) to 4 (continuous problem/unable to do it). The Dementia Rating Scale (DRS) is a 36-task and 32-stimulus card individually administered instrument designed to assess the level of cognitive functioning in individuals with brain dysfunction. The DRS consists of a professional manual, scoring booklets and 32 stimulus cards. The DRS assesses cognitive functioning on five subscales: Attention (ATT, 8 items); Initiation-Perseveration (I-P, 11 items); Construction (CONST, 6 items); Conceptualization (CONCEPT, 6 items); and Memory (MEM, 5 items). The test-retest reliability correlation coefficient was .97 with subscale correlation coefficients ranging from .61 to .94. The DRS was administered twice with a 1-week interval between administrations to a group of 30 patients diagnosed with dementia of the Alzheimer's type. The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report measure, with seven items forming a depression subscale and another seven measuring anxiety. Each item is rated on a four-point scale, ranging from 0 to 3, with 3 indicating higher symptom frequency. Total scores for each subscale range from 0 to 21 and are categorised as normal (0–7), mild (8–10), moderate (11–14) or severe (15–21). Participants read and answer the questions themselves in the presence of an interviewer. Results for the Depression "D" scale and Anxiety "A" scales will be examined.

Results

Patients who were older than 77 years old scored significantly lower than patients who were under 77 years old in the working memory and alternating verbal fluency subtest (t (6)=3.092, P < 0.01) and (t (6)=4.031, P < 0.01)). Scores on the PD¬CRS subtests of verbal memory, delayed free recall, alternating verbal fluency and action verbal fluency were significantly higher in the group with more than six years of education (t (14) = -2.060, p < 0.05; t (14) =¬2.696, P < 0.05; t (14) = ¬2.281, P < 0.05; t (14)= ¬2.163, P < 0.05). Scores

on the PDCRS subtest of working memory were significantly lower in the group of PD patients who had a duration of illness above 10 years (t (9) = 2.53, $P < 0.05$).

The scores for all PDCRS subtests, except those for verbal memory, delayed free recall, alternating verbal fluency and action verbal fluency, were significantly negatively correlated with anxiety and depression. This indicates that the higher the PDCRS score, the lower the probability that patients experience anxiety and depression (Table 1-5). There is a significant positive correlation between all PDCRS subtests and all DRS subscales, including total score. This indicates that the higher the PDCRS scores the more likely patients with Parkinson's disease will have a higher score in dementia, which means they are less likely to have dementia.

Discussion

This study describes the cognitive profiles of PD patients and their correlation with dementia, anxiety and depression. A cut-off age of 77 years was used to separate the patients into two groups because differences were found to be significant at this age. This is supported by

Table 1: Demographic data of Parkinson's Disease patients

	n	Percentages (%)
Age		
Below 77 years	24	80
Above 77 years	6	20
Gender		
Male	15	50
Female	15	50
Years of Education		
< 7 years	16	53.3
> 7 years	14	46.7
Duration of disease		
< 10 years	21	70
> 10 years	9	30
Ethnicity		
Malay	3	10
Chinese	27	90
Dementia		
Non-dementia	19	63
At risk	11	37

Table 2: Cognitive profiles comparison with age range

PD-CRS subtests	Age range	Mean (SD)	t	P
Verbal memory	< 77 years	5.29 (1.46)	0.645	0.524
	> 77 years	4.83 (1.94)		
Confrontation naming	< 77 years	14.36 (4.62)	-0.893	0.379
	> 77 years	16.17 (3.13)		
Sustained attention	< 77 years	4.50 (4.04)	1.408	0.170
	> 77 years	2.00 (3.10)		
Working memory	< 77 years	3.33 (2.68)	3.092	0.009**
	> 77 years	0.67 (1.63)		
Unprompted clock drawing	< 77 years	8.00 (2.92)	0.722	0.476
	> 77 years	7.00 (3.52)		
Copy clock drawing	< 77 years	8.36 (3.28)	-0.688	0.497
	> 77 years	9.33 (1.63)		
Delayed free recall	< 77 years	2.96 (2.48)	1.654	0.109
	> 77 years	1.17 (1.83)		
Alternating verbal fluency	< 77 years	4.04 (4.91)	4.031	0.001**
	> 77 years	0.00 (0.00)		
Action verbal fluency	< 77 years	6.38 (4.83)	-0.139	0.891
	> 77 years	6.67 (3.39)		

**significant at $P < 0.05$.

Table 3: Cognitive Profiles comparison with years of education

PD-CRS subtests	Education years	Mean (SD)	*t*	*P*
Verbal memory	Below 6 years	4.69 (1.49)	-2.060	0.049*
	> 6 years	5.79 (1.42)		
Confrontation naming	Below 6 years	14.50 (4.65)	-0.307	0.761
	> 6 years	15.00 (4.21)		
Sustained attention	Below 6 years	3.81 (4.09)	-0.273	0.787
	> 6 years	4.21(3.95)		
Working memory	Below 6 years	1.94 (2.67)	-1.953	0.061
	> 6 years	3.79 (2.49)		
Unprompted clock drawing	Below 6 years	7.44 (3.22)	-0.699	0.490
	> 6 years	8.21 (2.81)		
Copy clock drawing	Below 6 years	8.25 (3.38)	-0.606	0.549
	> 6 years	8.93 (2.64)		
Delayed free recall	Below 6 years	1.56 (1.86)	-2.696	0.013*
	> 6 years	3.79 (2.55)		
Alternating verbal fluency	Below 6 years	1.50 (3.63)	-2.281	0.032*
	> 6 years	5.21 (5.06)		
Action verbal fluency	Below 6 years	4.81 (3.06)	-2.163	0.043*
	> 6 years	8.29 (5.28)		

*significant at $P < 0.0$.

Table 4: Cognitive Profiles comparison with Duration of disease

PD-CRS subtests	Duration of disease	Mean (SD)	*t*	*P*
Verbal memory	< 10 years	5.19 (1.5)	-0.051	0.960
	> 10 years	5.22 (1.72)		
Confrontation naming	< 10 years	14.48 (4.71)	-0.485	0.632
	> 10 years	15.33 (3.67)		
Sustained attention	< 10 years	4.14 (4.20)	0.297	0.768
	> 10 years	3.67 (3.54)		
Working memory	< 10 years	3.48 (2.73)	2.530	0.020*
	> 10 years	1.22 (2.00)		
Unprompted clock drawing	< 10 years	7.86 (2.92)	0.156	0.877
	> 10 years	7.67 (3.39)		
Copy clock drawing	< 10 years	8.52 (2.99)	-0.117	0.908
	> 10 years	8.67 (3.28)		
Delayed free recall	< 10 years	3.05 (2.46)	1.571	0.127
	> 10 years	1.56 (2.19)		
Alternating verbal fluency	< 10 years	4.05 (4.79)	1.488	0.148
	> 10 years	1.33 (4.00)		
Action verbal fluency	< 10 years	7.10 (4.76)	1.235	0.227
	> 10 years	4.89 (3.69)		

*significant at $p < 0.05$.

Table 5: Association among Parkinson's Disease Cognitive Rating Scale, Parkinson's Disease Quality of Life (39), Dementia Rating Scale and Hospital Anxiety and Depression Scale

	Parkison Disease Cognitive Rating Scale (PDCRS) subtests								
	Verbal memory	Confrontation naming	Sustained attention	Working memory	Unprompted clock drawing	Copy clock drawing	Delayed free recall	Alternating verbal fluency	Action verbal fluency
PDQ39									
Mobility	-0.109	-0.288	-0.570**	-0.549**	-0.219	-0.161	-0.221	-0.197	-0.279
ADL	-0.066	-0.081	-0.623**	-0.426*	-0.163	-0.155	0.079	-0.425*	-0.449*
Emotional well-being	-0.161	-0.375*	-0.507**	-0.401*	-0.549**	-0.497**	-0.025	-0.218	-0.338
Stigma	0.084	-0.597**	-0.444*	-0.185	-0.342	-0.366*	0.053	-0.027	-0.394*
Social support	0.135	-0.100	-0.476**	-0.158	-0.389*	-0.302	0.182	-0.248	-0.294
Cognition	-0.616**	-0.204	-0.436*	-0.437*	-0.336	-0.265	-0.480	-0.317	-0.312
Communication	0.076	-0.222	-0.275	-0.132	-0.239	-0.211	-0.010	0.008	-0.218
Bodily discomfort	-0.093	-0.250	-0.405*	-0.264	-0.292	-0.347	-0.067	0.095	0.134
HADS									
Anxiety	-0.076	-0.374*	-0.552**	-0.479**	-0.622**	-0.526*	-0.003	-0.341	-0.354
Depression	-0.199	-0.194	-0.556**	-0.524**	-0.447*	-0.400**	-0.178	-0.259	-0.276
DRS									
Attention	-0.039*	0.160	0.238	0.207	0.279	0.192	-0.139	0.223	0.314
Initiation	0.175	0.271	0.421*	0.605**	0.482**	0.443*	0.203	0.178	0.514**
Construction	-0.085	0.296	0.330	0.255	0.446*	0.614**	-0.046	0.155	0.146
Conceptualization	-0.066	0.147	0.213	0.493**	0.515**	0.317	0.372*	0.259	0.286
Memory	0.062	0.258	0.284	0.595**	0.512**	0.560**	0.161	0.279	0.390*
Total score	0.034*	0.281	0.401*	0.624**	0.600**	0.528**	0.209	0.340	0.531**

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

other research (5,6) showing that PD and dementia both increase with age. These investigators found that the age of PD patients is one of the most important predictors of dementia risk. However, it is very important to note the differences in age distribution among studies.

The results of this study strongly support the finding of other investigators that a higher educational level is associated with a reduced risk of cognitive decline (3). Their study hypothesised that life experience may provide a cognitive reserve against the clinical expression of degenerative diseases. However, researchers are still debating this mechanism. The most plausible explanations are the "brain reserve" and "brain battering" hypotheses. We found that patients who had received education for more than six years were likely to have better verbal memory, delayed free recall, alternating verbal fluency and action verbal fluency.

Disease duration is also an important risk factor for dementia in PD, and the longer the follow-up, the higher the cumulative prevalence of PD with dementia. The current findings demonstrate that the patients with cognitive impairment who had shorter disease duration were most likely to have higher scores on the working memory scale in the PDCRS. Parkinson's disease patients are more likely to struggle with cognitive challenges in their everyday lives, and they are more likely to have difficulty in inhibiting attention to distracting stimuli, reduced ability in cognitive shifting and impaired working memory.

Previous literature has established that in the early stages of PD, cognitive dysfunction occurs most frequently in executive functions, working memory, and spatial behaviour. These cognitive functions are sensitive to frontal lobe dysfunction. In the middle stages of the disease, PD patients frequently show temporal lobe¬-like dysfunction of learning and memory. In some PD patients,

the cognitive decline progresses to a syndrome of dementia, the aetiology of which remains largely unclear. The cognitive profile of PD with dementia has been described as a progressive dysexecutive syndrome with memory impairment in the absence of aphasia, apraxia, and agnosia (7). In this study, positive correlations between dementia and PD were found in working memory, verbal fluency and clock drawing (as a reflection of spatial behaviour).

Among the PD patients recruited in this study, 37 percent were at risk of dementia. Other investigators (8) have stated that there are no specific or operationalised criteria to diagnose dementia in PD. However, the Mattis Dementia Rating Scale (MDRS) used in this study is a commonly used screening test that has excellent discriminating ability in diagnosing dementia in PD (9).

We found that those patients who had difficulty with sustained attention, working memory and movement also had significant anxiety and depression symptoms. This is supported by a study (10) in which HADS was used with PD patients. They reported that almost 50% of the patients displayed symptoms of anxiety and nearly 40% showed signs of depression. As an explanation of this observation, the anxiety and depressive symptoms may reflect a psychological reaction to the stress of having the illness or could be due to changes in neurochemical pathways (11).

Conclusion

Cognitive impairment is reported to be common in PD, even in patients who have not been diagnosed with dementia (5,6). PD affects the patient's quality of life, not only through the physical symptoms but also through multi¬modality function, including psychological symptoms. Dementia in PD is difficult to recognise at an early stage due to a lack of appropriate diagnostic tools and confounding variables such as severe motor symptoms, medications and depression. Early identification of these patients is important for optimizing the planning of future care (12). Psychopathological symptoms in cognitive, behavioural and emotional modalities are common in PD and expose patients to a higher risk of anxiety and depression. One limitation of this study is the challenge in distinguishing between mild cognitive impairment and the early onset of dementia. Future research into PD needs standardise assessment tools to collect unified data and coherent reporting of non¬physical symptoms of PD.

Acknowledgement

We are grateful to the participants who volunteered for this study and the clinic staffs who helped facilitate this study. We are also thank Emily Hong in her assistance as a translator throughout the study.

Funds

None.

Conflicts of Interests

None.

Authors' Contributions

Analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, administrative, technical, or logistic support, collection and assembly of data: WNAWM, NCD, NI

Correspondence

Dr Wan Nor Azlen Wan Mohamad
MCP (UKM)
Department of Neurosciences
School of Medical Sciences
Health Campus USM
16150 Kubang Kerian
Kelantan, Malaysia
Tel : +609-7676300
Email : wnorazlen@usm.my

References

1. Riedel O, Klotsche J, Spottke A, Deuschl G, Forstl H, Henn F, et al.Cognitive Impairment in 873 patients with idiopathic Parkinson's disease: Results from the German Study on Epidemiology of Parkinson's disease with Dementia (GEPAD). *J Neuro*. 2008;**255(2)**:255–264. doi: 10.1007/s00415-008-0720-2.

2. Pagonabarraga J, Kulisevsky J. Cognitive impairment in Parkinson's Disease: tools for diagnosis and assessment. *Mov Disord*. 2009;**24(8)**:1103–1110. doi: 10.1002/mds.22506.

3. Poletti M, Emre M, Bonuccelli U. Mild Cognitive Impairment and Cognitive Reserve in Parkinson's Disease. *Parkinsonism Rel Disord*. 2011;**17(8)**:579–586. doi: 10.1016/j.parkreldis.2011.03.013.

4. Zhao YJ, Tan LCS, Lau PN, Au WL, Li SC, Luo N. Factors affecting health related quality of life amongst Asian patients with Parkinson's disease. European. *J Neuro*. 2008;**15**:737–742. doi: 10.1111/j.1468-1331.2008.02178.x.

5. Janvin C, Aarsland D, Larsen JP, Hugdahl K. Neuropsychological profile of patients with Parkinson's disease without dementia. *Dement Geriatr Cogn Disord*. 2003;**15(3)**:126–131. doi: 10.1159/000068483.

6. Foltynie T, Brayne CE, Robbins TW, Barker RA. The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. *Brain*. 2004;**127(Pt 3)**:550–560.

7. Pagonabarraga J, Kulisevsky J. Cognitive impairment and dementia in Parkinson's disease. *Neurobiol Dis*. 2012;**46(3)**:590–596 doi: 10.1016/j.nbd.2012.03.029.

8. Aarsland D, Zaccai J, Brayne C. A systematic review of prevalence studies of dementia in Parkinson's disease. *Mov Disord*. 2005;**20(10)**:1255–1263. doi: 10.1002/mds.20527.

9. Llebaria G, Pagonabarraga, Kulisevssky J, GarciaSanchez C, PascualSedano B, Gironell A, Martinez Corral M. Cutoff score of the Mattis Dementia Rating Scale for screening dementia in Parkinson's Disease. *Move Disord*. 2008; **23(11)**;1546–1550. doi: 10.1002/mds.22173.

10. Marinus J, Leentjens AFG, Martine V, Stiggelbout AMS, van Hilten JJ. Evaluation of the Hospital Anxiety and Depression Scale in Patients with Parkinson's Disease. *Clin Neuropharmacol*. 2002;**25(6)**:318–324.

11. Walsh K, Bennett G. Parkinson's Disease and Anxiety. *Postgrad Med J*. 2001;**77**:89–93. doi: 10.1136/pmj.77.904.89.

12. Kaszas B, Kovacs N, Balas I, Kallai J, Aschermann Z, Kerekes Z, et al. Sensitivity and Specificity of Addenbrooke's Cognitive Examination, Mattis Dementia Rating Scale, Frontal Assessment Battery, Mini Mental State Examination for diagnosing dementia in Parkinson's Disease. *Parkinsonism Relat Disord*. 2012;**18(5)**:553–556.