Clinical Neurology and Neurosurgery 151 (2016) 65–69

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Cognitive impairment in patients with Parkinson's disease: A 30-month follow-up study

Ling Chen[a,1], Cuiyu Yu[b,1], Ning Zhang[c], Junjun Liu[d], Weiguo Liu[b,*]

[a] Department of Clinical Psychology, Jiangsu Province Geriatric Institute, Nanjing, 210024, China
[b] Department of Neurology, Nanjing Brain Hospital Affiliated with Nanjing Medical University, Nanjing, 210029, China
[c] Department of Clinical Psychology, Nanjing Brain Hospital affiliated with Nanjing Medical University, Nanjing, 210029, China
[d] Department of Psychiatry, Shanhai Meishan Hospital, Nanjing, China

ARTICLE INFO

Article history:
Received 14 December 2015
Received in revised form
19 September 2016
Accepted 30 September 2016
Available online 4 October 2016

Keywords:
Parkinson's disease
Cognitive impairment
Follow-up
Mini-mental state examination
Montreal cognitive assessment (MoCA)

ABSTRACT

Objective: A longitudinal (30-month) study of the cognitive changes in Parkinson's disease patients and analysis of influencing factors.
Methods: The cognitive function and related symptoms of 102 patients with idiopathic Parkinson's disease were assessed using the Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), and relevant scales, at baseline and 30-month follow-up. The *t*-test, nonparametric tests, and regression analyses were used to evaluate cognitive decline and investigate risk factors for cognitive impairment.
Results: From baseline to follow-up, the MMSE and MoCA scores significantly decreased, respectively, from 28.16 ± 2.29 to 26.18 ± 3.64, and from 24.60 ± 4.23 to 21.94 ± 5.47 (both $P < 0.001$). Impairment was observed in multiple cognitive areas, significantly in naming, delayed recall, and orientation ($P < 0.01$). Patients at baseline with postural instability and gait disturbance (PIGD), lower MoCA scores, or depression had a higher risk of cognitive impairment at follow-up ($P < 0.01$).
Conclusion: Cognitive impairment is highly prevalent in Parkinson's disease patients, especially for those with lower MoCA scores, PIGD, and depression.

1. Introduction

Parkinson's disease (PD) was once considered a disorder of movement solely, but evidence now indicates that cognitive impairment very common and a progressive feature of PD [1]. Whether mild or constituting dementia, cognitive impairment in PD significantly affects patients' survival and quality of life [2].

A longitudinal study in Norway showed that PD patients had a 3- to 5-fold higher risk of developing dementia, compared with the non-PD control group matched for age [3]. We have long recognized that PD patients are susceptible to concurrent cognitive decline, termed PD dementia, and there have been many studies that explored the factors that influence the development of cognitive impairment in PD patients. Adler et al. [4] reported that age, time of onset, duration, severity of motor symptoms, depression, and hallucinations could affect cognitive function in PD. A study conducted by Levy and colleagues [5] suggested that the combined effects of increased age and extrapyramidal signs were the primary factors contributing to an elevated risk of dementia in PD patients. Our previous studies [6] also reported several risk factors for dementia in patients with PD, including older age, less education, and more severe motor symptoms. However, little is known about the process of cognitive impairment in PD patients.

Although the prevalence of dementia in PD patients is ~30%, severe cognitive impairment is often not recognized by clinicians during routine examination [7]. Furthermore, dementia commonly develops late in PD, although it is possible to detect subtle cognitive decline much earlier [8]. Because PD is a neurodegenerative disease, impairments in cognition are generally irreversible. Therefore, early diagnosis of cognitive impairment in PD is extremely important.

For the present study, cognitive assessments of PD patients were conducted using the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) (http://www.mocatest.org/). The Mini-Mental State Examination (MMSE) is a clinical cognitive screening scale that is widely used, but researchers have reported that its sensitivity is not as satisfactory as the MoCA for identifying early cognitive impairment in PD [9]. Thus,

* Corresponding author.
E-mail addresses:
hubbub_kennel@163.com (L. Chen), 363422440@qq.com (C. Yu), zn6360@126.com (N. Zhang), g6115124@163.com (J. Liu), liuweiguo1111@sina.com (W. Liu).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.clineuro.2016.09.021
0303-8467/

for PD patients the MMSE is appropriate only for simple cognitive screening. On the other hand, the MoCA is also a simple, widely used assessment tool, with good sensitivity and specificity. The MoCA is now the most commonly used clinical assessment scale for rapid screening of cognition in PD [10].

Previous studies [11,12] using the MoCA scale have determined a cutoff value for impaired cognitive function of 26 points. However, some subsequent clinical researchers found that the MoCA score of patients with normal cognition was below 26 points. In particular for the present study, this cutoff value may not be suitable for Chinese patients with PD; previous studies using the MoCA scale assessment in a Chinese population showed that the scores were influenced by age and educational level [13]. In the present study, we chose screening cutoff scores with reference to Lu et al.'s [14] study of Chinese population-based norms, which included the elderly. Lu et al.'s recommended cutoff values differed according to level of education, and we consider that this is more appropriate for our studies.

Currently, follow-up studies of cognitive function in PD patients in China are rare. To contribute to the understanding of cognitive impairment in Chinese patients with PD, herein we report a 30-month follow-up study of PD patients in China. We investigated the amount of decline during the 30 months according to the MMSE and MoCA, and the associations between clinical features and changes in cognitive functions in these patients.

2. Methods

The Ethics Committee of Nanjing Brain Hospital approved this study. All participants signed informed consent before their basic demographic information was obtained.

2.1. Participants

From 2009 to 2010, 102 patients with PD were enrolled in this study at the Neurology Clinic of Nanjing Brain Hospital in Nanjing, China. The patients were evaluated for cognitive assessments and other PD-related motor and non-motor symptoms. Diagnoses of idiopathic PD were based on the UK PD Brain Bank diagnostic criteria for PD [15] and performed by a movement disorder specialist (author WL). Patients with the following were excluded from the study: cerebrovascular disease, encephalitis, trauma, drug-induced Parkinson's disease, Parkinson syndrome, idiopathic tremor, cancer, severe visual and hearing impairment, or serious mental illness.

Patients were followed up from 2012 to 2013. Eighteen patients were lost to contact, and hence 102 patients completed the follow-up study. All participants were able to speak Mandarin. No patient had ever taken rivastigmine or memantine to improve intelligence. Seven patients had taken citicoline sodium.

2.2. Assessments

To assess cognitive function, all subjects were tested with the MMSE and MoCA. Both the MMSE and MoCA assess a range of cognitive skills on a scale from 0 to 30 points, with higher scores indicating better performance. Patients were tested twice using the MoCA scale, and the results for each individual were averaged. With reference to Lu et al.'s [14] study, the MoCA screening cutoff score varied with the educational level of the PD patients: 13/14 for illiterate individuals, 19/20 for individuals with 1–6 years of education, and 24/25 for individuals with $\geq$7 years of education. Patients whose average MoCA score was above the cutoff value for their educational level were defined as cognitively normal, the rest were considered cognitively impaired.

The following instruments were administrated to PD patients to assess PD motor and non-motor symptoms: part II and part III of the United Parkinson's Disease Rating Scale (UPDRS) [16], the Hamilton Depression Rating Scale (HAM-D) [17], and the Hamilton Anxiety Rating Scale (HAM-A) [18]. All scales were administered by 2 trained neurologists using standardized survey language.

The 102 PD patients were divided into 3 motor subtypes, based on calculated tremor points and postural instability/gait disturbance (PIGD) points determined by UPDRS scores. Using the modified ratio based on the UPDRSIII, with a numerical ratio derived from the mean tremor and akinetic-rigidity scores, tremor was assessed using a 9-item scale that included history of left or right arm tremor (2 items); rest tremor of the face/lips/chin and each limb (5 items); as well as postural tremor of the right and left upper extremities (2 items).The 14-item akinetic-rigidity scale assessed passive range of motion rigidity of the neck and each extremity (5 items); rapid opening/closing of hands (2 items); finger tapping (2 items); rising from a chair (one item); posture and postural instability (2 items); gait (one item); and body bradykinesia (one item). Each item was rated 0–4 with 0 representing absence of symptoms (or normal activity) and 4 the presence of significant symptoms or impairment. The mean of each scale was calculated and then the ratio (tremor/akinetic-rigidity score) determined. A score $\leq$1 was considered PIGD, 1-1.5 was intermediate PD, and $\geq$1.5 was recorded as tremor-dominant PD.

2.3. Statistical analysis

All statistical analyses were performed using SPSS version 18.0 software (SPSS, Chicago IL). Wilcoxon rank tests (Z-tests), and *t*-tests were used to compare the MoCA and MMSE scores and other variables between the cognitively normal and cognitively impaired groups. The data for normally distributed variables is presented as the mean $\pm$ standard deviation. Non-normally distributed continuous data is presented as the median and interquartile range (IQR). Categorical data is shown as the rate and 95% confidence interval (CI). Bivariate logistic regression analyses were performed at follow-up to find predictors of cognitive impairment. A probability value $P < 0.05$ was considered statistically significant.

3. Results

The 102 PD patients who completed the follow-up were from Nanjing and the surrounding area; 55 were men. The men and women patients were comparable in age, age of PD onset, and duration and severity of disease (UPDRS III score). At baseline, the women patients had attained less education and MoCA scores than the men. At enrollment, the patient's ages were 36–80 y (64.32 ± 9.00 y). The age at PD onset was 26–77 y (57.89 ± 10.24 y), the average duration of PD was 6.43 ± 4.55 y. Their UPDRS III score of these patients was 18.76 ± 10.29; the Hoehn-Yahr stage 2–4. Subjects had achieved an average of 9.71 ± 4.06 y of education. The educational levels of the patents were as follows: 6 (5.88%) patients were illiterate; there were 14 (13.73%), 28 (27.45%), and 24 (23.53%) whose highest educational attainment was the completion of primary, junior, and high school, respectively. Those who had more years of education included 17 (16.67%) who graduated from technical college and 12 (11.76%) with a bachelor's degree or higher. Regarding motor subtypes, 41 (40.20%), 16 (15.67%), and 45 (44.12%) patients were PIGD, intermediate, and tremor-dominant.

The PD patients' cognitive scale scores (MMSE and MoCA) at the 30-month follow-up were significantly lower than that at the baseline ($P < 0.001$, both; Table 1). Specifically, the mean MMSE score was 28.16 ± 2.29 at baseline, and 26.18 ± 3.64 after 30 months; the MoCA score at baseline was 24.60 ± 4.23, and 21.94 ± 5.47 at follow-up.