Journal of Clinical Neuroscience 22 (2015) 981–985

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Clinical Study

A neurophysiological profile in Parkinson's disease with mild cognitive impairment and dementia in China

Ya-qin Wang [a,d], Bei-sha Tang [a,b,c,f], Xin-xiang Yan [a,c,f], Zhi-heng Chen [d], Qian Xu [a,c], Zhen-hua Liu [a], Kai Li [a], Kai Wang [e], Ji-feng Guo [a,b,c,f,*]

[a] Department of Neurology, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha 410008, Hunan, People's Republic of China
[b] State Key Laboratory of Medical Genetics, Changsha, Hunan, People's Republic of China
[c] Neurodegenerative Disorders Research Center, Central South University, Changsha, Hunan, People's Republic of China
[d] Department of Healthy Management Center, The Third Xiangya Hospital, Central South University, Changsha, Hunan, People's Republic of China
[e] Neuropsychological Laboratory, Department of Neurology, First Hospital of Anhui Medical University, Hefei, Anhui, People's Republic of China
[f] Key Laboratory of Hunan Province in Neurodegenerative Disorders, Changsha, 410008 Hunan, People's Republic of China

ARTICLE INFO

Article history:
Received 24 September 2013
Accepted 25 November 2014

Keywords:
Dementia
Mild cognitive impairment
Neuropsychological assessment
Parkinson's disease

ABSTRACT

Mild cognitive impairment (MCI) and dementia (D) are frequent features of Parkinson's disease (PD) but widely disparate criteria have been used. Our understanding of the prevalence and cognitive profile of Chinese PD patients remains limited. In order to determine the frequency and pattern of cognitive dysfunction and identify risk factors for cognitive dysfunction in the Chinese Han PD population we performed a cross-sectional study in a cohort of 330 PD patients and 163 healthy controls. Five cognitive domains (executive function, attention, praxis and visuospatial function, memory, and language) and mood/behavior were evaluated. According to the Movement Disorder Society Task Force consensus criteria, up to 29.1% of PD patients were classified as PD-MCI and 32.1% as PD-D. Impairments occur in a range of cognitive domains with dysexecutive profile predominating. Healthy controls also outperformed cognitively preserved PD patients in tasks of executive function and attention. Logistic regression indicated that PD-MCI may be predicted by lower educational level and apathy. Additionally, later disease onset, longer disease duration, more severe motor symptoms and higher neuropsychiatric inventory score were associated with a faster transition from PD-MCI to PD-D. These findings suggest that all PD patients should undergo routine cognitive screening. For high-risk patients early recognition and therapeutic intervention is imperative.

1. Introduction

There is compelling evidence that Parkinson's disease (PD) is much more than a movement disorder and cognitive deterioration is inherent [1]. The presence of cognitive impairment has been noted even at the very beginning of the disease [2]. Clinical manifestations range from modest deficits only demonstrated by means of comprehensive neuropsychological testing up to dementia (PD-D). Associated with normal aging and Alzheimer's disease, the construct of mild cognitive impairment (MCI) has also been applied to PD. In PD, MCI has been used to describe the earliest stage of cognitive decline and prodromal PD-D [3]. Estimates of the mean point prevalence of PD-D are up to roughly 30% and the 8 year cumulative prevalence is reported to be 78% [4,5]. Likewise, PD-MCI is common, occurring in about 19–38% of nondemented PD patients [6].

The onset of cognitive impairment in PD is insidious, often making it difficult for the patient and the family to identify. In clinical practice, only 25% of PD-D patients are recognized by clinicians [7]. The clinical features of cognitive impairment in PD are heterogeneous and encompass a broad spectrum. A subcortical pattern predominates in both PD-MCI and PD-D [8,9]. For PD-MCI there are also four clinical subtypes with both nonamnestic and amnestic cognitive domains affected and single and multiple-domain impairment [10]. This heterogeneity may reflect differences in the neurobiological substrates.

Historically, the existing criteria for PD-D is based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders which emphasizes memory function and not characteristics of cognitive deficits in PD-D. The manual also diagnoses PD-MCI differently and uses many variable definitions. In order to allow more accurate clinico-pathological correlation studies and help to determine the natural history of cognitive impairment in a more systematic way, the Movement Disorder Society Task

* Corresponding author. Tel.: +86 731 84327398; fax: +86 731 84327332.
E-mail address: guojifeng2003@163.com (J.-f. Guo).

http://dx.doi.org/10.1016/j.jocn.2014.11.030
0967-5868/

Force (MDSTF) proposed consensus criteria for both PD-D and PD-MCI [11,12].

To date, a large body of clinical literature exists that focuses on different clinical features and risk factors associated with PD-D and PD-MCI but very few studies have used a comprehensive neuropsychological test battery comprising all cognitive function domains and neuropsychiatric symptoms simultaneously. Especially in Asian countries, research in cognitive impairment in PD is limited and the sample sizes are relatively small (no more than 50 patients with PD-MCI or PD-D) [13,14]. The objective of this study is to provide a more accurate prevalence rate, cognitive profile and description of neuropsychiatric symptoms in PD with no cognitive impairment (PD-NC), PD-MCI and PD-D and to explore risk factors for cognitive impairment in these groups.

2. Patients and methods

2.1. Study samples

A sample of 330 consecutive PD patients were studied from the outpatient neurology clinics of Xiangya Hospital, Central South University. All PD patients fulfilled the research diagnostic criteria for idiopathic PD [15]. We excluded those with atypical or secondary Parkinsonism, known causes of dementia and prior neurosurgery. The 163 age, gender and education matched healthy controls were enrolled from patients' spouses or medical checkup participants who reported no subjective cognitive decline on interview and were free from Parkinsonism and dementia. People who were illiterate, color blind, deaf, suffered major depression (Hamilton depression rating scale $\geqslant$14 points) [16] and psychosis were excluded.

2.2. Neurological and neuropsychological assessment

The study was formally approved by the Medical Ethical Committee of Central South University. Patients or their power of attorney gave written informed consent prior to participating in the study. All assessments were done during the on-motor state. For PD patients, detailed demographic and clinical information were obtained. Standardized evaluations using Unified Parkinson's Disease Rating Scale (UPDRSIII), Hoehn and Yahr scale and activities of daily living scale were also documented. The patients were classified into postural instability gait difficulty (PIGD), tremor-dominant or indeterminate motor subtypes using the approach proposed by Jankovic et al. [17].

The psychometric evaluations were made by impartial individuals who were blinded to the demographic and clinical characteristics of the patients. A battery of cognitive and neuropsychiatric tests were performed: (1) overall cognitive status: mini-mental state examination (MMSE), the Beijing version of the Montreal cognitive assessment; (2) attention and working memory: digit span forward and backward, the Stroop Color-Word test, Serial 7s (a subtest of MMSE); (3) executive functions: semantic fluency test, phonological fluency test, frontal assessment battery; (4) praxis and visuospatial ability: clock-drawing test, judgment of line orientation test; (5) memory function: Hopkins verbal learning test, three word recall (subtest of MMSE); (6) language: similarities, naming (subtest of MMSE and the Beijing Montreal cognitive assessment); (7) mood/behavior: Hamilton depression rating, apathy scale and neuropsychiatric inventory.

2.3. Definition of cognitive status of PD

The diagnosis for PD-D was made according to MDSTF criteria and operationalized according to the diagnostic algorithm outlined by Dubois et al. [11]. The definition of PD-MCI was also adopted from the recently proposed MDSTF criteria [12] then the remaining portion was classified as PD-NC. Four subtypes of PD-MCI were further determined: nonamnestic single-domain cognitive impairment, amnestic single-domain cognitive impairment, amnestic multiple-domain cognitive impairment and nonamnestic multiple-domain cognitive impairment [18].

2.4. Statistical analyses

All statistical analysis was performed using SPSS statistics software (version 18.0, IBM Corporation, Armonk, NY, USA). Descriptive statistics were expressed as mean ± standard deviation. Group differences were compared on means (one way analysis of variance or Kruskal–Wallis) or proportions (chi-squared test) as appropriate. Multivariable logistic regression analyses were performed to assess risk factors and predict cognitive performances in PD patients. Independent factors which correlated at a significant level in the bivariate analysis were included in a subsequent multivariate logistic regression model with the PD-NC and PD-MCI, PD-MCI and PD-D as the dependent variables. Differences were interpreted as significant at $p < 0.05$.

3. Results

3.1. Prevalence of cognitive impairment in PD patients

Of all the 330 PD patients, 96 patients were considered to be PD-MCI (29.1%; 95% confidence interval [CI] 24.2–34.0) and 106 patients met the criteria for probable PD-D (32.1%; 95% CI 27.1–37.2; Fig. 1A). The distribution of four subtypes in PD-MCI is shown in Figure 1B.

3.2. Demographic and clinical characteristics in PD-NC, PD-MCI and PD-D patients

Table 1 shows the general characteristics of different groups. No difference was observed among these groups for side of motor onset. There were significant differences for educational level and UPDRSIII scores between the three groups and PD-MCI mean values were intermediate.

3.3. Cognitive profile in healthy controls and PD patients

An overview of neuropsychological results for each group is outlined in Table 2. Compared to the healthy controls, the PD-NC patients were impaired on the digit span forward and semantic fluency tests and neuropsychiatric symptoms were more common. As expected, most results of the examined neuropsychological assessments and neuropsychiatric symptoms differed significantly across the three groups in the order of PD-D < PD-MCI < PD-NC. The proportion of patients showing impairment in PD-MCI and PD-D followed a similar pattern, in the order of executive function (43.8% and 93.4%, respectively) > memory (37.5% and 78.3%) > attention (35.4% and 53.8%) > visuospatial function (25.5% and 50.0%) > language (8.3% and 41.5%).

3.4. Factors associated with cognitive impairment in PD

Multivariable logistic regression revealed that educational level and apathy were independently associated with PD-MCI and age at disease onset, disease duration, UPDRSIII and neuropsychiatric inventory score showed a significant effect on PD-D status (Table 3).