Parkinsonism and Related Disorders 20 (2014) 1071–1075

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Severity of mild cognitive impairment in early Parkinson's disease contributes to poorer quality of life

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ARTICLE INFO

Article history:
Received 13 December 2013
Received in revised form
14 May 2014
Accepted 8 July 2014

Keywords:
Parkinson's disease
Mild cognitive impairment
Quality of life

ABSTRACT

Background: Poor quality of life (QoL) is a feature of people with Parkinson's disease (PD) who develop dementia. The relationship between mild cognitive impairment in PD (PD-MCI) and QoL is less clear. To address this, we studied the impact of varying severities of cognitive impairment on QoL in a cohort of non-demented patients with early PD.

Method: Patients with newly diagnosed PD ($n = 219$) and age and sex matched healthy controls ($n = 99$) completed a schedule of neuropsychological tests, in addition to scales assessing QoL (PDQ-39), depression, sleep, neuropsychiatric symptoms and a clinical examination. The Movement Disorder Society criteria were used to define and classify PD-MCI.

Results: Participants with PD-MCI were significantly older than those with normal cognition, had more severe motor symptoms, scored higher for depression and had poorer quality of life. Logistic regression showed that mild cognitive impairment, independent of other factors, was an indicator of poorer QoL. Using cognitive performance 2.0 standard deviations (SD) below normative data as a cut-off to define PD-MCI, there was a significant difference in QoL scores between patients with PD-MCI and those classified as having normal cognition. Subjects with less severe mild cognitive impairment did not exhibit significant differences in QoL.

Conclusions: PD-MCI is a significant, independent factor contributing to poorer QoL in patients with newly diagnosed PD. Those classified with greatest impairment (2.0 SD below normal values) have lower QoL. This has implications for clinical practice and future interventions targeting cognitive impairments.

1. Introduction

Poor quality of life (QoL) and impaired wellbeing are common in Parkinson's disease dementia (PDD) [1], a frequent complication of Parkinson's disease (PD). The point prevalence of PDD is 25–30%, which is six times higher than an aged-matched general population [2]. Cumulatively the prevalence of PDD is estimated to be up to 80% [3]. PDD is associated with increased risk of falls, caregiver burden, nursing home placement and increased mortality [1–3]. In addition, fractures, urinary incontinence, hallucinations and neuropsychiatric symptoms are also common in PDD and impact on QoL.

The Movement Disorder Society (MDS) Task Force defines mild cognitive impairment in PD (PD-MCI) as performing 1 to 2 standard deviations (SD) below appropriate normative values in neuropsychological tests with no impairments of activities of daily living (ADL) [4]. It is a potential early marker for the development of PDD [5–7] so may also be associated with poorer QoL [8]. The prevalence of PD-MCI is between 15 and 40% at the time of PD diagnosis [1,6,7]. This variability may be due to a lack of consensus in defining PD-MCI, which did not exist until the proposed diagnostic MDS criteria were agreed upon in 2011. A recent review of the literature showed a wide variation in the tests used to diagnose PD-MCI and inconsistencies in the criteria used [9]. The lack of consistent cut-offs leaves much room for variation across studies. A cut-off of below 1.5 SD of normative data of age-matched controls was the most common criterion used.

The relationship between PD-MCI and QoL is unclear; currently only two studies have used the MDS Task Force diagnostic criteria

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http://dx.doi.org/10.1016/j.parkreldis.2014.07.004

to investigate QoL in PD-MCI [1,8]. It is vital to understand the contribution MCI and cognitive decline has on PD patients, in addition to the motor and non-motor symptoms, and the extent to which it influences QoL. Understanding the impact of PD-MCI would help guide clinicians as to what pharmacological and non-pharmacological interventions might be particularly effective [10–12]. We therefore investigated whether the degree of severity of PD-MCI independently influences QoL in patients with newly diagnosed PD. This is also the first study to examine the effects of PD-MCI on QoL in a large cohort of early PD and to explore the impact that different operational cut-offs for diagnosing PD-MCI have on QoL. We hypothesized that those with PD-MCI would have a poorer QoL compared to those with normal cognition.

2. Methods

2.1. Participants

This study was approved by the Newcastle and North Tyneside Research Ethics Committee and performed according to the Declaration of Helsinki. All participants provided written informed consent.

Participants were recruited from community and outpatient clinics through general practitioners, neurologists, geriatricians and PD nurse specialists in Newcastle upon Tyne, Gateshead and Cambridgeshire as part of the Incidence of Cognitive Impairments in Cohorts with Longitudinal Evaluation-Parkinson's Disease (ICICLE-PD) study. All patients were newly diagnosed with idiopathic PD by a movement disorder specialist and fulfilled Queen's Square Brain Bank criteria [13]. All participants underwent detailed clinical assessment, including carer interviews, to exclude dementia. Participants were excluded if they had significant cognitive impairment at presentation (Mini Mental State Examination (MMSE) < 24) that impaired ADL, met DSM-IV criteria for dementia or a diagnosis of dementia [2]. Age-sex matched healthy controls were recruited through word of mouth and local advertising to provide normative data.

2.2. Scales and assessments

Participants and controls completed a schedule of neuropsychological tests. Global cognitive function was assessed using the MMSE [14] and Montreal Cognitive Assessment (MoCA) [15]. Table 1 shows the neuropsychological assessments used. Selective tests from the computerized Cognitive Drug Research (CDR) battery [16] and Cambridge Neuropsychological Test Automated Battery (CANTAB) [17] were used to assess attention, memory and executive function. The phonemic fluency test asked participants to generate as many words as they could in 60 s beginning with the letter F [18]. Similarly, the semantic fluency test asked participants to list as many animals as they could in 90 s [18]. Visuospatial function was evaluated using the pentagon copying item within the MMSE [14] and was graded using a modified 0–2 rating scale [19].

Consistent with the MDS Task Force criteria [4], participants were classified as having PD-MCI if they scored 1 to 2 SD below the means of appropriate norms (controls) on at least two neuropsychological tests across five cognitive domains: attention, executive function, visuospatial function, memory and language. For data that was not normally distributed and could not be transformed appropriately, percentiles derived from a normal distribution were used to estimate cut-offs 1 SD (16th percentile), 1.5 SD (7th percentile) and 2 SD (2nd percentile), therefore the cut-offs give approximately the correct percentage of people impaired. For example, the pentagon score was assessed as 2 (shape includes 10 angles and clear intersection), 1 (two intersecting figures, one with five angles) or 0 (less acceptable copy); using corresponding percentiles from the control group, participants scoring 1 were classified as having impairment at the 1 SD and 1.5 SD level, and participants scoring 0 were classified as having impairment at the 2 SD level.

Implementation of our schedule of neuropsychological tests preceded the establishment of MDS criteria. However, broadly we were able to meet Level II criteria with our testing, despite having only one test specific for visuospatial impairment. We investigated the differences using 1 SD, 1.5 SD and 2 SD. These three cut-offs have been used in other studies, although 1.5 SD is the most common [8]. Additionally, subjective cognitive decline and functional independence of participants were determined through semi-structured interviews with participants and/or their carers.

Quality of life was measured using the Parkinson's Disease Questionnaire (PDQ-39) [20], which is widely used in PD research and clinics [6]. It includes a 39 item Likert scale covering eight domains: mobility, ADL, emotional wellbeing, stigma, social support, cognition, communication and bodily discomfort. The single index of this scale was used as a global measure of QoL in PD. The single index scores range from 0, (best possible QoL), to 100 (worst possible QoL).

Demographic information, including age, sex and education was collected. Participants also completed the MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III [21]. Premorbid intelligence was measured using the National Adult Reading Test (NART) [22]. Depression was assessed using the Geriatric Depression Score (GDS-15) [23]; a cut-off of ≥5 suggested possible depression. Neuropsychiatric symptoms were measured by the Neuropsychiatric Inventory (NPI-D) [24]. Participants were assessed when "on." Levodopa equivalent dose was calculated for all dopaminergic medications [25].

Table 1
Neuropsychological tests.

Domain	Test
Attention	CDR:
	Power of attention
	Digit vigilance
Executive function	CANTAB: One touch tower of London (OTS)
	Phonemic fluency
	Semantic fluency
Visuospatial function	Pentagons
Memory	CANTAB:
	Pattern recognition memory (PRM)
	Spatial recognition memory (SRM)
	Paired associate learning (PAL)
Language	MoCA:
	Naming
	Language

CDR = Cognitive Drug Research Battery, CANTAB = Cambridge Neuropsychological Test Automated Battery, MoCA = Montreal Cognitive Assessment.

2.3. Statistical analysis

Statistical analyses were performed using SPSS software (Version 19.0; SPSS, Inc., Chicago, IL). Data were examined for normality of distribution with visual histograms and Kolmogorov–Smirnov's test. Comparisons of means between two groups were performed using independent *t*-tests or Mann–Whitney *U* test as appropriate. For more than two group comparison one way ANOVAs or Kruskal–Wallis tests were used as appropriate. Multiple comparisons were corrected using Bonferroni's correction; the cut-off for significance was calculated using α/n where α is the significance level (0.05) and n is the number of tests. Logistic regression was used to build a model to predict QoL; data were dichotomized using the median, such that scores below the median were low and scores above the median were high.

3. Results

Participants ($n = 219$) were aged between 35 and 87 years (mean of 65.9, SD = 9.7); 63.9% were male ($n = 140$). Mean time since diagnosis was 5.5 months (SD = 5.0), 83% were rated as Hoehn and Yahr stage 1 or 2 and 16% were drug naïve. The ages of the control subjects ($n = 99$) ranged from 48 to 88 years (mean of 67.9, SD = 8.2) and 55% were male ($n = 54$). There was no significant difference between age ($p = 0.06$) and sex ($p = 0.11$) of PD participants and controls. Neither was there a significant difference between PD participants and controls in terms of number of years of education (mean of 13.1 SD = 3.4 and 12.8 SD = 3.6, respectively; $p = 0.36$) and NART scores (mean of 115.8, SD = 8.7 and 114.3, SD = 10.3, respectively; $p = 0.37$).

The clinical characteristics of the cohort according to different levels of PD-MCI are shown in Table 2. PD participants classified as normal cognition (PD-CN) scored within 1 SD of normative data. Three MCI groups were defined: MCI 1 SD which included those with a score of ≥1 SD but <1.5 SD below normative data (23.2%); MCI 1.5 SD which included those with a score ≥1.5 SD but < 2 SD below normative data (21.1%); and MCI 2 SD who scored ≥2 SD below normative data (22.4%). In each group, participants scored below the means of appropriate norms (controls) on at least two neuropsychological tests for that standard deviation.

As a group, participants with PD-MCI (≥1 SD below normative data) were most commonly impaired in executive function (67%), memory (61%) and attention (51%) domains. They were significantly older, had spent fewer years in education and had a lower premorbid IQ (NART) ($p < 0.01$) than PD-CN. They also had a higher MDS-UPDRS III score ($p < 0.01$) and Hoehn and Yahr stage