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Short Communication

Quality of Life and Mild Cognitive Impairment in Early Parkinson's Disease: Does Subtype Matter?

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Abstract. We evaluated the association between mild cognitive impairment (MCI) subtypes and quality of life (QoL) in 219 newly diagnosed Parkinson's disease (PD) patients without dementia. Participants completed neuropsychological tests of attention, executive function, visuospatial function, memory, and language, and reported QoL using the Parkinson's Disease Questionnaire. Impairments were most common in executive function, memory and attention. MCI subtypes were classified according to Movement Disorder Society Task Force criteria. More severe cognitive impairment was associated with poorer quality of life ($p = 0.01$), but subtype of impairment was not ($p > 0.10$), suggesting that the nature of cognitive impairment is less significant than its severity.

Keywords: Parkinson's disease, quality of life, mild cognitive impairment, subtypes

INTRODUCTION

For the individual living with Parkinson's disease (PD), the development of dementia (PDD) has a significant impact upon quality of life (QoL) [1]. Mild cognitive impairment in PD (PD-MCI) may be a precursor to PDD, and thus may also impact on QoL [2]. Furthermore, QoL may be affected by particular subtypes of MCI [1], where impairments in multiple domains may have greater cognitive burden and thus may cause greater difficulties in activities of daily

living (ADL) and poorer QoL [3, 4]. Additionally, specific domains, e.g. deficits in attention and executive function which are common in PD, may be more detrimental to ADL and QoL [4–6].

To the authors' knowledge, there are currently no studies investigating whether QoL in people with PD-MCI differs between subtypes. Such information could help guide clinicians as to what pharmacological and non-pharmacological interventions might be particularly effective [7]; e.g. cholinesterase inhibitors for attention could improve QoL [5, 8].

We evaluated the impact of PD-MCI subtypes upon QoL in a large cohort of patients with newly diagnosed PD. We hypothesised that PD-MCI would negatively affect QoL and that the effect across the different MCI subtypes would not be equal, with executive dysfunction and attention having a greater impact.

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PARTICIPANTS AND METHODS

Newly diagnosed idiopathic PD patients, as per Queen's Square Brain Bank criteria [9], were recruited from community and outpatient clinics. Participants and age-sex matched healthy controls completed a schedule of neuropsychological assessments covering five cognitive domains: attention, executive function, visuospatial function, language and memory [10]. Attention was assessed using Power of Attention and Digit vigilance from the Cognitive Drug Research Battery [11]. Executive function was assessed using the One touch Tower of London from the Cambridge Neuropsychological Test Automated Battery (CANTAB) [12], phonemic fluency (number of words generated in 60 seconds beginning with the letter F) and semantic fluency (number of names of animals generated in 90 seconds) [13, 14]. Memory was assessed using Spatial and Pattern Recognition Memory, and Paired Associate Learning subsets from the CANTAB. Visuospatial dysfunction was measured using a modified scoring for copying interlocking pentagons [15]. Language dysfunction was measured using the naming and language scores from the Montreal Cognitive Assessment (MoCA) [16]. Premorbid intelligence was measured using the National Adult Reading Test (NART) [17].

As our study design predated the Movement Disorder Society (MDS) Task Force PD-MCI criteria, we used a modified Level II criteria, which is described in full elsewhere [10], at cut offs of 1.0, 1.5 or 2.0 standard deviations (SD) below normative values (controls) to classify PD-MCI. For non-normally distributed neuropsychological scores, an approximation to the normal distribution was used to calculate cut-offs. Single-domain PD-MCI was defined as impairment in two tests in the same domain; multi-domain classification required at least one impaired test in more than one domain [18]. Participants were then classified according to impairments in specific domains.

The Parkinson's Disease Questionnaire (PDQ-39) single index score was used to assess QoL [19], where a score of 0 indicates best QoL and a maximum score of 100 indicates worst QoL. This questionnaire is widely used and recommended for measuring QoL in PD [20].

This study was approved by the Newcastle and North Tyneside Research Ethics Committee. All participants provided written informed consent.

Statistical analyses were performed using SPSS Version 19.0. Comparisons of means between two groups or more than two groups were performed using independent *t*-tests, Mann-Whitney U test or Kruskal-Wallis tests as appropriate..

RESULTS

There were no significant differences between PD participants ($n=219$) and controls ($n=99$) in terms of age (mean of 65.9 ± 9.7 vs 67.9 ± 8.2 years; $p=0.06$), sex (males 63.9% vs 55%; $p=0.11$), level of education (mean of 13.1 ± 3.4 vs 12.8 ± 3.6 years; $p=0.36$) and NART scores (mean of 115.8 ± 8.7 vs 114.3 ± 10.3 ; $p=0.37$). Mean duration of PD was 5.5 ± 5.0 months, 83% were rated as Hoehn and Yahr stage 1 or 2.

Using our modified MDS criteria 66% ($n=144$) were classified as having PD-MCI (≥ 1 SD below normative data); they were significantly older ($p<0.01$), had completed fewer years of education ($p<0.01$) and more severe motor symptoms ($p<0.01$). QoL scores were significantly worse for participants with PD-MCI (mean of 24.3 ± 19.4 vs 31.2 ± 23.3 ; $p=0.03$).

Participants were grouped by MCI severity, participants scoring: ≥ 1 SD but <1.5 SD below normative data (PD-MCI 1SD, $n=51$); ≥ 1.5 SD but <2 SD below normative data (PD-MCI 1.5 SD, $n=44$); and ≥ 2 SD below normative data (PD-MCI 2 SD, $n=49$). *Post hoc* analysis showed PDQ-39 scores were significantly worse using the 2 SD PD-MCI cut off (mean of 38.2 ± 25.2 ; $p=0.01$) compared to 1 SD and 1.5 SD cut off (mean of 26.6 ± 21.9 and 28.8 ± 21.2 respectively), suggesting that more severe MCI was a major contributor to poor quality of life in the MCI group.

Subtypes of mild cognitive impairment

The MDS PD-MCI criteria identified 22 subtypes (Fig. 1). Significantly more subjects were classified as having multi-domain than single-domain MCI ($p<0.01$). Executive function (67%), memory (61%) and attention (51%) were most frequently impaired. The most common subtypes were memory+executive function (22%), attention+executive function (13%) and attention+memory+executive function (13%). Figure 1 also shows that the number of participants in each subtype was relatively small; the first seven subtypes accounted for the majority of participants, with those after the divide making up less than 5% of participants in each subgroup.

Figure 2 shows a radar plot of the seven most frequent subtypes and PDQ-39 score by PD-MCI cut off; values extending from the centre of plot indicate worse QoL. In most subtypes, QoL decreased as cognitive impairment increased. Single-domain attention and multi-domain attention+memory+executive function tended to be associated with poorer QoL at the 2 SD cognitive cut off compared to other cut offs, but

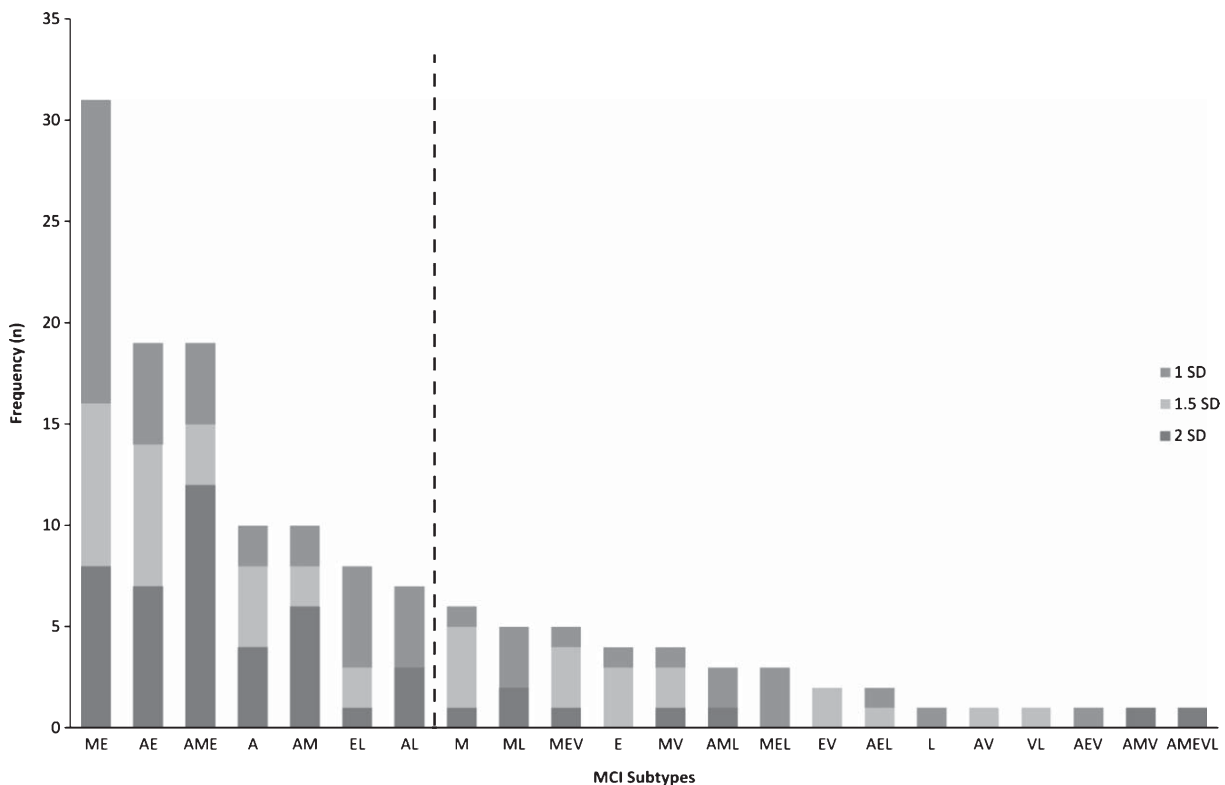


Fig. 1. Subtypes of mild cognitive impairment in participants with newly diagnosed Parkinson's disease. Subtypes of mild cognitive impairment (MCI): A = Attention; E = Executive function; L = Language; M = Memory; V = Visuospatial function.

overall there were no significant differences in QoL between MCI subtypes ($p > 0.10$).

We conducted a secondary analysis using classifications outlined by Marras, et al. [21], which required two tests impaired in at least one domain. This identified fewer PD-MCI participants (≥ 1 SD below normative data; $n = 104$) with significantly more single-domain impairments (76%). The most common subtypes were single-domain executive function (25%) and memory (19%); memory+executive function remained the most common multiple-domain subtype (5%). There were no significant differences in QoL between subtypes ($p > 0.10$).

DISCUSSION

In this large incidence cohort, we found that QoL decreased as severity of MCI increased. We identified a number of PD-MCI subtypes and found more multi-domain impairments than single-domain, although there were no significant differences in QoL between subtypes. This may suggest that in PD-MCI it is the

severity of cognitive impairment, rather than the nature of impairment, that impacts on QoL.

Impairment was most common in executive function, memory and attention. Two thirds of PD-MCI participants had executive dysfunction. A recent study has also observed high frequencies of executive dysfunction in PD-MCI [22], which can impair ADL [8]. Memory was the second most common impaired domain, which was also reported by Goldman, et al. [22], and has been shown to negatively impact on QoL [23, 24]. Half of PD-MCI participants had attentional dysfunction, which was also the most common single-domain subtype. This has also been observed in a previous study [25] and has been shown to significantly impact physical functioning and social interaction [5]. Significantly, only 15% of PD-MCI subjects had single-domain impairment. The high proportion of multi-domain impairments has also been found in other studies [21, 22, 26, 27].

To our knowledge, this is the first study to explore the relationship between QoL and PD-MCI subtypes. More severe impairment in single-domain attention and multi-domain attention+memory+executive

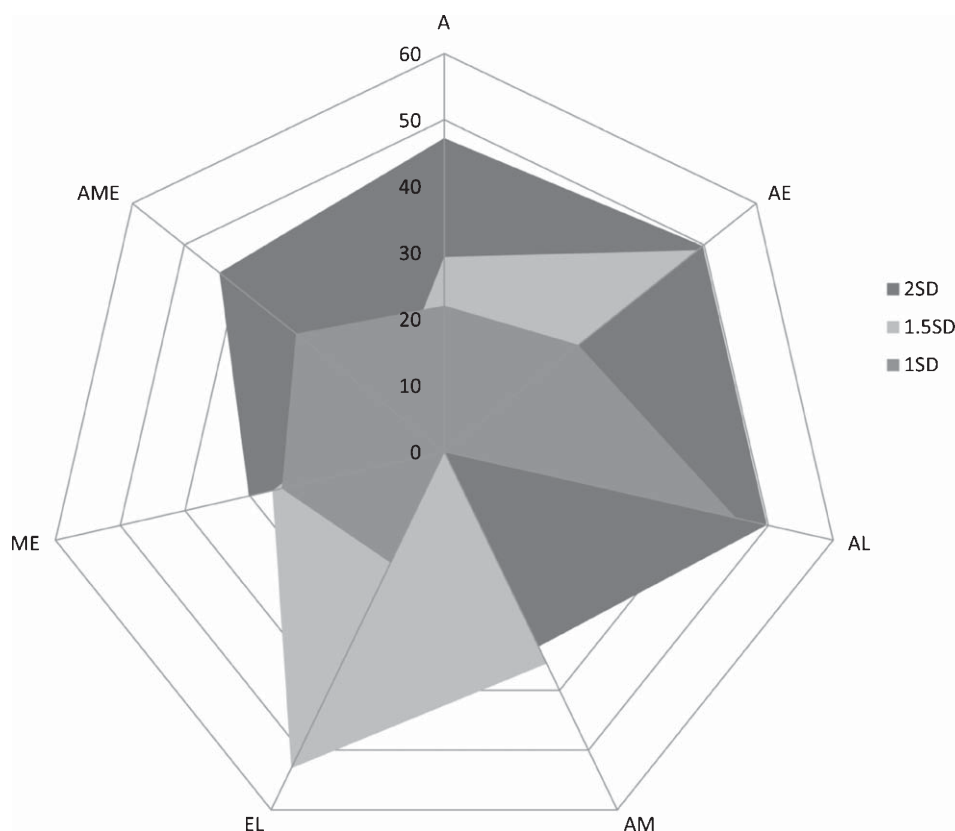


Fig. 2. Subtypes of mild cognitive impairment and PDQ-39 scores. Radar plot of mean PDQ-39 scores of each cut-off, (1 SD, 1.5 SD and 2 SD below normative values) for the most frequent subtypes of mild cognitive impairment. Scale on graph is PDQ-39 score, where higher values indicate worse quality of life. A = Attention; E = Executive function; L = Language; M = Memory; V = Visuospatial function; PDQ-39 = Parkinson's Disease Questionnaire.

function subtypes tended to be associated with poorer QoL, although we did not find any significant differences in QoL score between subtypes. Previous studies have variable findings between cognitive domains. Attention and memory problems have been associated with worse QoL [23], whilst another study found visuospatial function, executive function and attention in PD participants affected QoL [4]. Impairment in specific domains can inhibit everyday functioning and ADL [5], or results in less effective coping strategies [6]. Therefore, there may be an interaction between PD-MCI and other lifestyle variables; those with higher premorbid functioning may find the challenge of having MCI greater [24].

The strength of this study is in the large cohort of newly diagnosed PD participants with an age-matched control group. Limitations include its design that preceded the publication of the MDS PD-MCI criteria. We therefore used a modified version with an unequal numbers of tests per domain comprising only one test for visuospatial function and more than two tests for

memory and executive function. This has implications for subtyping and may increase the frequency of impairments in these domains. The small number of participants in each subtype reduced statistical power, decreasing the sensitivity of our study to detect subtle differences between subtypes.

In summary, PD-MCI is complex with severity of impairment, rather than subtype, affecting QoL. It could be inferred that the current MDS guidelines for subtyping PD-MCI may not be optimal, we identified 22 subtypes using the proposed guidelines. Numerous subtypes may be impractical in clinical settings; this could indicate that subtyping is of no real significance to patients and that their QoL is not affected by the specific nature of the impairment.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to report.

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