



## Cognitive profile and determinants of poor cognition in people without dementia in Parkinson's disease

Max Barnish<sup>1</sup>, David J Daley<sup>2</sup>, Katherine HO Deane<sup>3</sup>, Allan B Clark<sup>2</sup>, Richard J Gray<sup>4</sup>, Simon MC Horton<sup>3</sup>, Zoe R Butterfint<sup>3</sup>, Phyo K Myint<sup>\*5</sup>

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### Abstract

**Background:** The Montreal Cognitive Assessment (MoCA) has been recommended as a cognitive screening tool for clinical practice and research in Parkinson's disease (PD), yet no normative data have been published for MoCA in PD without dementia.

**Methods:** We undertook a pooled secondary analysis of data from two studies (one cross-sectional design and one clinical trial) conducted in the East of England region. All participants were aged 18 years or over, met UK Brain Bank criteria for PD and did not have clinical dementia. Cognitive status was assessed using MoCA at baseline in both studies. The influences of age, gender, disease duration, medication load (LEDD) and mood (HADS) on cognition were examined using regression analysis.

**Results:** Data from 101 people with PD without dementia were available (mean age 71 years, 66% men). Median (IQR) MoCA was 25(22, 27). Age was found as the only predictor of MoCA in this sample. People aged over 71 had poorer MoCA (Beta=0.6 (95%CI 0.44, 0.82)) and an increased odds of MoCA <26 (Beta=0.29 (95%CI 0.12, 0.70)) as well as poorer scores on several MoCA sub-domains.

**Conclusion:** We present the normative data for MoCA in people with PD without clinical dementia. Age appeared to be the only associated factor for lower level of cognition, suggestive of Mild cognitive impairment in PD (PD-MCI) in PD without clinical diagnosis of dementia.

**Keywords:** Neuropsychology, Cognition disorders, Parkinson disease, Geriatrics

**Conflicts of Interest:** None declared

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### Introduction

Parkinson's disease (PD) is a common neurodegenerative condition affecting around 1.5% of people over 65 in Europe (1). Mild cognitive impairment in PD (PD-MCI) is found in over a quarter of patients (2), may be present at diagnosis (3) and is predictive of the risk of developing dementia (2), an outcome that occurs in over 80% of patients (4).

There exist a range of tools that can be used to assess cognitive status in PD. However, long-established assessment tools such as the Mini Mental State Examination (MMSE) (5) have been shown to be insensitive to mild cognitive impairment in PD (6). The Montreal Cognitive Assessment (MoCA) (7) is a brief screening tool that, based on its good psychometric properties,

**Corresponding author:** Phyo K Myint, [phyo.myint@abdn.ac.uk](mailto:phyo.myint@abdn.ac.uk)

<sup>1</sup> Institute for Health Research, College of Medicine and Health, University of Exeter, Exeter, UK

<sup>2</sup> Norwich Medical School, University of East Anglia, Norwich, UK

<sup>3</sup> School of Health Sciences, University of East Anglia, Norwich, UK

<sup>4</sup> Department of Nursing, La Trobe University, Melbourne, Australia

<sup>5</sup> Aging Clinical and Experimental Research (ACER) Team, School of Medicine, Medical Sciences, and Nutrition, University of Aberdeen, Aberdeen, UK

#### ↑What is "already known" in this topic:

- Mild cognitive impairment in PD (PD-MCI) is found in over a quarter of patients, may be present at diagnosis and is predictive of the risk of developing dementia.
- The Montreal Cognitive Assessment (MoCA) has been recommended as a cognitive screening tool for clinical practice and research in PD.

#### →What this article adds:

- We present the normative data for MoCA in people with PD without clinical dementia.
- Age appeared to be the only associated factor for lower level of cognition suggestive of PD-MCI in PD without clinical diagnosis of dementia.

has been recommended for clinical practice and research (8) and approved by the Movement Disorder Society for the Level 1 criteria for PD-MCI diagnosis (9).

The potential advantages of MoCA over more traditional cognitive diagnostic tools such as MMSE have been studied for a considerable period of time. For example, Mamikonyan et al (6) found that MoCA detected mild cognitive impairment in 29% of people with PD with normal age- and education-adjusted MMSE scores. Hoops et al (10), Zadikoff et al (11), and Dalrymple-Alford et al (12) all also found MoCA to be superior to MMSE in detecting mild cognitive impairment in PD. Moreover, Biundo et al (13) found MoCA to be superior to MMSE in assessing cognitive change.

However, the focus has been largely on psychometrics rather than epidemiological investigation. Although normative data for PD with dementia have been published in the Greek setting (14), there were only 19 participants in the study. Moreover, to our knowledge, no normative data for MoCA in people with PD without dementia have been previously reported, with existing studies instead focusing on assessing parameters such as test-retest reliability or convergent validity compared to other test instruments. Normative data would be useful for future research and practice. In addition to a lack of normative data for MoCA in people with PD without dementia, the pathophysiology of PD-MCI remains poorly understood (15) and the contribution of clinical and demographic risk factors for cognitive impairment in PD remains unestablished. One study has assessed the sensitivity and specificity of the domain-specific subsections of MoCA (16).

Given the lack of identified MoCA-specific normative data for people with PD without dementia, and the advantages such descriptive epidemiological data would offer in terms of guiding further research and better understanding cognitive impairment in PD and how this recommended tool can profile it, we undertook the analyses presented in this article. The aims of the study, therefore, are to i) present normative data for MoCA in people with PD without dementia; ii) assess the associations with potential risk factors for PD-MCI as measured by MoCA score.

## Methods

### Design and data sources

This article presents a pooled secondary analysis of de-duplicated anonymised data from two studies (17, 18) conducted in the East of England region. One was a cross-sectional observational study of functional communication in PD (17), while the other was a pilot randomised controlled trial of adherence therapy to improve medication adherence and quality of life in PD (18). These studies received Ethics approval from the National Research Ethics Service East of England Cambridge Central and Norfolk committees, respectively.

### Eligibility criteria

In order to be eligible for this analysis, participants had to: be aged 18 years or over, have a diagnosis of PD according to the UK Brain Bank Criteria (19), and have no clinical indication of dementia. Additionally, due to the specific requirements all participants in the study by Barnish et al (17) had to: have some degree of self-reported speech or communication difficulty, and have no history of other serious medical conditions likely to affect cognition, speech or communication. All participants from Daley et al (18) had to: be prescribed one or more antiparkinsonian medications, be on a stable medication regime, and have a Morisky Medication Adherence Score (20) of at least 1.

### Measures

Cognitive status was assessed using MoCA (7) in both studies at the time of study enrolment. Scores for MoCA subsections were also collected. Medication load was assessed using Levodopa Equivalent Daily Dose (LEDD) (21). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) (22). Age, gender and disease duration in years were also extracted from the respective study databases.

MoCA has been shown in a Parkinson Study Group (PSG) Cognitive/Psychiatric Working Group task force systematic review (8) to be feasible to administer in a PD context, able to stand alone as a brief cognitive assessment taking <15 minutes, assess all the major cognitive domains, be able to identify subtle cognitive impairment and have PD-specific psychometric data showing good test-retest reliability, inter-rater reliability and convergent validity across studies, have good sensitivity, some limitations in terms of specificity, and be able to identify mild cognitive impairment not detected by the MMSE. LEDD is an algorithm that was validated in a PD context through a systematic review (7) which provided the evidence base to derive the LEDD formulae. HADS is recommended as both a depression and an anxiety scale in PD according to Movement Disorder Society (MDS) task force systematic reviews (23-24). For depression, HADS was found across studies to have good internal consistency and test re-test reliability, acceptable sensitivity with some limitations in terms of specificity, it contained >50% psychological items, and benefitted from having <25% somatic items, resulting in little overlap with non-depressive symptoms of PD (23). For anxiety, HADS was found across studies to have satisfactory internal consistency and test-retest reliability, and to have a fair to moderate correlation with quality of life measures, but be unable to discriminate between anxiety and depression in PD (24). Therefore, we did not use HADS to measure anxiety and depression as separate constructs.

### Statistical analysis

Statistical analysis was conducted using STATA software (25). Descriptive statistics were used to pro-

file age, gender, disease duration, LEDD, HADS total score, MoCA total score and MoCA subsection scores (visuospatial, naming, attention, language, abstraction, delayed recall and orientation) using  $n$  (%), mean (SD) and median (IQR) as appropriate. MoCA total score was also profiled according to these potential risk factors for poor cognition. Then, regression models were constructed to assess the relationship between the following potential predictors: age, using median age of the cohort as a categorical cut off point (age 72 or over vs age 71 or below), gender, disease duration, HADS (<15 vs.  $\geq$ 15), quartiles of LEDD and MoCA score and MoCA subsection scores.

Full case analysis was used with logistic transformation applied. Relationships with the naming subscale could not be assessed due to insufficient variation in outcome scores.

## Results

A total of one hundred and one participants with PD were included in this study. The dataset from Barnish et al (17) provided 45 participants, while the dataset from Daley et al (18) provided an additional 56 participants. Twenty people participated in both studies and are therefore counted only once. The mean age (SD) of included participants was  $71.3 \pm 8.8$  years. Sixty-seven participants (66%) were men and the median disease duration was 8.0 years (IQR 4.0 to 13.0). The median LEDD score was 660.6 units (IQR 444.8 to 1109.4). The mean (SD) total HADS score was  $10.3 (\pm 5.7)$ .

Descriptive scores for total MoCA, potential risk factors of interest and the individual subsections of MoCA are provided in Table 1. The distribution of total MoCA scores is shown in Figure 1. The median value was 25 (IQR 22, 27), which is indicative of cognitive impairment in at least 50% of people with PD without apparent dementia. Sex-specific analysis showed (Fig. 2) that the cognitive profiles are comparable between men (mean 24.3, 95% CI 23.3, 25.4) and women (mean 24.6, 95% CI 23.4, 25.8). Similarly, MoCA scores did not differ substantially as a function of LEDD, HADS or disease duration.

Nevertheless, older participants had consistently lower MoCA scores (Fig. 3). For example, among participants in the 45-54 years age category, the mean

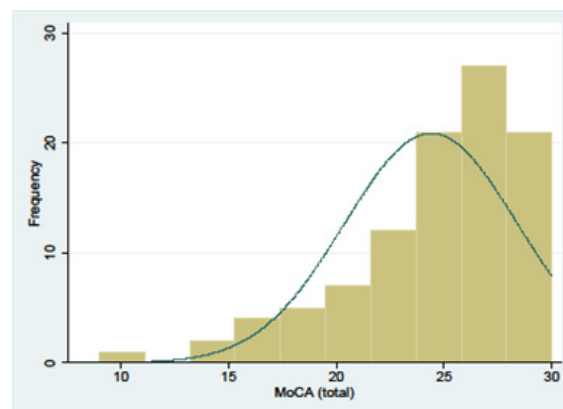


Fig. 1. Distribution of MoCA scores

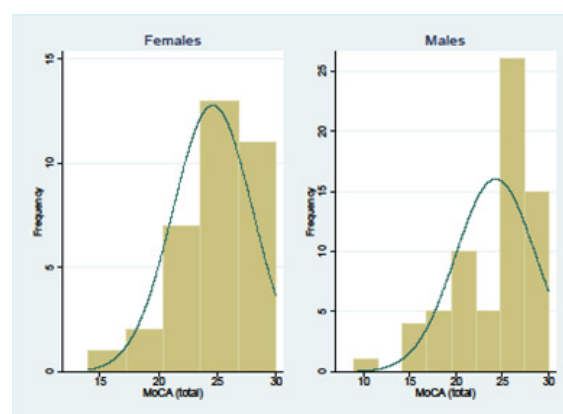


Fig. 2. Distribution of MoCA subdivided by gender

(95% CI) MoCA score was 28.0 (26.2, 29.8), whereas among over 75s, it was 23.1 (21.5, 24.7)

In inferential regression analysis, older age was a significant predictor of lower MoCA total score (Beta= 0.6, 95% CI 0.44, 0.82,  $p < 0.001$  for age below median vs age above median). Older age is associated with greater odds of cognitive impairment defined as a MoCA score  $\leq 26$  (OR=3.45, CI: 1.43, 8.33,  $p=0.006$ ), indicating cognitive impairment. Gender, disease duration, HADS score and LEDD score did not significantly predict MoCA total score or the odds of a MoCA score  $\leq 26$ . With regard to MoCA subscales, older age was a significant predictor of lower scores on the delayed recall (Beta=0.29, 95%CI: 0.11, 0.78,  $p=0.014$ ), attention (Beta=0.44, CI: 0.2, 0.99,  $p=0.046$ ) and

Table 1. Descriptive profile of MoCA total, risk factors and subsection scores

Measure	Mean; SD	Median; IQR	N; %
Age	71.3 (8.8)	-	-
Gender (male)	-	-	67; 66.3
Disease duration (years)	-	-	8.0; 4.0-13.0
LEDD	-	660.6; 444.8-1109.4	-
HADS total	10.3 (5.7)	-	-
MoCA total	-	25.0; 22.0-27.0	-
MoCA visuospatial	-	4.0; 3.0-5.0	-
MoCA naming	-	3.0; 3.0-3.0	-
MoCA attention	-	6.0; 5.0-6.0	-
MoCA language	-	3.0; 2.0-3.0	-
MoCA abstraction	-	2.0; 2.0-2.0	-
MoCA delayed recall	-	3.0; 2.0-4.0	-
MoCA orientation	-	6.0; 6.0-6.0	-

The most appropriate type of value is shown here for each outcome

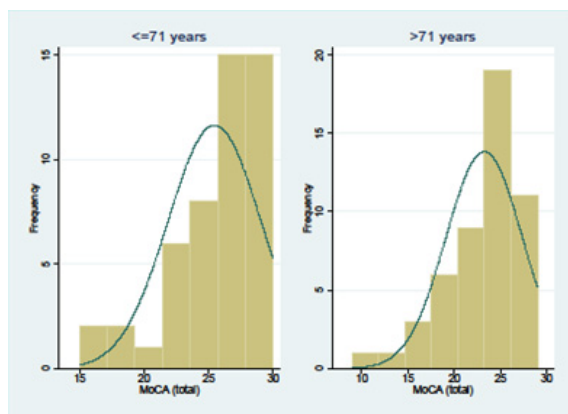


Fig. 3. Distribution of MoCA subdivided by age bands

visuospatial function (Beta=0.34, 95% CI: 0.15,0.78,  $p=0.010$ ) subscales.

### Discussion

To our knowledge this is the first study to present normative data for MoCA in people with PD without clinical dementia and to present associations between potential risk factors and MoCA score as the proxy marker of PD-MCI in this population. We found that more than half of participants with PD have cognitive impairment according to MoCA despite no overt dementia. Our study benefited from the use of MoCA as a sensitive indicator of PD-MCI as suggested by the literature in this field (8, 10-12).

We also present a graphical depiction of the distribution of MoCA scores to better understand the descriptive epidemiology of cognition in the context of PD without clinical dementia. We provide descriptive information for the different domains of MoCA, although no cut-off scores are available for the MoCA domains, unlike the MoCA total score. However, our results are suggestive of impairment across a broad range of cognitive areas, and are broadly congruent with the results of a recent meta-analysis (not MoCA-specific) in this respect (26). We found no gender differences in cognitive profile of people with PD across wide range of people with PD. Of our potential risk factors for PD-MCI, we only found a statistically significant association with age. In particular, we found that older people had poorer total MoCA scores. They also had poorer scores on the delayed recall, attention and visuospatial subscales, as well as an increased likelihood of having a total MoCA score lower than 26, which indicates cognitive impairment. This suggest that factors such as LEDD and disease duration may be less important for predicting the onset of cognitive decline in PD, and that age should be specifically acknowledged when planning potential interventions targeting cognition. Whether age in addition to disease duration, or other potential risk factors, further helps predict cognitive decline remains unknown and represents an area of further investigation.

Our study has several strengths. Through pooling two studies that specifically excluded people with clin-

ical dementia, we were able to present the first normative data for people with PD exclusively without apparent clinical dementia. Moreover, pooling these studies that shared a number of key clinical measures allowed us to study a sample size over five times larger than a prior study that provided some initial MoCA data in PD with dementia (14).

There are also some limitations we should consider. This is a secondary analysis, meaning that the sample size was powered on the objectives of the primary studies and the data available depend on what these studies collected. Therefore, regression analysis may be underpowered and has potential for missing possible associations. Also, this is a single- centre study with both primary studies having recruited from the same large academic medical centre in the East of England region with an overrepresentation of Caucasian individuals.

Future studies should seek to confirm the cognitive profile we present for people with PD without dementia, conduct further assessment of risk factors for PD-MCI using MoCA, assess prognosis and also consider the role of social factors such as keeping mentally and physically active. Such a programme of research could enable consideration of how cognitive risk scores could be calculated and used, as well as how to potentially slow or avoid cognitive decline in PD. The cognitive profile we present here could be an important foundation for this future research. In turn, such research could assess whether cognitive assessment for PD should be integrated into routine clinical practice and what benefits this might bring for patient outcomes.

### Conclusion

We present an analysis and graphical profile of MoCA scores in people with PD without dementia. More than half of participants had MoCA scores indicating cognitive impairment despite no overt dementia. Age predicted MoCA score, although no other variables were found to be predictive. Older people had poorer MoCA scores and were more likely to have a total MoCA score lower than 26 indicating cognitive impairment.

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### Conflict of Interests

The authors declare that they have no competing interests.

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