The Mini-Mental Parkinson’s (MMP) as a cognitive screening tool in people with Parkinson’s disease.

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**ABSTRACT**

**Introduction**

Cognitive decline is common in Parkinson’s disease (PD) but may not be adequately identified by the mini-mental state examination (MMSE), which is better suited to Alzheimer’s disease. The mini-mental Parkinson (MMP) examination is a cognitive screening tool designed in French specifically for PD. We aimed to establish the validity and reliability of the English language version of the MMP compared with the MMSE.

**Methods**

People with various stages of PD underwent testing with the MMP and MMSE, which was then compared with a reference standard battery of neuropsychological tests to identify those with significant cognitive impairment.

**Results**

Forty-nine patients were recruited. Both the MMP and MMSE were significantly correlated with scores on all the neuropsychological tests in the validation battery. The median MMP score was proportionally lower (80% of maximum) than the MMSE (90% of maximum) in PD patients with cognitive impairment and those with prior neuropsychiatric complications but there was no difference between the MMP and MMSE in areas under the curves (0.84) for detecting cognitive impairment. Test-retest reliability of the MMP was good (intra-class correlation coefficient 0.793). An MMP of 28 or lower out of 32 detected cognitive impairment with 87% sensitivity and 76% specificity.

**Discussion**

The English language version of the MMP has now been validated. It detects more cognitive deficits in PD patients than the MMSE and identifies significant cognitive impairment in those with PD at least as well as the MMSE.

**BACKGROUND**

In a recent systematic review, dementia was found to affect 25% to 30% of those with Parkinson’s disease (PD), and PD dementia (PDD) was found to account for 3% to 4% of all dementia. [1] Furthermore, the prevalence of dementia increases with increased duration of PD. One study reported that 60% of patients were diagnosed with dementia during 12 years of follow-up [2] and another that 83% of those surviving 20 years suffered from dementia.[3] PDD is more common with increasing age, increasing severity of motor symptoms, and where treatment-induced hallucinations are present.[4] Dementia in PD is associated with a poorer quality of life for patients [5] and their carers, [6,7] increased mortality, [8] and increased risk of nursing home admission. [4,9]

Many quick cognitive screening tools used in modern practice were developed in populations suffering from Alzheimer’s type dementias, and focus on orientation, attention, memory function and visuospatial abilities. However, the pattern of cognitive decline in PDD differs from that seen in these dementias. [10] Typically, there are marked deficits in executive function and attention as well as visuospatial and constructional abilities, with relative sparing of recall when compared with Alzheimer’s disease.

One of the most commonly used cognitive screening tools is the mini-mental state examination (MMSE). [11] Tools like the MMSE are not completely effective in identifying cognitive impairments in PD patients as they do not test for the deficits in executive functioning associated with the disease. Indeed, recent studies have found cognitive deficits to be detectable in people with PD in whom no deficit is detected using the MMSE. [12-15] The MMSE in particular may also be difficult to use in people with more advanced PD because patients’ performance in writing and drawing tasks is likely to be hampered by the motor features of the disease.

With these difficulties in mind, Mahieux *et al* [16] developed the Mini-Mental Parkinson (MMP) test. This tool is based on the MMSE, altered to specifically assess the cognitive deficits seen in PDD. It has the advantage of including no assessments requiring manual dexterity and is quick to administer (taking around 5 to 10 minutes). Whilst one study has validated the Spanish language version of the test, [17] further validation of the MMP is necessary because: (1) only two studies have been carried out so far in people with PD, and these have included a limited number of participants; (2) no validation has been carried out in people with PD using the English language version of the test; (3) comparison with established tools (particularly the MMSE) has been limited; (4) no assessment has been made of test-retest reliability; (5) no cut off score (similar to that used with the MMSE) has been established to allow use of the MMP for screening for cognitive impairment in people with PD.

We, therefore, compared the MMP and MMSE scores of a group of people with various stages of PD with their scores on formal standardised neuropsychological testing in order to establish (1) the validity and reliability of the MMP in people with PD whose first language was English and (2) whether the MMP was a more sensitive and specific measure of cognitive deficits in PD than the MMSE.

**METHODS**

**Participants**

People with various stages of PD (mild, moderate and severe) were invited to take part. The clinical diagnosis of PD was made by a consultant neurologist with a specialist interest in movement disorders, based on UK Brain Bank criteria [18]. Mild PD was defined as a Hoehn & Yahr score (H&Y) [19] of I or II. Moderate PD was defined as H&Y III without severe motor fluctuations. Severe PD was defined as H&Y IV or V or marked motor fluctuation causing periodic disability. All participants had to be able to give informed consent and, therefore, those with overt dementia were excluded. In addition, those with severe language impairment, those with significant pre-morbid psychiatric history and those with another coexisting condition affecting cognition were excluded.

We aimed to include 20 patients in each group, although no formal sample size calculation was undertaken. People with mild PD were recruited from a pilot incidence study. [20] Those with moderate or severe PD were recruited either from PD outpatient clinics or from PD patients admitted to hospital wards during the period of the study. All participants gave their written, informed consent.

**Assessments**

Initial assessment was carried out by a PD nurse or a trainee in Geriatric Medicine. Age, gender, educational background, time since diagnosis, disease severity and the nature and duration of treatment were recorded. PD medication was converted to levodopa equivalent daily doses (LEDD) where the equivalent bioavailable dose of 100mg of controlled release levodopa was taken to be 70mg of immediate release levodopa [21] and 100mg levodopa was equivalent to 1.5mg pramipexole as salt, 6mg ropinirole, 1mg pergolide, 1mg cabergoline, and 10mg apomorphine. [22-24] Specific information about prior or ongoing hallucinations, confusion and memory problems was collected from the participants, their carers, and review of their medical records. An MMSE and an MMP were recorded at the initial interview. MMP was used as per Mahieux paper except that animal fluency was for the letter ‘c’ as we felt that fewer animals began with letter ‘l’ in English compared to French (Supplementary box 1, supplementary figures 1 to 3).

A second interview was arranged for further neuropsychological testing and to repeat the MMP. This interview was conducted by a trained neuropsychologist who was blind to the initial MMP and MMSE scores. At this interview, a battery of neuropsychological tests was carried out including: the Block Design test from the revised Wechsler Adult Intelligence Scale (WAIS-R) (perceptual and executive functioning ); [25] Digit Span [25] to assess registration (Digit Span Forward) and working memory (Digit Span Backward); the California Verbal Learning Test (Short form) (CVLT) ( a test of memory and learning with an executive component); [26] Category Fluency (semantic memory); Letter Fluency (executive functioning: mental flexibility); and the Stroop test (executive functioning: response suppression and distractibility). [27] These tests were chosen in order to test the cognitive domains where people with PD are known to have particular deficits. [10]

**Definition of cognitive impairment**

For the purposes of this study cognitive impairment in patients was defined as deficits in three or more of eight selected neuropsychological tests, given that less than 5% of the normal population would be expected to have abnormalities on 3 or more tests by chance. [28] Cut offs for deficits were defined as: digit span scaled score ≤5; CVLT total correct from trials 1 to 4 T-score <35; CVLT short delay, long delay and cued recall >1.5 standard deviations (SD) below normative mean; Stroop word number correct in eighth percentile or lower; Category fluency number correct T-score <35; and Letter fluency T score <35.

**Statistical analysis**

To facilitate direct comparison, MMP and MMSE scores were converted to percentage of maximum possible score (30 for MMSE, 32 for MMP).

Statistical analysis was carried out using SPSS 14.0 for Windows. Normally distributed data were compared using Student’s t-test, and non-parametric scale variables were compared using the Mann-Whitney U-test. Proportions were compared using the χ2 test or Fisher’s exact test as appropriate, and the linear-by-linear association Chi-squared test used for assessing trends in ordinal variables (such as severity score). Correlation was assessed using Spearman’s rank correlation coefficient for non-normally distributed variables and Pearson’s correlation coefficient for normally distributed variables.

**RESULTS**

Forty-nine patients were recruited. Demographics and symptoms by severity group are presented in Table 1. Two participants from the moderate disease group and three from the severe disease group attended for the initial assessment but did not return for detailed neuropsychological testing. There was no difference in gender (χ2=0.32, degrees of freedom (DF) =1, p=0.57), educational level (χ2=0.36, DF=1, p=0.55), or cognitive impairment on neuropsychological testing (χ2=1.48, DF=1, p=0.22) between groups. Self reported hallucinations (χ2=13.73, DF =1, p<0.001), previous confusion (χ2=10.75, DF=1, p=0.01), and ongoing confusion (χ2=10.73, DF=1, p=0.001), and self or proxy reported memory problems (χ2=5.88, DF=1, p=0.15) increased with severity of disease, though in the latter case this was not statistically significant.

As expected, patients with more severe disease had been diagnosed (p<0.001) and been on treatment (p<0.001) for longer, were on receiving higher total LEDD (p<0.001) and were more likely to be taking levodopa (χ2=9.07, DF=1, p=0.003).

*Table 1: Baseline Characteristics.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | | Mild  (n=17) | Moderate  (n=18) | Severe  (n=14) |
| Mean Age (Standard deviation) | | | 71.94 (9.13) | 73.86 (8.69) | 68.06 (11.44) |
| Gender (M:F) | |  | 10:7 | 6:12 | 7:7 |
| Educational level | | School | 12 (70.5%) | 8 (50%) | 6 (55%) |
| (% of those with recorded level) | | GNVQ | 2 (12%) | 7 (44%) | 3 (27%) |
|  | | Degree | 3 (17.5%) | 1 (6%) | 2 (18%) |
| Hallucinations\* | |  | 11.8% | 44.4% | 78.6% |
| Previous confusion | |  | 0% | 22.2% | 50% |
| Ongoing confusion\* | |  | 0% | 5.6% | 42.9% |
| Self reported Memory problems\* | |  | 0% | 33.3% | 35.7% |
| Cognitive impairment†  (% of those completing tests) | |  | 5 (29%) | 4 (25%) | 6 (55%) |
| Median years diagnosed at time of testing (IQR) \* | |  | 1.0 (0.5-1.4) | 5.8 (2.9-10.4) | 15.0 (9.3-16.9) |
| Median duration of treatment in months (IQR)\* | |  | 6 (2-15) | 66 (30-96) | 150.5 (88.5-189.0) |
| % on dopamine agonist | |  | 29% | 44% | 50% |
| % on Levodopa\* | |  | 53% | 78% | 100% |
| Median LEDD in mg (IQR)\* | |  | 260 (0-360) | 578 (300-670) | 700 (500-1137) |

*GNVQ= General National Vocational Qualification*

*LEDD= levodopa equivalent daily dose.*

*†Defined as impairment on 3 or more of 8 selected cognitive tests (see text).*

*\*Statistically significant increase with severity (see text).*

**Construct validity**

The total scores of the MMP and MMSE in people with PD were significantly correlated with all the tests in the neuropsychology validation battery (Table 2), with correlation tending to be stronger with the MMP than the MMSE.

Compared with MMSE, there was a trend towards greater correlation between MMP or MMSE and age (rs for MMP= -0.26, p=0.077; rs for MMSE= -0.18, p=0.213), disease duration (rs for MMP= -0.25, p=0.087; rs for MMSE= -0.21, p=0.155), or levodopa equivalent daily dose (rs for MMP= -0.24, p=0.087; rs for MMSE= -0.16, p=0.271), though none of these correlations were statistically significant.

*Table 2- Construct validity. Level of correlation between validation battery tests, MMP and MMSE in patients with PD.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variable | Raw score  Median (IQ) | MMP | | MMSE | |
| rs | p | rs | p |
| Digit span forward (n=44) | 11 (8 to 12) | 0.43 | 0.003 | 0.33 | 0.03 |
| Digit span backward (n=44) | 6 (5 to 8) | 0.48 | <0.001 | 0.52 | <0.001 |
| CVLT total correct (n=44) | 23 (16 to 27) | 0.67 | <0.001 | 0.64 | <0.001 |
| CVLT short delay correct (n=44) | 6 (4 to 7) | 0.74 | <0.001 | 0.66 | <0.001 |
| CVLT long delay correct (n=44) | 5 (3 to 8) | 0.72 | <0.001 | 0.58 | <0.001 |
| CVLT cued recall correct (n=44) | 5 (3 to 8) | 0.65 | <0.001 | 0.60 | <0.001 |
| Stroop Colour (n=43) | 112 (86 to 112) | 0.44 | 0.003 | 0.38 | 0.01 |
| Stroop Word (n=41) | 58 (19 to 72) | 0.66 | <0.001 | 0.55 | <0.001 |
| Semantic animal fluency (n=44) | 14 (11 to 20) | 0.48 | 0.001 | 0.50 | <0.001 |
| Letter fluency (n=43) | 33 (17 to 42) | 0.52 | <0.001 | 0.51 | <0.001 |
| Block design scaled score (n=41) | 8 (5 to 10) | 0.56 | <0.001 | 0.49 | 0.001 |

*IQ= interquartile range, rs= Spearman’s rank correlation coefficient.*

There was a non-significant trend for worsening disease severity to be associated with lower scores on MMSE (p=0.17) and MMP (p=0.06; Table 3). This reached significance for MMP (p=0.020) but not MMSE (p=0.067) when those with moderate or severe disease were compared with patients with mild disease. The differences seen in MMP scores between severity groups were larger than those seen in MMSE scores (Table 3).

MMP and MMSE scores were significantly lower in those reporting neuropsychiatric or cognitive symptoms and in those with cognitive impairment on neuropsychological testing than in those without (Table 3). Again, there was a greater difference in MMP scores than in MMSE scores between groups.

*Table 3: Median cognitive test scores (as percentage of maximum score), by reported presence or absence of neuropsychiatric symptoms.*

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Median MMSE % (IQR) | Median MMP % (IQR) |
| Hallucinations | Yes (n=21) | 93 (80-97)# | 81 (70-92) *\*\** |
| No (n=28) | 97 (93-100)# | 94 (88-97) *\*\** |
| Hallucination, confusion and/or self or proxy-reported memory problems | Yes (n=26) | 95 (85-97)\* | 83 (73-92) *†* |
| No (n=23) | 97 (97-100)\* | 94 (88-97) *†* |
| Cognitive impairment*††* | Yes (n=15) | 90 (80-97) *†* | 80 (69-88) *†* |
| No (n=29) | 98 (97-100) *†* | 94 (91-97) *†* |
| Severity*‡* | Mild (n=17) | 97 (93-100) | 97 (88-97) |
| Moderate (n=18) | 97 (93-97) | 88 (78-94) |
| Severe (n=14) | 92 (77-100) | 88 (72-94) |

*††As defined by impairment on 3 or more of 8 neuropsychological tests (see text).*

*Statistically significant difference on Mann-Whitney U test between those with and without symptom at †p<0.001, \*\*p<0.005, \*p<0.01,#p=0.017.*

*‡See text.*

**Reliability**

The test-retest reliability assessment of the MMP between initial assessment and repeat testing (median time between tests 28 days; IQR 8-42) showed an intra-class correlation coefficient of 0.797 (p<0.001) for total MMP, 0.498 (p<0.001) for time orientation, 0.601 (p<0.001) for place orientation, 0.571 (p<0.001) for total orientation, 0.582 (p<0.001) for visual registration, 0.634 (p<0.001) for attention and mental control, 0.419 (p=0.002) for two-set fluency, 0.666 (p<0.001) for visual recall, 0.665 (p<0.001) for mental shifting, and 0.603 for concept processing (p<0.001). The mean difference (±2SD) in MMP between tests was -0.23 (±6.10). There was no correlation between absolute difference in MMP scores and time between these assessments (rs= 0.17, p=0.282).

**Criterion validity**

There was no difference in the area under the receiver-operator characteristics curves for the initial MMP and MMSE compared to the reference standard of cognitive impairment as defined by impairment on 3 of more of the eight selected neuropsychological tests (Figure 1). The sensitivity and specificity of a variety of cut off scores for MMP and MMSE for detection of cognitive impairment are shown in table 4. An MMP score of 27 or less out of 32 predicted cognitive impairment on neuropsychological testing with 86% specificity and 73% sensitivity and hallucinations with 86% specificity and 57% sensitivity. A score of 28 or less out of 32 predicted cognitive impairment on neuropsychological testing with 76% specificity and 87% sensitivity and hallucinations with 71% specificity and 67% sensitivity.

An MMSE score of 29 or less out of 30 predicted cognitive impairment with 93% sensitivity and 41% specificity. A score of 28 or less out of 30 predicted cognitive impairment with 80% sensitivity and 79% specificity.

When items common to the MMSE and MMP (orientation in time and place and attention) were removed, the remaining items in the MMP performed better than those in the MMSE at predicting cognitive impairment on neuropsychological testing, with an area under the ROC curve of 0.844 compared with 0.740.

*Figure 1: Receiver-operator characteristics for MMP and MMSE in predicting cognitive impairment on formal neuropsychological testing in people with Parkinson’s disease.*

*Table 4: Sensitivity and specificity of selected cut off scores for MMP and MMSE in detection of cognitive impairment in people with Parkinson’s disease.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cut off for cognitive impairment on MMSE or MMP\* | MMP | | MMSE | |
| Sensitivity | Specificity | Sensitivity | Specificity |
| 29 or less | 87% | 59% | 93% | 41% |
| 28 or less | 87% | 76% | 80% | 79% |
| 27 or less | 73% | 86% | 53% | 93% |
| 26 or less | 60% | 86% | 53% | 93% |
| 25 or less | 53% | 90% | 40% | 97% |

*\*MMP scores are out of 32, MMSE scores are out of 30.*

**DISCUSSION**

The English language version of the MMP is a valid cognitive screening tool for use in patients with PD. It is comparable to the MMSE in diagnosing significant cognitive impairment on formal neuropsychological testing in terms of area under receiver-operator characteristic curves, but median MMP is significantly lower than median MMSE in those with cognitive impairment (median MMP 80% of maximum possible score vs. median MMSE 90% of maximum possible score, Table 4). Greater deficits were observed in the MMP than the MMSE in those with symptomatic hallucinations or cognitive problems, and in those with moderate or severe PD (compared with those with mild PD), suggesting that the MMP may be more sensitive to the early cognitive deficits in PD. A cut-off score of 28 out of 32 on the MMP appears to be relatively sensitive for detection of cognitive deficits in PD and a score of this or below may suggest the need for more detailed cognitive assessment. The specificity of the MMP at this cut off was less good, but this may be seen as less important in a screening test. A cut off of 28 out of 30 for the MMSE was less sensitive but a little more specific, which may make it less useful as a screening tool.

Correlation of the MMP with individual neuropsychological tests was “very good” (rs 0.61-0.80) with the CVLT and Stroop Word test and “satisfactory” (rs 0.41-0.60) with the other tests. In people with PD, the MMP had similar or better correlation than the MMSE with all the individual neuropsychological tests aside from Digit Span Backwards and Category Fluency. These tests cover working memory and semantic memory, both of which are assessed in the MMSE. Test-retest reliability of the MMP was good over a period of two months. When items common to both tests were removed from each test, the remaining items in the MMP performed better in predicting cognitive impairment than the remaining items in the MMSE, suggesting that the items specific to the MMP detect some deficits not picked up by the MMSE.

This study was carried out in a well defined group of patients with PD diagnosed on the basis of accepted research criteria. Stratification by severity of PD allowed assessment of validity of the MMP in a wide range of patients. In particular, this study included patients with early disease who may have been excluded from other studies. It is the first study to compare the performance of the MMP and the MMSE in screening for cognitive impairment in people with PD as defined by “reference standard” neuropsychological testing. A recent study looking at the Spanish language version of the MMP found it to be similar to the MMSE in predicting cognitive symptoms in PD, but did not include formal neuropsychological testing. [31]

A number of the limitations of this study are worth highlighting. Firstly, this was a relatively small study and repetition in a larger cohort will be necessary before any firm conclusions can be drawn regarding the relative utility of the MMP and MMSE. Additionally, it may be that a true correlation between MMP and/or MMSE and age, disease duration, or LEDD may have been missed due to lack of power. Secondly, this study was limited to those PD patients not suffering from overt dementia. This limits the generalisability of any conclusions that are drawn regarding the use of the MMP as a measure of the severity of cognitive impairment. However, their exclusion should have little bearing on the use of the MMP as a screening tool for cognitive impairment since people with overt dementia are likely to be diagnosed clinically without need for screening and, by definition, are already known to suffer from cognitive impairment.

The MMP is a cognitive test that has now been validated in people with PD in English, French and Spanish language versions. Its ability to detect cognitive deficits in PD is at least comparable to that of the MMSE and it has the advantage that it lacks any component that may lead to the estimate of cognitive performance being limited by the problems with manual dexterity seen in PD, and has measurable cut off values that are both sensitive and specific for cognitive impairment as defined here. Further larger studies will be required to determine whether these cut offs are reproducible in other populations and to develop cut offs for overt dementia.

One commonly accepted difficulty with the use of the MMSE for cognitive screening is its variation with age and educational attainment. [29] The current study was not large enough to explore this issue but we found that in a group of 265 community-based non parkinsonian controls recruited as part of a large incidence study [unpublished data from ref 20 and 30] there was a significant negative correlation between MMP and age (rs -0.40; p<0.0001) but a statistically non-significant difference between median MMP in those whose maximum educational attainment was secondary (median MMP 29, IQ 28-31) and tertiary (median MMP 30, IQ 29-31; p=0.23). These factors should be born in mind when interpreting MMP scores.

We have used the MMP as a PD-specific cognitive assessment tool for follow-up of an incident cohort of parkinsonian patients and controls. [20, 30] This will, in time, give further information on the ability of the MMP to detect change over time in cognition in parkinsonian patients and to predict dementia. When we established the incidence study the MMP was one of the few PD specific tools available but it should be noted that, in the interim, other scales have been developed and validated although few have been directly compared to the MMP. These include the Parkinson neuropsychometric dementia assessment (PANDA) [31] and the Montreal cognitive assessment (MOCA), [32] both of which have been shown to be superior to the MMSE in the assessment of cognitive deficits in those with PD. [12-15] The Spanish language version of the MMP has recently been compared with the Scales for Outcomes in Parkinson’s Disease- Cognition (SCOPA-COG), another PD-specific cognitive screening tool. No clear difference between the tests was found, though there was some suggestion that the SCOPA-COG had greater discriminative ability. [33] The MMP has potential advantages over some of the other cognitive scales used in PD such as the Mattis Dementia Rating Scale (MDRS) and the Parkinson’s Disease Cognitive Rating Scale (PD-CRS) in that it is shorter to administer (5-10 minutes compared with 20-25 minutes for the MDRS and 17-26 minutes for the PD-CRS [34,35]) and has no manual tasks, which can be difficult for people with advanced PD. These advantages have a clear impact on the utility of these tools in routine clinical practice.

While the MMP was designed to assess the specific cognitive deficits found in people with PD, it is possible that it would also be useful in other dementias. One previous study comparing it with the MMSE in a Memory Clinic setting found it to be acceptable to patients and easy to administer, with performance at least equivalent to the MMSE.[34] It is not clear whether selection of test by syndrome of presentation may improve diagnostic utility and this may bear further study.

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**CONFLICT OF INTEREST**

RC, CH and JG have been employed as part of a grant from Parkinson’s UK.

**Supportive/Supplementary Material**

*Supplementary box 1: The mini-mental Parkinson*

*Supplementary figure 1: Mini-mental Parkinson visual registration cards*

*Supplementary figure 2: Mini mental Parkinson set shifting cards*

*Supplementary figure 3: Mini mental Parkinson visual recall cards*

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