VALIDATION OF MALAYALAM VERSION OF
MONTREAL COGNITIVE ASSESSMENT FOR KERALITE
PATIENTS WITH PARKINSON’S DISEASE

Thesis submitted in partial fulfilment of the rules and regulations
for DM degree Examination

By

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<table>
<thead>
<tr>
<th>1</th>
<th>Introduction</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Review of literature</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Objectives</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Materials and Methods of the study</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>Statistical Analysis</td>
<td>36</td>
</tr>
<tr>
<td>6</td>
<td>Results</td>
<td>37</td>
</tr>
<tr>
<td>7</td>
<td>Discussion</td>
<td>51</td>
</tr>
<tr>
<td>8</td>
<td>Conclusion</td>
<td>55</td>
</tr>
<tr>
<td>9</td>
<td>Bibliography</td>
<td>57</td>
</tr>
<tr>
<td>10</td>
<td>Annexure</td>
<td>71</td>
</tr>
</tbody>
</table>
INTRODUCTION

Parkinson’s disease (PD), the second most common neurodegenerative disorder was initially known as a ‘motor” disorder characterized by tremor, bradykinesia, rigidity and postural abnormalities. It is now known that nonmotor manifestations are very common in PD, and contribute to disability and impaired quality of life in patients. Cognitive impairment is one among the important non-motor manifestations of PD. Non-motor manifestations, including cognitive dysfunction dominate the clinical picture in the later stages of the disease. Cognitive dysfunction is an important non-motor manifestation, with significant impacts on functioning, quality of life and caregiver burden. The spectrum of cognitive dysfunction range from mild cognitive impairment (PD-MCI) to PD dementia (PDD). Cognitive dysfunction increases the risk of nursing home placement and contribute to personal and socioeconomic burden in patients with Parkinson’s disease PD-MCI is common and appears to place patients at risk of progressing to dementia. Dementia occurs upto 83% of patients with PD over 20 years. Even mild cognitive deficits in PD are associated with functional impairment and worse QOL.
Early identification is very important to start early interventions to improve functioning and quality of life. Brief and sensitive neuropsychological tests are required to administer in these patients for early identification of the cognitive decline. Cognitive domains affected in PD are attention, working memory, executive function, language, memory and visuospatial function.\textsuperscript{5,6,13} Validated neuropsychological tests sensitive for detection of cognitive dysfunction in these domains are available in English and other languages. Tests requiring long time are difficult to use in PD patients in the clinic. Many short neuropsychological tests have been developed and validated in PD patients. The Montreal Cognitive Assessment was designed by Nasreddine et al.\textsuperscript{19} as a brief screening tool for MCI and has become an increasingly popular screening tool for cognitive dysfunction not only in PD but also in the setting of Alzheimer disease, stroke, vascular dementia, traumatic brain injury, and frontotemporal dementia. This screening tool tests short-term memory, visuospatial function, executive function, attention, concentration and working memory, language and orientation in 10 minutes time.\textsuperscript{19}

The usefulness of MoCA as a suitable, accurate, and brief test for screening all levels of cognition in PD has also been established.\textsuperscript{20} In the present study, we aimed to create a cross cultural adaptation of MoCA (MoCA-Malayalam - “MoCA-M”), and test its metric properties and
reliability for use in Malayalam-speaking patients with PD. We hope that MoCA-M will be a novel screening tool useful for detecting cognitive impairment in its early stage itself, for use in Keralite population.
REVIEW OF LITERATURE

Parkinson’s disease is the second most common neurodegenerative disorder with increased prevalence in males and age more than 60 years and is a common cause of disability. PD was initially described by Dr James Parkinson in “An essay of the shaking palsy”. The description of the disorder was similar to how we describe it today, as a progressive disease due to probable degenerative pathology in the central nervous system. The main symptoms were characterized by resting tremor, flexed posture and shuffling gait. The intellect and senses were described as being intact in the initial description; cognitive dysfunction not considered as part of disease till 1960s. There have been many diagnostic criteria proposed for the clinical diagnosis; the United Kingdom Parkinson’s Disease Society Brain Bank (UKPDSBB) criteria is the most widely used one and is well validated.
UK PARKINSON’S DISEASE SOCIETY BRAIN BANK CLINICAL DIAGNOSTIC CRITERIA

1. Diagnosis of Parkinsonian Syndrome

- Bradykinesia

- At least one of the following

  1. Muscular rigidity
  2. 4-6 Hz rest tremor
  3. Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction

2. Exclusion criteria for Parkinson’s disease

- History of repeated strokes with stepwise progression of parkinsonian features

- History of repeated head injury

- History of definite encephalitis

- Oculogyric crises

- Neuroleptic treatment at onset of symptoms

- More than one affected relative
• Sustained remission

• Strictly unilateral features after 3 years

• Supranuclear gaze palsy

• Cerebellar signs

• Early severe autonomic involvement

• Early severe dementia with disturbances of memory, language, and praxis

• Babinski sign

• Presence of cerebral tumor or communication hydrocephalus on imaging study

• Negative response to large doses of levodopa in absence of malabsorption

• MPTP exposure

3. Supportive prospective positive criteria for Parkinson’s disease

Three or more required for diagnosis of definite Parkinson’s disease in combination with step one

• Unilateral onset
• Rest tremor present

• Progressive disorder

• Persistent asymmetry affecting side of onset most

• Excellent response (70-100%) to levodopa

• Severe levodopa-induced chorea

• Levodopa response for 5 years or more

• Clinical course of ten years or more

**Prevalence of PD**

The prevalence of PD in people over 65 years of age is around 1-2% and increases from 0.6% in the ages 65-69 to 2.8% in the ages 85-89 years.\textsuperscript{23,24} The cumulative incidence (the life time risk) of PD up to 89 years of age is close to 3%.\textsuperscript{24} The mean age at symptom onset is in the late 60’s and population based studies report age at diagnosis to around 70 years of age.\textsuperscript{25}

**Non motor symptoms of PD**

PD is classically considered as a motor disorder but a diverse range of nonmotor symptoms (NMS) including cognitive dysfunction occur in the majority and dominate the clinical picture in the later stages of the
disease.\textsuperscript{1,2} The nonmotor symptoms (NMS) of PD are increasingly recognized as being critical to identify and treat because of their impact on quality of life in PD perhaps having an even greater impact than motor symptoms.\textsuperscript{4,26} The most commonly described primary NMS of PD are autonomic dysfunction, cognitive abnormalities, sleep disorders, mood disorders, pain, and sensory disorders.\textsuperscript{27} Non-motor symptoms in PD include neuropsychiatric symptoms with depression, apathy, hallucinations, cognitive impairment and dementia, sleep disorders with restless legs, REM sleep behavior disorder, excessive daytime somnolence, vivid dreaming and insomnia, autonomic symptoms with bladder disturbances, orthostatic hypotension and sweating, sensory symptoms with olfactory disturbance, pain and visual dysfunction and gastrointestinal symptoms with constipation.\textsuperscript{4,27} There are also NMS in PD that are secondary to treatment, such as impulse control disorders and psychosis.\textsuperscript{27} Recent studies show that NMS may be present in the early PD\textsuperscript{28} or may be the presenting symptom in some patients.\textsuperscript{29} NMS are missed in 50% of patients with PD in routine consultations.\textsuperscript{28}

**Cognitive dysfunction in PD**

Patients with PD have an almost six-fold increased risk of developing dementia compared with age-matched individuals without PD.\textsuperscript{30} Cognitive dysfunction in PD may present in varying degrees.
Occurrence is common even among patients with mild motor symptoms, and includes difficulties such as bradyphrenia, or slowing of thinking, and executive dysfunction, such as impairment of planning and goal-directed behaviors. Subtle cognitive impairment is common in early disease and one study has reported that over a third of patients have deficits at the time of their diagnosis. Cognitive dysfunction is an important non-motor manifestation, with significant impacts on functioning, quality of life and caregiver burden.

Although the cognitive deficits in PD have traditionally been classified as being ‘‘subcortical’’ in nature, a range of cognitive domains are impaired in PD patients without dementia. The spectrum of cognitive dysfunction range from mild cognitive impairment (PD-MCI) to PD dementia (PDD). Cognitive dysfunction in PD not only increases the risk of nursing home placement, but also contribute to a more malignant course of illness, and exacerbate personal and socioeconomic burden. PD-MCI is common and appears to place patients at risk of progression to dementia; even mild cognitive deficits in PD are associated with functional impairment and worse QOL.
Pathogenesis of cognitive decline in PD

PD is characterized by a progressive widespread diffusion of the Lewy body neuropathology from subcortical to cortical structures, therefore at different disease stages, PD patients present different loads of Lewy body neuropathology and different involvements of subcortical and cortical structures. PD is associated with cortical Lewy pathology including limbic and neocortical regions and AD related changes, including the hippocampus suggesting that both PD and AD pathologies contribute to cognitive decline in PD. Lewy bodies and neuronal loss in the substantia nigra occurs concurrently with accumulation of α-synuclein deposition in cholinergic neurons of the BF. Loss of midbrain dopaminergic neurons of the substantia nigra pars compacta, results in striatal dopaminergic denervation. Cholinergic projection losses that vary from 5% to 25% in PD subjects both with and without dementia.

Pathogenesis of cognitive dysfunction in PD is heterogeneous and may differ between individuals and between subtypes. Clinicopathological studies showed brainstem predominant LB disease in majority and less frequent brainstem-limbic forms (33%) and neocortical type of LB disease in PD-MCI. Multiple pathogenic substrates in PDD include dysfunctions of the subcortico-cortical networks resulting from neuronal loss and atrophy in amygdala and limbic areas, cholinergic deficits in cortex.
and thalamus associated with neuronal loss in the nucleus basalis of Meynert (NBM) and decreased nicotinic acetylcholine receptors.\textsuperscript{43,44} The number of LBs in the frontal cortex or of LB densities in the limbic cortex may be a better predictor of dementia in PD.\textsuperscript{45}

Cognitive deficits in early PD are associated with impaired nigrostriatal dopaminergic function, which results in abnormal processing in the frontostriatal circuit with reduced prefrontal and parietal metabolism.\textsuperscript{46}

**Parkinson’s disease -mild cognitive impairment (PD-MCI)**

PD-MCI is thought to be common in non-demented PD patients and is associated with increasing age, disease duration and disease severity. PD-MCI is thought to predict the development of PD-D.\textsuperscript{13,47} The concept of PD-MCI is now well supported by a number of studies showing an association between electrophysiological, imaging, biochemical and neuropathological variables and cognitive impairment in PD patients without dementia.\textsuperscript{48-58} The QEEG measures of background rhythm frequency and relative power in the theta band are potential predictive biomarkers for dementia incidence in PD and EEG measures have potential use as biomarkers in the study of both early and late cognitive deterioration in PD.\textsuperscript{48} SPECT studies done in PD patients with normal cognition had limited areas of hypometabolism in the frontal and occipital cortices and in
the PDMCI patients, there were extensive areas of hypometabolism in the posterior cortical regions, including the temporo-parieto-occipital junction, medial parietal, and inferior temporal cortices suggest that posterior cortical dysfunction is the primary neuroimaging feature of PD patients at risk for dementia.\textsuperscript{50,51}

In noncomplicated PD, structural neuroimaging (cranial computed tomography and MRI) may be normal or show mild diffuse brain atrophy and temporal lobe changes in early PD. Hippocampal atrophy and lateral ventricular enlargement are structural biomarkers for PD-MCI. Marked gray matter atrophy occurs in PDD, whereas far fewer extensive changes are evident in PD-MCI.\textsuperscript{52} Studies on cerebrospinal fluid (CSF) biomarkers suggest that CSF Aβ-42, and tau predict cognitive decline in PD.\textsuperscript{55,56}

**Prevalence of PD-MCI**

The studies done so far indicate that 18.9% -38.2 % of non-demented PD patients have PD-MCI.\textsuperscript{47,59-65} In nondemented PD patients mean prevalence was 27%; range, 19%–38% and is associated with the subsequent development of PD Dementia(PDD) .The frequency of MCI increases with age and with duration and severity of PD.\textsuperscript{13} Studies on newly diagnosed PD patients also have shown significant cognitive decline over
years.\textsuperscript{66,67} Nonamnestic, single-domain impairment (i.e., any single nonmemory domain) is the most common subtype of PD-MCI.\textsuperscript{13}

\textbf{Figure 1.} Flowchart for the diagnosis of mild cognitive impairment and its subtypes
Risk factors for PD-MCI

Different studies showed that increasing age, male gender, lower levels of education, later onset of disease, greater PD severity and longer disease duration are associated with PD-MCI.\textsuperscript{68,69}

Patterns of cognitive deficit in PD-MCI

Cognitive domains typically affected in PD include executive function, attention, processing speed, visuospatial, learning and memory.\textsuperscript{68} PD-MCI may affect a range of cognitive domains, but single domain impairment is more common than multiple domains and within a single domain, nonamnestic impairment is more common than isolated amnestic deficits.\textsuperscript{13} In the nonamnestic single domain, high proportion of visuospatial and executive function deficits observed such as problem solving and working memory. Attentional-executive dysfunction is common in most PD patients without dementia and up to half of these may also experience visuospatial and free recall memory problems.\textsuperscript{68}

Definition of PD MCI

PD MCI denotes cognitive decline that is not normal for age but with essentially normal functional activities (fail to meet the criteria for PD-D) and could be present even at the time of diagnosis of PD and prior to
initiation of dopaminergic therapy. This operational definition was uniformly followed in the longitudinal \(^{47,54}\) and cross-sectional \(^{56-61}\) studies done so far, but there was no uniformity in the number of impaired cognitive tests required in each domain, the number of involved domains and the degree of involvement in each domain, to be classified as PD-MCI.

The need for formal diagnostic criteria for PD-MCI has been highlighted\(^{13}\) and the Movement disorder Society (MDS) commissioned a task force to review the available literature on PD-MCI and formulate a diagnostic criteria. The MDS task force diagnostic criteria have been published recently.\(^{70}\) The MDS Task Force diagnostic criteria include (1) characterization of the clinical syndrome and (2) methods for its diagnosis.

**PD-MCI Criteria**

The diagnosis of PDMCI needs satisfaction of the inclusion and exclusion criteria specified; two levels of diagnostic categories and various subtypes of PD-MCI have been defined. PD-MCI is a syndrome defined by clinical, cognitive, and functional criteria.\(^{70}\) The MDS Task Force criteria are rooted in the MCI criteria previously described, but modified to address issues relatively specific to PD. The criteria were also designed to be consistent with the MDS proposed PDD criteria and thereby allow transitions between categories of normal cognition, MCI, and dementia.\(^{71}\)
I. **Inclusion criteria**

1. Diagnosis of Parkinson’s disease as based on the UK PD Brain Bank Criteria \(^{17}\)

2. Gradual decline, in the context of established PD, in cognitive ability reported by either the patient or informant, or observed by the clinician

3. Cognitive deficits on either formal neuropsychological testing or a scale of global cognitive abilities (detailed in section III)

4. Cognitive deficits are not sufficient to interfere significantly with functional independence, although subtle difficulties on complex functional tasks may be present.

II. **Exclusion criteria**

1. Diagnosis of PD dementia based on MDS Task Force proposed criteria \(^{57}\)

2. Other primary explanations for cognitive impairment (e.g., delirium, stroke, major depression, metabolic abnormalities, adverse effects of medication, or head trauma)
3. Other PD-associated comorbid conditions (e.g., motor impairment or severe anxiety, depression, excessive daytime sleepiness, or psychosis) that, in the opinion of the clinician, significantly influence cognitive testing

III. Specific guidelines for PD-MCI level I and level II categories

A. Level I (abbreviated assessment)

1. Impairment on a scale of global cognitive abilities validated for use in PD or

2. Impairment on at least two tests, when a limited battery of neuropsychological tests is performed (i.e., the battery includes less than two tests within each of the five cognitive domains, or less than five cognitive domains are assessed)

[scales of global cognitive abilities validated in PD are – MoCA, SCOPA-COG(Scales for Outcomes of Parkinson’s disease–Cognition) , PD-CRS(Parkinson’s Disease-Cognitive Rating scale), MDRS(Mattis Dementia Rating Scale)]
B. Level II (comprehensive assessment)

1. Neuropsychological testing that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive, language, memory, and visuospatial)

2. Impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains

3. Impairment on neuropsychological tests may be demonstrated by:
   - Performance approximately 1 to 2 SDs below appropriate norms or
   - Significant decline demonstrated on serial cognitive testing or
   - Significant decline from estimated premorbid levels

IV. Subtype classification for PD-MCI (optional, requires two tests for each of the five cognitive domains assessed and is strongly suggested for research purposes)\textsuperscript{a}

\textsuperscript{a} Subtype classifications are applicable only to those PD-MCI who have had at least two tests within each of the five cognitive domains administered.
1. **PD-MCI single-domain**—abnormalities on two tests within a single cognitive domain (specify the domain), with other domains unimpaired or

2. **PD-MCI multiple-domain**—abnormalities on at least one test in two or more cognitive domains (specify the domains)

**Neuropsychological tests for the five cognitive domains**

**Attention and working memory**

- WAIS-IV (or earlier version) Letter Number Sequencing,
- WAIS-IV Coding (or earlier version) or other substitution task, written or oral
- Trail Making Test,
- Digit span backward or digit ordering,
- Stroop color-word test.

**Executive function**

- Wisconsin Card Sorting Test (CST), or modified CST(Nelson’s modification)
- Tower of London test–Drexel version, or Stockings of Cambridge (CANTAB)
Review of Literature

- Verbal fluency test, such as letter fluency (COWAT or similar tests),
- Category fluency (animals, supermarket, or similar), or alternating fluency tasks (if a well-standardized version is used).
- 10 points Clock Drawing Test

Language

- WAIS-IV (or earlier version) Similarities
- Confrontation naming task, such as Boston Naming Test (or short-form validated in PD) or Graded Naming Test

Memory

- Word list learning test with delayed recall and recognition conditions, such as Rey’s Auditory Verbal Learning Test, California Verbal Learning Test, Hopkins Verbal Learning Test, and Selective Reminding Test
- Prose recall test with a delayed recall condition, such as Wechsler Memory Scale-IV Logical Memory subtest (or earlier version) or Rivermead Behavioural Memory Test, paragraph recall subtest
- Brief Visuospatial Memory Test–Revised (BVMT-R)
Visuospatial function

- Benton’s Judgment of Line Orientation
- Hooper Visual Organization Test
- Clock copying (e.g., Royall’s CLOX)

The level I category allows for the diagnosis of PDMCI based on an abbreviated cognitive assessment, because comprehensive testing may not always be practical or available. Level I criteria provide less diagnostic certainty than level II. When a limited battery of neuropsychological tests is performed, impairment must be present on at least two tests to diagnose PD-MCI by level I criteria. Level I criteria do not allow complete subtyping of PD-MCI.

For the diagnosis of PD-MCI by level II criteria and PD-MCI subtyping, the task force recommends formal, comprehensive neuropsychological testing that includes at least two tests for each of the five cognitive domains previously listed. Impairment should be present on at least two tests, either within a single cognitive domain or across different cognitive domains.
Risk of progression to PDD

Mild cognitive impairment in Parkinson's disease is an important predictor for the progression to PDD. Longitudinal studies on non-demented PD patients show that 20-60% develop PD dementia over 2-5 years. Information on the conversion of PD-MCI to PDD is scanty. Around 60% of PDMCI are converted to PD-D over 4 years, compared to 20% of PD patients with normal cognition. Cognitive decline correlating with the neuropathologic stage of PD demonstrated in a clinicopathological study also support PDMCI as a risk factor for PD-D. It has been shown that majority of PD patients develop dementia over time. The cumulative prevalence of PDD for patients surviving more than 10 years is at least 75%. The point prevalence of PD-MCI and PD-D are similar. Thus, PDMCI precedes PDD and majority of PD-MCI are converted to PDD over time.

PDD

Diagnosis of PD dementia must be based on the presence of deficits in at least two of the four core cognitive domains (attention, memory, executive and visuo-spatial functions) as shown in clinical and cognitive examination, and be severe enough to affect normal functioning. The
Movement Disorder Society (MDS) Task Force defined the clinical diagnostic criteria for PD-D.\textsuperscript{71}

**Features of dementia associated with Parkinson’s disease**

I. **Core features**

1. Diagnosis of Parkinson’s disease according to Queen Square Brain Bank criteria.

2. A dementia syndrome with insidious onset and slow progression, developing within the context of established Parkinson’s disease and diagnosed by history, clinical, and mental examination, defined as:
   - Impairment in more than one cognitive domain
   - Representing a decline from premorbid level
   - Deficits severe enough to impair daily life (social, occupational, or personal care), independent of the impairment ascribable to motor or autonomic symptoms.

II. **Associated clinical features**

1. **Cognitive features**
   - **Attention**: Impaired. Impairment in spontaneous and focused attention, poor performance in attentional tasks; performance may fluctuate during the day and from day to day.
• **Executive functions:** Impaired. Impairment in tasks requiring initiation, planning, concept formation, rule finding, set shifting or set maintenance; impaired mental speed (bradyphrenia)

• **Visuo-spatial functions:** Impaired. Impairment in tasks requiring visual-spatial orientation, perception, or construction

• **Memory:** Impaired. Impairment in free recall of recent events or in tasks requiring learning new material, memory usually improves with cueing, recognition is usually better than free recall

• **Language:** Core functions largely preserved. Word finding difficulties and impaired comprehension of complex sentences may be present

2. **Behavioral features:**

• **Apathy:** decreased spontaneity; loss of motivation, interest, and effortful behavior

• **Changes in personality and mood** including depressive features and anxiety

• **Hallucinations:** mostly visual, usually complex, formed visions of people, animals or objects

• **Delusions:** usually paranoid, such as infidelity, or phantom boarder (unwelcome guests living in the home) delusions

• **Excessive daytime sleepiness**
Based on these features, clinical diagnostic criteria for probable and possible PD-D are described.

**Scientific and clinical significance of identifying PD-MCI**

As discussed above, PD-MCI is common and precede PD-D. Most PD patients develop dementia,\(^{80-83}\) the impact of which is substantial. PD-D has major consequences for psychiatric morbidity,\(^ {84}\) functioning,\(^ {15,85,86}\) caregiver burden,\(^ {87,88}\) nursing home placement\(^ {9}\) and mortality.\(^ {89,90}\) Even mild cognitive deficits affect functioning and quality of life in PD.\(^ {15-18}\) Early identification is very important and help early interventions to improve functioning and QOL as well as drug development and other measures aimed to delay the development of PDD. This has got public health importance, considering the commonness of PD.\(^ {91}\) Early recognition of cognitive impairment could offer a window for novel therapeutic interventions, aiming to alter the course of this natural history.

**Tools for Assessment of Cognition in PD**

There are a number of issues that are not fully resolved in the cognitive testing in PD, including the ideal cut-off scores, number of tests to be done in each domain, number of tests/domains to be involved to classify as PD-MCI, the potential non-linear nature of cognitive decline in PD, and the issue of whether different cognitive domains decline at same or different
Assessment of cognition in PD can be complicated by disease- or medication-related effects, such as bradykinesia, fatigue, sleepiness, and mood disorders, which can adversely affect test results regardless of cognitive abilities. The recently published MDS PD-MCI diagnostic criteria specifies two levels of diagnosis; level I is the “abbreviated assessment” and level II, “Comprehensive assessment”.

Level I requires impairment on a scale of global cognitive abilities validated for use in PD or impairment on a limited battery of neuropsychological tests. Level II requires testing with at least two cognitive tests, assessing each of the five cognitive domains (Attention and working memory, executive function, language, memory and visuospatial function). As each of the recommended tests take 5-15 minutes a minimum of 1-1 ½ hours may be required for the individual patient. This has practical challenges; hence the level I testing may be more suitable in the clinic settings and require only impairment in a scale of global cognitive abilities validated for use in PD or a limited battery of cognitive tests.

Neuropsychological Scales for Assessing Global Cognitive Abilities validated for use in PD are Montreal Cognitive Assessment (MoCA); Parkinson’s Disease-Cognitive Rating scale (PD-CRS); Scales for Outcomes of Parkinson’s disease–Cognition(SCOPA-COG) and Mattis Dementia Rating Scale(MDRS). Based on the Movement disorder Task
Force’s evaluation criteria the Montreal Cognitive Assessment (MoCA), appeared to be the most suitable measure and recommended consideration of the MoCA as a minimum cognitive screening measure in clinical trials of PD.$^{13,70}$

**The Montreal Cognitive Assessment (MoCA)**

The MoCA was designed by Nasreddine et al.$^{19}$ in English language as a brief screening tool for MCI and has become an increasingly popular screening tool for identifying cognitive impairment. As it is brief (can be administered in around 10 minutes)$^{13}$ and can be easily administered even by non-specialist staff it has become very useful and common screening test. MoCA covers a range of executive functions and addresses frontal functions better than the widely used Mini-Mental Status Examination (MMSE).$^{92}$ The MoCA is divided into 7 subscores: visuospatial/executive (5 points); naming (3 points); memory (5 points for delayed recall); attention (6 points); language (3 points); abstraction (2 points); and orientation (6 points). One point is added if the subject has < 12 years of education.$^{19}$ MoCA has high sensitivity and specificity for MCI and has good test-retest reliability, internal consistency and content validity.$^{92}$ It has been studied in patients with MCI, Alzheimer's disease (AD), Vascular Cognitive Impairment, post stroke, PD, Huntington’s disease, Epilepsy, traumatic brain injury, Frontotemporal dementia, multiple sclerosis and
Review of Literature

tumors of brain and found to be a useful screening tool in all these conditions.  

The usefulness of MoCA as a suitable, accurate and brief test for screening all levels of cognition in PD, has been demonstrated. MoCA doesn’t have the pronounced ceiling effect seen with MMSE and is a more sensitive tool to identify early cognitive impairment in PD, especially PD-MCI. It has also been found that approximately half of the patients with normal MMSE have cognitive impairment based on MoCA. Based on these findings, the MDS task force has recommended MoCA as a neuropsychological scale to test the global cognitive abilities in PD, to make a “level I” diagnosis of PD-MCI. The optimal MoCA screening cut-off values for PD-D and PD-MCI have recently been defined as 21/30 and 26/30 respectively. The scale was originally designed in English and cross-cultural adaptation and validation was done for use in 43 other languages.

Addenbrooke’s Cognitive Examination

The Addenbrooke’s Cognitive Examination (ACE), a global cognition screening battery, is a reliable and sensitive tool consists of six components evaluating separate cognitive domains. A maximum score of 100 is weighted as orientation(10), attention(8), memory(35), verbal fluency(14)
Review of Literature

, language(28), and visuospatial ability(5). Scores for each of the six domains can be calculated separately and their sum gives the composite score on the ACE. The MMSE score can also be calculated from this. The ACE can be administered in 15 to 20 minutes. Addenbrookes Cognitive Examination is validated for dementia evaluation in PD, with a cut-off score of 83 points. It is adapted into Malayalam and validated for use in our population and normative data for different ages and educational levels are available.

Mini Mental Status Examination

The Mini Mental Status Examination (MMSE) (Folstein et al., 1975), is a widely used cognition screening test in many parts of the world, modified and adapted into many local languages. Malayalam version of MMSE with normative scores are published earlier. MMSE is being used for long time for testing cognition in PD. But it is less sensitive for the detection of cognitive impairment seen in early PD. It shows a ceiling effect in patients and normal controls. Studies in patients with PD showed that approximately half of patients with a normal MMSE score have cognitive impairment by testing with MoCA.
Aims and objectives of the study

1. Cross-cultural adaptation of Montreal Cognitive assessment (MoCA) scale into the regional language (Malayalam)

2. Study the validity and reliability of Montreal Cognitive assessment-Malayalam (MoCA-M) for cognitive assessment in Parkinson’s disease patients.
Materials and Methods of the study

Cross-cultural adaptation of MoCA to Malayalam (MoCA-M)

MoCA is copyright protected cognitive assessment tool required written permission of the copyright holder for translation and use for research purpose. We contacted the copyright holder and obtained permission for translation (to Malayalam) and use for this project. The copyright holders have also provided guidelines for translation of MoCA to Malayalam. The English version was used as a base for translation. The 5-word recall and sentence repetition items was adapted to the language and culture, based on the guidelines provided. In order to ensure accurate translation of the test and instructions, a back translation (from Malayalam to English) was done and compared with the original English version. The translation and back-translation was done independently by two bilingual experts, who are clinical psychologists well versed with similar tasks and consensus was obtained. The final version was discussed and approved within an internal committee consisting of the bilingual experts as well as the investigators.
Validation of Montreal Cognitive assessment-Malayalam (MoCA-M)

Study design and setting

The study was a hospital based cross-sectional study. The subjects were selected from among the patients attending the movement disorder clinic of our tertiary care University hospital (Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram).

Study period:

The study was conducted over a period of 18 months from January 2013 to June 2014.

Methods

For validation, the test (MoCA-M) was administered to 100 consecutive patients with Parkinson’s disease, attending the Movement Disorders clinic of SCTIMST and satisfying the entry criteria, and 100 normal controls. The controls were selected from the hospital staff, friends and relatives of hospital staff and visitors of the in-patients in the hospital who agreed to participate.
Ethical considerations:

Written informed consent was obtained from all the subjects participating in the study. The study was approved by the Institutional Ethics Committee. (SCT/IEC/438/DECEMBER-2012)

Inclusion criteria (for PD patients):

1. Diagnosis of PD, as per standard diagnostic criteria (United Kingdom Parkinson’s Disease Society Brain Bank Diagnostic Criteria)\(^{22}\)

2. Ability to read, understand and write Malayalam well.

3. Ability to provide written informed consent.

Inclusion criteria (for Controls)

1. No known neurological disorders.

2. Normal neurologic examination (except for assessment of higher functions)

3. Age, gender and level of education matched with patients.

4. Ability to read, understand and write Malayalam well.

5. Ability to provide written informed consent.
Exclusion criteria (for PD patients and Controls)

1. Clinically significant depression (Beck’s Depression Inventory (BDI) Score $\geq 20$)$^{102}$

2. Any significant neurological, psychiatric or medical co-morbidity interfering with cognitive testing or affecting cognitive functions in the judgement of the investigators.

The Malayalam version of MoCA(MoCA-M) was applied to consecutive patients with PD diagnosed using the United Kingdom Parkinson’s Disease Society Brain Bank Diagnostic Criteria, attending the Movement Disorders clinic of our hospital having at least 10 years of formal education and able to read, write and understand Malayalam. MoCA-M was also applied to age and education-matched healthy controls without any neurological disorders. All the patients underwent a formal neurological examination including assessment using Unified Parkinson’s Disease rating Scale (UPDRS I-IV)$^{103}$ The UPDRS part III (motor examination) was done in the “off” state in patients having motor fluctuations. The severity of motor symptoms of PD was assessed by the Hoehn and Yahr stage. The age of onset of motor symptoms of PD, duration of motor symptoms and details of ongoing treatment was collected by directly interviewing the patients /
Materials and Methods

caregivers and by review of hospital files. The controls also underwent a neurological examination to ensure that they have no neurological disorders.

The neuropsychologic evaluation was done in the “On” (well medicated) state with the help of the qualified Neuropsychologist, attached to the Movement Disorders Program of the Institute. All the subjects (PD patients and controls) were undergone neuropsychological assessment using the MoCA-M, Addenbrooke’s Cognitive Examination –Malayalam (ACE-M)\textsuperscript{100}, and Beck depression inventory (BDI). Those with clinically significant depression (Beck’s Depression Inventory score >20)\textsuperscript{102} or any significant neurological, psychiatric, or medical co-morbidity affecting cognitive functions or interfering with cognitive testing in the judgment of the investigators were excluded.

The ACE has several advantages (The MMSE is also included in it, is validated for use in Parkinson’s disease,\textsuperscript{98} adaptation is available for use in Malayalam speaking population\textsuperscript{100} and cut-off scores are well defined in our population, adjusted for age and level of education.\textsuperscript{101} The normative data for each of the individual domains of ACE also has been published\textsuperscript{101} making it ideal as a standard for validating the new scale. The Malayalam version of ACE (M-ACE)\textsuperscript{100} was used for the study. A subgroup of subjects were re-examined using the MoCA-M after an interval of 2 weeks to determine the test-retest reliability.
**Statistical analysis**

Cronbach’s alpha was calculated to assess the internal consistency of MoCA-M. Pearson correlation coefficient was used to assess test-retest reliability as well as to assess the relationship between MoCA-M scores and the performance in other cognitive tests. The data were analyzed using statistics software (Statistical Package for the Social Sciences (SPSS) Inc, Illinois, Chicago) with guidance from the Medical Statistics expert of the institute.
Results

Baseline clinical characteristics

There were 100 patients with PD and 100 healthy controls. Mean age of patient group was 57.8(± 9.3) years, range 35-78 years. In the control group mean age was 58.94(±8.42), range 39-85 years.

The mean years of education was 12.19(±3.46) in patient group, and 13.6(±3.20) in the control group.

Table 1 Demographic data of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.8(± 9.3)</td>
<td>58.94(±8.42)</td>
<td>0.38</td>
</tr>
<tr>
<td>Education (years)</td>
<td>12.19(±3.46)</td>
<td>12.2 (±1.97)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Age and education were similar in the patient and control groups and there was no statistically significant difference.

In the patient group 71% were men and 29% were women and in the control group 53% were men and 47% were women.
The mean duration of motor symptoms was 6.58 (±4.04) years, range from 2-18 years. The mean age of onset of symptoms was 52.42(±10.02) years range from 30-76 years. The mean Levodopa equivalent dose (LED) was 615(±295.51)mg.

The severity of motor symptoms according to Hoehn and Yahr (H and Y) stage was as follows: Stage 1- 7% (7patients), stage 2–44% (44patients), stage 3–43% (43patients), stage 4–6% (6 patients). Majority of the patients were in stages 2 and 3.
Figure 3  Number of patients distributed in various H&Y stages
Neuropsychology Test Results:

Patients

The mean MoCA score was 24.41 (±4.04) ranging from 8-30 in patients with PD. ACE mean score was 83.99(±9.99)ranging from 49-99 . MMSE mean score was 28.55±1.73 ranging from 21-30 .

Controls

The mean MoCA score was 27.78±1.67ranging from 23-30 in normal controls. ACE mean score was 91.56±4.98 ranging from 80-99 . MMSE mean score was 29.220±0.98 ranging from 23-30 .

Table 2. Mean scores in cognitive testing in patients

<table>
<thead>
<tr>
<th></th>
<th>No of patients</th>
<th>Minimum score</th>
<th>Maximum score</th>
<th>Mean score</th>
<th>Std dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>MoCA</td>
<td>100</td>
<td>8</td>
<td>30</td>
<td>24.4</td>
<td>4.04</td>
</tr>
<tr>
<td>ACE</td>
<td>100</td>
<td>49</td>
<td>99</td>
<td>83.99</td>
<td>9.99</td>
</tr>
<tr>
<td>MMSE</td>
<td>100</td>
<td>21</td>
<td>30</td>
<td>28.55</td>
<td>1.73</td>
</tr>
</tbody>
</table>
The mean MoCA-M, MMSE, and ACE scores of the patients and healthy controls are shown in Table 4. The scores in all the three tests differed significantly between patients and normal controls.

Table 4. The MoCA-M, MMSE, and ACE scores of patients and healthy controls
Results

Mean BDI score was 3.9(±4.84), range from 0-20 in the patient group. In the control group mean score was 3(±4.5) ranging from 4-12. There was no significant difference between patient and control group.

Table 5. BDI scores of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std dev</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>3.9</td>
<td>4.84</td>
<td>4-20</td>
</tr>
<tr>
<td>Control</td>
<td>3</td>
<td>4.4</td>
<td>0-12</td>
</tr>
</tbody>
</table>

There was no correlation between age and the scoring in cognitive tests, in the patient group (pearson correlation R 0.023 and p value 0.82) or in the control group (R -0.04 and p value 0.69).

Table 6. Correlation of age and MoCA scores

<table>
<thead>
<tr>
<th>Correlations</th>
<th>MoCA_TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) patient</td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>0.023</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.823</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td>Age (years) control</td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>-0.040</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.690</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
</tbody>
</table>
Results

There was no significant difference in scores between males and females in the patient group (p value 0.83) or the control group (p value 0.873).

Table 7. MoCA score in male and female in control group

<table>
<thead>
<tr>
<th>GENDER</th>
<th>Mean</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>27.76</td>
<td>53</td>
<td>1.55</td>
<td>28.00</td>
<td>25.0</td>
<td>30.0</td>
</tr>
<tr>
<td>female</td>
<td>27.81</td>
<td>47</td>
<td>1.81</td>
<td>28.00</td>
<td>23.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Total</td>
<td>27.78</td>
<td>100</td>
<td>1.67</td>
<td>28.00</td>
<td>23.0</td>
<td>30.0</td>
</tr>
</tbody>
</table>

Table 8. MoCA score in male and female in patient group

<table>
<thead>
<tr>
<th>GENDER</th>
<th>Mean</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>24.47</td>
<td>71</td>
<td>3.57</td>
<td>26.00</td>
<td>14.0</td>
<td>30.0</td>
</tr>
<tr>
<td>female</td>
<td>24.28</td>
<td>29</td>
<td>5.07</td>
<td>26.00</td>
<td>8.0</td>
<td>29.0</td>
</tr>
<tr>
<td>Total</td>
<td>24.41</td>
<td>100</td>
<td>4.04</td>
<td>26.00</td>
<td>8.0</td>
<td>30.0</td>
</tr>
</tbody>
</table>

There was no correlation between duration of PD and the scoring in cognitive testing in MoCA, R was .057 and p value is 0.57. There was no correlation between age onset of symptoms and scoring in cognitive testing R -.012 and p value was .91. There was no correlation between LEDD and MoCA scores, R -.053 p value was 0.60
Table 9. Correlation of MoCA score with demographics of patients

<table>
<thead>
<tr>
<th>Correlations</th>
<th>MoCA total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration in years</strong></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.057</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.574</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td><strong>Age of onset years</strong></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>-.012</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.909</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td><strong>Daily L-dopa dose</strong></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>-.012</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.904</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
<tr>
<td><strong>LEDD</strong></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>.053</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.601</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
</tr>
</tbody>
</table>

The mean MoCA score in H&Y stage 1 was 23.71±7.36, stage 2 was 24.34±3.65, stage 3 was 24.28±3.95 and stage 4 was 26.67±2.34. There was no significant difference in the MoCA score in different H&Y stages and the p value was 0.51.
Results

Table 10. MoCA score in various H&Y stages in the off state of patients

<table>
<thead>
<tr>
<th>H&amp;Y stage off</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>7</td>
<td>23.71</td>
<td>7.36</td>
<td>27.00</td>
<td>8.0</td>
<td>29.0</td>
</tr>
<tr>
<td>2.0</td>
<td>44</td>
<td>24.34</td>
<td>3.65</td>
<td>26.00</td>
<td>14.0</td>
<td>28.0</td>
</tr>
<tr>
<td>3.0</td>
<td>43</td>
<td>24.28</td>
<td>3.95</td>
<td>26.00</td>
<td>14.0</td>
<td>30.0</td>
</tr>
<tr>
<td>4.0</td>
<td>6</td>
<td>26.67</td>
<td>2.34</td>
<td>26.50</td>
<td>24.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>24.41</td>
<td>4.04</td>
<td>26.00</td>
<td>8.0</td>
<td>30.0</td>
</tr>
</tbody>
</table>

There was no correlation between H&Y stage of PD and the scoring of cognitive testing in MoCA, MMSE or ACE.

Figure 4. Scoring in cognitive tests in each H&Y stages
**Table 11.** Scores in cognitive tests in each H&Y stage

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MoCA mean score</strong></td>
<td>23.71±7.36</td>
<td>24.34±3.65</td>
<td>24.28±3.95</td>
<td>26.67±2.34</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>ACE mean score</strong></td>
<td>82.28±16.24</td>
<td>84.51±9.5</td>
<td>82.91±9.64</td>
<td>91.00±5.34</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>MMSE mean score</strong></td>
<td>28±3.10</td>
<td>28.69±1.53</td>
<td>28.40±1.76</td>
<td>29.33±0.81</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Results did not show any significant difference in the test scores in patients with various H&Y stages. There was no correlation between H&Y stage and MoCA score.
Results

Validity and Reliability of MoCA-M

MoCA-M showed good internal consistency; the Cronbach’s alpha for MoCA-M was 0.72 in patients with PD and 0.40 in controls.

There was also excellent test-retest reliability for the total score of MoCA-M, as well as for the individual items.

Table 12. Test-retest reliability of MoCA-M

<table>
<thead>
<tr>
<th>Cognitive domains</th>
<th>Pearson’s correlation coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visuo spatial/executive</td>
<td>0.87</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Naming</td>
<td>0.63</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Attention</td>
<td>0.96</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Language</td>
<td>0.95</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Abstraction</td>
<td>0.96</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>0.96</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Orientation</td>
<td>0.58</td>
<td>0.001</td>
</tr>
<tr>
<td>Total</td>
<td>0.97</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

The scores of MoCA, MMSE and ACE differed significantly between patients and normal controls with a significant p value. There was significant difference in the scores of MoCA-M and ACE between healthy controls and patients and p value was <0.001. Though the difference in the MMSE scores of controls and patients was less it was significant statistically and the p value was 0.003.
Table 13. The MoCA-M, MMSE, and ACE scores of patients and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Healthy controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MoCA-M</td>
<td>24.41 ±4.04</td>
<td>27.78±1.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.55±1.73</td>
<td>29.220±0.98</td>
<td>0.003</td>
</tr>
<tr>
<td>ACE</td>
<td>83.99±9.99</td>
<td>91.56±4.98</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The MoCA-M scores correlated well with the MMSE (R = 0.67; P < 0.0001) and ACE (R=0.81;P<0.0001) scores in patients with PD.

Table 14. Correlation of MoCA scores with MMSE and ACE in patient group

<table>
<thead>
<tr>
<th></th>
<th>MoCA_TOTAL</th>
<th>ACE_TOTAL</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.807**</td>
<td>.670**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.000</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).
The healthy controls showed good correlation of MoCA scores with ACE (R = 0.49; \( P < 0.0001 \)); however, correlation with MMSE scores (R = 0.23; \( P = 0.02 \)) was weak.

**Table 15.** Correlation of MoCA scores with MMSE and ACE in control group

<table>
<thead>
<tr>
<th></th>
<th>MoCA_TOTAL</th>
<th>ACE_TOTAL</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Correlations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MoCA_TOTAL</td>
<td>Pearson Correlation</td>
<td>1</td>
<td>.489**</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
<td>.000</td>
<td>.020</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>ACE_TOTAL</td>
<td>Pearson Correlation</td>
<td>.489**</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MMSE</td>
<td>Pearson Correlation</td>
<td>.233*</td>
<td>.229*</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
<td>.020</td>
<td>.022</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).**

*, Correlation is significant at the 0.05 level (2-tailed).
**Table 16.** Correlation of MoCA score with ACE and MMSE score of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>ACE patient</th>
<th>ACE control</th>
<th>MMSE score patient</th>
<th>MMSE score control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MoCA score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson correlation R</td>
<td>0.81</td>
<td>0.49</td>
<td>0.67</td>
<td>0.23</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Discussion

There is increasing evidence that dementia is common in advancing PD, affecting up to 80% of patients followed long term. Recognition of cognitive impairment at its initial stage will enable clinicians to educate patients and family members about prognosis and to allow informed decisions about the risks and benefits of therapeutic interventions. Screening tests used in PD should be brief and sensitive for the type of cognitive dysfunction seen in these patients as it is difficult to do long tests due to the motor dysfunction. MoCA is well-recognized as a suitable screening test for cognition in PD as it is a brief test, has demonstrated good test–retest and interrater reliabilities and high intraclass correlation coefficients in patients with PD and has been translated to many languages. The cognitive domains tested by MoCA include executive and visuospatial function, memory, language, and attention. The domains of executive and visuospatial function are known to be affected relatively early in PD and hence MoCA could be a useful instrument to screen for cognitive dysfunction in PD.

In this study we translated and adapted MoCA into our regional language Malayalam and demonstrated the usefulness of the Malayalam version of MoCA for screening cognitive functions in PD. We created
MoCA-M (the test and instructions for testing have been posted at the official website of MoCA\textsuperscript{93} and are available on line at www.mocatest.org) by translating MoCA to Malayalam and cross-culturally adapting the relevant items. We have changed the 5 words in the delayed recall item relevant to our language and culture. Back translation of the test and instructions was done by bilingual experts and compared with the original English version, and consensus was obtained. The back translations were accepted by the group who invented the original version of MoCA and hold the copyright.

The mean duration of motor symptoms of PD in our patient group was 6.58 years. The mean age of patients was 57.8 years which was comparable with the control group. The mean age of onset of symptoms was $52.42 \pm 10.02$ years. Most of the patients were in the H and Y stage 2 or 3 and there was no patients in the stage 5. There was no significant relation between the H&Y stage and scoring in cognitive testing in our study. Males were more in the patient group which was expected as PD is more common in males.

The MoCA-M takes about 10 minutes to administer. MoCA-M was compared with ACE for several reasons—it is a brief test battery encompassing all the cognitive domains,\textsuperscript{98} its validity in PD has been
demonstrated, its validated adaptation for Malayalam speaking population is available, and it also gives the MMSE score.

MoCA-M showed good internal consistency, and the test-retest reliability was excellent. We found that MoCA-M scores of patients correlated well with their performance in ACE. The MoCA-M scores also showed good correlation with MMSE scores in patients with PD. MoCA-M is more brief and easy to administer compared to ACE. MoCA’s superiority for testing cognition in PD, compared to MMSE has already been demonstrated. The cognitive dysfunction in PD is characterized by a frontal, attentional-executive dysfunction in most patients, in addition to visuospatial defects and memory problems. The utility of MoCA for screening cognition in PD and its superiority over MMSE are well described and it tests frontal functions better than MMSE, in addition to testing the other cognitive domains.

We also examined 100 age and education matched healthy volunteers and demonstrated good correlation of MoCA-M scores with performance in ACE. However, unlike the observation in patients with PD, correlation of MMSE scores with MoCA–M scores of control group was weak. The MMSE scores were significantly higher for healthy volunteers, and the poor correlation between MoCA-M and MMSE scores in this group is
attributable to the ceiling effect of MMSE,\textsuperscript{65,72} which is not observed for MoCA.

We found that the performance of patients with PD in all the three tests was significantly worse compared to controls. The MoCA-M mean score in the patient group was 24.41(±4.04) versus 27.78(±1.67) in the control group. The mean MoCA-M score of the patients was falling below the cut-off levels defined for MCI, for the original version of MoCA\textsuperscript{19}. The ACE score was 83.99(±9.99) in the patient group and 91.56(±4.99) in the control group. The significantly low MoCA-M and ACE scores in patients, compared to controls is not surprising, considering the mean duration of PD in our patient group; a considerable number of them are expected to have MCI. MoCA-M is a cross-cultural adaptation of MoCA, its normative data and cut-off scores for MCI in PD and PD-D need to be separately defined by further studies.

In this study we have done cross cultural adaptation of MoCA into Malayalam and demonstrated the reliability and validity of the Malayalam version for screening cognition in patients with PD.
CONCLUSION

1. MoCA –M is a cross cultural adaptation of MoCA for use in Malayalam speaking patients. MoCA’s validity for screening cognition for patients with all stages of PD, is already well established.

2. We showed that the MoCA –M had good test-retest reliability and internal consistency, similar to the original version of MoCA.

3. The comparison of MoCA-M with other standard cognitive tests used in patients with PD, showed good correlation.

4. MoCA-M scores differed significantly between patients with PD and healthy volunteers, paralleling the observation in a more elaborate and established cognitive testing instrument - the Malayalam version of ACE.

5. MoCA-M is valid and reliable, similar to the original English version, for screening for cognitive dysfunction in Malayalam speaking PD patients.
SUMMARY

We created a cross-cultural adaptation of MoCA (MoCA-M), for use for cognitive screening in Malayalam speaking patients, especially with PD. We have shown that it is a valid and reliable tool for the purpose.


27. Nonmotor Symptoms in Parkinson’s Disease Expanding the View of Parkinson’s Disease Beyond a Pure Motor, Pure Dopaminergic Problem Victor W. Sung.; Neurol Clin 31 (2013)


43. Martijn L.T.M. Müller, Cholinergic Dysfunction in Parkinson’s Disease, Curr Neurol Neurosci Rep. 2013 September ; 13(9): 377


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93. www.mocatest.org


Annexure

Abbreviations

**ACE**- Addenbrooke’s Cognitive Examination  
**AD**- Alzheimers disease  
**BDI**- Beck’s Depression Inventory  
**H&Y** stage- Hoehn and Yahr stage  
**LEDD**- Levodopa equivalent dose  
**MCI**- Mild cognitive impairment  
**MDRS**- Mattis Dementia Rating Scale  
**MDS**- Movement Disorder Society  
**MMSE**- Mini-Mental Status Examination  
**MoCA**- Montreal Cognitive Assessment  
**MoCA-M**- Montreal Cognitive Assessment-Malayalam  
**NMS**- Nonmotor symptoms  
**PD**- Parkinson’s disease  
**PD-CRS**- Parkinson’s Disease-Cognitive Rating scale  
**PDD**- Parkinson’s disease dementia  
**QOL**- Quality of life  
**SCOPA-COG**- Scales for Outcomes of Parkinson’s disease-Cognition  
**UKPDSBB**- United Kingdom Parkinson’s Disease Society Brain Bank criteria  
**UPDRS**- Unified Parkinson’s Disease rating Scale
PROFORMA- FOR NORMAL CONTROLS
Validation of the Malayalam Version of the Montreal Cognitive Assessment (MoCA) Scale and a Prospective Evaluation of Mild Cognitive Impairment in Parkinson’s disease Using the Malayalam version (“MoCA-M”).

Date of Evaluation:

1. Subject details and history:

Name:
Age:
Gender:
Level of Education: Total number of years of formal education:
Marital status:
Address:
Telephone No:
Details of any medical illnesses:

2. Details of any Medications which the subject is taking

<table>
<thead>
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<th>Present Medications</th>
<th>Total Daily Dose</th>
<th>Duration of Exposure</th>
<th>Dosing Schedule</th>
</tr>
</thead>
</table>

3. Clinical Examination:

4. Neuropsychological evaluation:

MoCA score: Total
ACE- Total score:
MMSE:
BDI score:

PROFORMA- FOR PD PATIENTS
Validation of the Malayalam Version of the Montreal Cognitive Assessment (MoCA-M) Scale and a Prospective Evaluation of Mild Cognitive Impairment in Parkinson’s disease Using Malayalam version (MoCA-M).

Date of Evaluation:

1. Patient’s details and history:

Name:
Hospital no:
Age: Gender: 
Level of Education: Total number of years of formal education: 
Marital status: 
Address: 

Telephone No: 
Duration of disease: Age at onset: 
Type of Parkinson’s disease: Tremor Dominant / Rigid Bradykinetic / mixed 
Side of onset: Right/ Left / Can’t say 
Motor fluctuations: Yes/ No 
Dyskinesia: Duration: Type: 
Other medical illnesses: 
Family History of PD: No of family members affected: 

Non-motor Symptoms: 
Sleep dysfunction: Description: 
Hallucinations: Description: 
Other psychotic features: 
Impulse control disorders: 
Memory dysfunction: 
Other Cognitive symptoms: Description: 
Urinary disturbances: 
Other autonomic symptoms: 
Constipation: 
Other GI symptoms: 
Any other non-motor symptoms: Description: 

2. Details of Medications

<table>
<thead>
<tr>
<th>Present Medications</th>
<th>Total Daily Dose</th>
<th>Duration of Exposure</th>
<th>Dosing Schedule</th>
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<td><strong>LEDD:</strong></td>
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<tr>
<td><strong>Past Medications:</strong></td>
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<td>Duration of Exposure</td>
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<tr>
<td>Amantadine:</td>
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</tbody>
</table>

3. Clinical Examination: 

“On” “Off” 

UPDRS I: 
UPDRS II: 
UPDRS III: 
UPDRS IV A: 
UPDRS IV B: 
Hoehn & Yahr stage: 

4. Neuropsychological evaluation: 

MoCA score: Total 
ACE- Total score: 
MMSE: 
BDI score: