



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
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From,

Dr Syam K,
Professor of Neurology,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Thiruvananthapuram,
Kerala

To,

Mr. Ishwar Likhari
Administrative Officer,
Division of NCD,
Indian Council of Medical Research
Ansari Nagar,
New Delhi - 110029

Subject: Submission of Final Report, two-page summary, final Statement of Accounts and Utilization Certificate, pertaining to the Ad-hoc Project Proposal, "Validation of the Malayalam version of Montreal Cognitive Assessment (MoCA) Scale and a prospective evaluation of MCI in Parkinson's disease using the Malayalam version (MoCA-M)". PI: Dr Syam K, Department of Neurology, SCTIMST, Trivandrum

Ref: (1) File No: 5/4-5/106/Neuro/2013-NCD-I

(2) Your letter to me, dated 24/02/2020

Dear Sir,

I am hereby submitting (1) the final report (2) a 2-page summary of the work done and (3) the final statement of accounts and utilization certificate, pertaining to the referenced project.

No non-expendable articles / equipment was purchased for the purpose of the project. The grant sanctioned has been fully utilized for the project and there is no unspent balance. The project staff appointed (Junior Research Fellow) was relieved on the date of completion of the project.

Because of the unfortunate and unprecedented situation through which our Institute (A health care worker getting affected with COVID-19 as a consequence of which the Institute's major share of work force has gone on quarantine, leading to a near stand-still state) , the State and the Nation are going through, the inevitable lock-down with only essential services remaining and health care professionals including myself focusing fully on COVID control, I am sending the scanned copies by e-mail initially and the original hard copies later as situations permit,

Thanking you,

SCTIMST

26/03/2020

Sincerely



Dr Syam K

Professor of Neurology, SCTIMST

(Principal Investigator)



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
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SUBMISSION OF FINAL REPORT

- Title of the Research Scheme:** 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"). (Ref No: 5/4-5/106/Neuro/2013-NCD-1)
- Name, Degree and Designation of the Officer-in Charge and Co-investigators:** **Principal Investigator:** Dr. Syam K., MD, DM. Professor of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala. Phone: 0471-2524268, 9847310745 E-mail: drsyam@sctimst.ac.in
Co-PI: (1) Dr. Asha Kishore, MD, DM. Professor of Neurology (Sr Grade), Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram. E-mail: asha@sctimst.ac.in
(2) Dr. Ramshekhar N Menon, MD, DM. Additional Professor of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram. E-mail: rsnmenon@sctimst.ac.in
- Name of the Institution:** Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala. PIN 695011
- Year in which the scheme was started:** 2017
- Date from which the scheme was sanctioned:** 1st March 2017
- ICMR grant sanctioned and the actual expenditure from the year of inception till the date of termination**

Year	Grant sanctioned	Actual Expenditure Incurred
Year 1	Rs. 3,81,100/-	Rs. 3,40,100/-
Year 2	Rs. 3,47,500/-	Rs. 3,88,500/-
Year 3	Rs. 5,46,940/-	Rs. 5,46,940/-

7. Aims and Objectives with which the scheme was started:

The study was done in 2 phases.

The aim of the first Phase: Cross-cultural adaptation of Montreal Cognitive assessment (MoCA) scale into the regional language (Malayalam) and study of its validity for cognitive assessment in Parkinson's disease (PD).

The aims of Phase 2: (1) Cognitive evaluation of a cross-sectional sample of patients with PD using the screening tool (Malayalam version of MoCA- the "MoCA-M") as well as using a detailed and comprehensive battery of neuropsychological tests as per standard recommendations for cognitive testing in PD. (2) Determining the prevalence of PD-MCI in the study population (3) Longitudinal neuropsychological follow-up of the cohort for a period of 2 years aiming at detecting the rate of decline of cognitive functions and whether the decline in MoCA-M correlate with the decline detected in other neuropsychological tests.

8. Details of the report of work done:

Materials and Methods used:

Phase 1 (Cross Cultural Adaptation of MoCA and Validation of MoCA-M): The study was conceived in 2013, and the proposal was submitted to ICMR for funding. Part of the study (first phase) was completed by 2015, during the waiting period for sanction of funds. The Phase 1 involved translation / cross-cultural adaptation of MoCA to Malayalam and its validation. Translation and cross-cultural adaptation were done after getting the permission from copyright holders of the original version of MoCA and following the standard guidelines for validation / cross-cultural adaptation of Neuropsychological tests. For validation, the test (MoCA-M) was administered to patients with Parkinson's disease, and matched healthy controls. Other standard neuropsychological tests (Addenbrooke's Cognitive Examination - ACE/ Mini Mental Status Examination -MMSE) were also applied for comparison. A subgroup of subjects was re-examined using the MoCA-M after an interval of 2 weeks to determine the test-retest reliability.

Phase 2: Estimation of the prevalence of PD-MCI and a longitudinal follow-up of PD-MCI using MoCA-M and other Neuropsychological test batteries: During the second phase, 192 patients were recruited and underwent comprehensive clinical and neuropsychological evaluation required to make a level II diagnosis of PD-MCI, as per the published Movement Disorder Society

Criteria (2012) for the same. 50 healthy control subjects were also recruited for normative data for the neuropsychological test battery, to define the cut-off scores for MCI. The patients underwent follow-up clinical and neuropsychological evaluation, to determine the decline in neuropsychological test performance over time and the ability of MoCA -M to detect the same.

Observations and Conclusions (Kindly note that the following pertain to the baseline data of the first 170 patients; the follow up data has been collected but yet to be analyzed. The final analysis including statistical analysis of follow up data has been hindered by the unexpected COVID -19 epidemic with a surge of cases in our locality, with a health care professional in our Institution also affected and a major part of our workforce going into quarantine and the remaining, including myself being directed to COVID control activities and preparatory work for a community spread)

Phase 1: Translation and cross-cultural adaptation of MoCA to Malayalam and its validation has been done and the results published (Cited below). We translated MoCA into Malayalam and cross-culturally adapted the relevant items, following standard guidelines. The Malayalam version (MoCA-M) was applied to 70 patients with Parkinson's disease and 60 age and education matched healthy controls. Metric properties were assessed and the scores were compared with performance in validated Malayalam versions of Mini Mental Status Examination (MMSE) and Addenbrooke's Cognitive Examination (ACE). MoCA-M showed good internal consistency and test-retest reliability and its scores correlated with MMSE (patients: $R=0.70$; $p<0.001$; healthy controls: $R=0.26$; $p=0.04$) and ACE (patients: $R=0.8$; $p<0.001$; healthy controls: $R=0.52$; $p<0.001$) scores. The reliability and validity of MoCA-M for assessing cognition in Malayalam speaking PD patients was thus established.

Phase 2: For the second phase, a comprehensive Neuropsychological battery consisting of MoCA-M, MMSE, ACE, and two tests in each of the five cognitive domains (Attention, Executive Functions, Memory, Language and Visuospatial Functions) was compiled. (Ref: Litvan I et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. *Mov Disord.* 2012 Mar;27(3):349-56.) The tests used include the following: (1) Attention – Digit Span Test and the Attention/ concentration sub-section of ACE (2) Executive Functions- Trail Making Test and Wisconsin Card Sorting Test (3) Memory: Visual Reproduction and Logical Memory Test of Weschler Memory Scale (4) Language: Frenchay's Aphasia Battery and the

Language section of ACE (5) Visuospatial Functions – Position Discrimination and Cube Analysis of the Visual Object and Space Perception Battery. In addition, Beck’s Depression Inventory for Screening for Depression, Neuropsychiatric Inventory (NPI) for Neuropsychiatric symptoms and Clinical Dementia Rating Scale are also being used.

The data from the 50 healthy volunteers who participated in the second part of the study was used to define the cut-off scores for PD-MCI as per the standard guidelines, and the patients were classified into PD-MCI – Single-domain, PD-MCI Multidomain and PD-Normal cognition. Analysis of baseline Neuropsychological data from our cohort showed that the prevalence of the PD-MCI in our population was 29.4%. Vast majority (87.5%) of the patients with MCI had multi-domain involvement. Executive functions were the most frequently affected domain, followed by memory.

Tables 1 and 2 show the baseline demographic and neuropsychological data of the first 170 patients recruited for the study.

Table 1: Baseline demographic details of the study cohort (Data shown in years, as Mean ± Standard Deviation)

	Patients	Controls
Age	54.54 ± 8.51	51.10 ± 10.06
Education	12.40 ± 2.90	14.40 ± 3.39
Duration of illness	6.12 ± 4.01	Not applicable

Table 2: Baseline Neuropsychological data of the study cohort (Data shown as Mean ± Standard Deviation)

Neuropsychological Test	Patients (N=140)	Healthy Volunteers (N=60)
ACE	86.14 ± 8.73	92.02 ± 6.82
MMSE	27.46 ± 1.98	28.93 ± 1.12
MoCA-M	25.64 ± 2.72	27.28 ± 2.06

BDI	9.76 ± 8.48	4.52 ± 6.44
NPI	4.96 ± 5.36	1.74 ± 3.62
CDR	0.27 ± 0.26	0.12 ± 0.22
ACE-Attention	7.33 ± 0.95	7.72 ± 0.59
Digits Span-total	10.48 ± 2.69	11.88 ± 3.40
Visual reproduction-Delayed	18.40 ± 10.11	26.71 ± 10.53
Logical memory-Delayed	12.72 ± 6.75	18.05 ± 7.47
WCST-Total errors	3.34 ± 3.36	2.26 ± 3.04
TMT (B)- Errors	1.97 ± 3.58	0.59 ± 0.92
ACE- Language	27.18 ± 1.26	27.64 ± 0.67
Frenchay's Aphasia battery	28.61 ± 1.18	29.11 ± 0.98
VOSP- Cube Analysis	8.12 ± 2.71	8.78 ± 2.42
VOSP-Position Discrimination	19.66 ± 0.74	19.93 ± 0.33

ACE- Addenbrooke's Cognitive Examination, BDI- Beck's Depression Inventory, CDR- Clinical Dementia Rating Scale, MoCA-M: Montreal Cognitive Assessment-Malayalam, NPI- Neuropsychiatric Inventory, TMT(B)-Trail Making Test(B), VOSP-Visual Object and Space Perception Battery, WCST-Wisconsin Card Sorting Test

9. An abstract, highlighting the results achieved by the research project for inclusion in the Council's research information bulletin:

Objective: We aimed to design a neuropsychological test battery, including the Malayalam Version of Montreal Cognitive Assessment (MoCA), to diagnose Mild Cognitive Impairment (MCI) and to estimate the prevalence of MCI in Malayalam-speaking patients with Parkinson's disease (PD) from South India. We also did a longitudinal follow up of cognitive functions in patients with PD to examine how the neuropsychological functions change over time and whether changes in MoCA reflect the changes in detailed neuropsychological tests. **Background:** MCI is common in PD and a risk factor for PD-Dementia. Guidelines for diagnosis of PD-MCI have been published. However, a comprehensive test battery as per published guidelines is currently unavailable for use in South Indian population speaking Malayalam, numbering around 40 million. There is also little data on the prevalence of MCI among Indian PD patients. **Methods:** The Malayalam version of MoCA has been validated and published by our group.[1] For detailed Neuropsychological assessment, we compiled a test battery comprising of two neuropsychological tests in Malayalam in each of the five cognitive domains, namely attention and working memory, executive functions, language, memory and visuospatial functions.

Normative data from 50 healthy volunteers was used to decide cut-off scores for defining PD-MCI. The test battery was applied to 192 consecutive non-demented patients with PD to estimate the prevalence and characteristics of PD-MCI. The patients were also followed up longitudinally with annual Neuropsychological assessments. **Results:** The baseline data of the first 170 consecutive patients has been analysed. Healthy volunteers and patients did not differ significantly with regard to age or level of education. 50 (29.4%) of the patients were found to have PD-MCI. Among the patients with PD-MCI, multi-domain involvement was seen in 43 and the rest had involvement of only one domain. Executive function, followed by memory were the most common domains affected. Patients with MCI were older (57.8 ± 8.3 years Vs 54.9 ± 8.6 years; $p= 0.04$), had longer duration of motor symptoms (9.3 ± 2.7 years Vs 5.0 ± 3.0 years; $p < 0.01$) and lower MoCA scores (23.8 ± 2.8 Vs 26.6 ± 2.1 ; $p < 0.01$) compared to those without. The follow up data will be analysed and published soon. **Conclusions:** We designed a neuropsychological test battery to diagnose PD-MCI in Malayalam speaking South Indian population. The prevalence of PD-MCI estimated with the battery is comparable to that reported from other populations. Multi-domain involvement was seen in the majority with MCI. Patients with PD-MCI performed poorer on the Malayalam version of MoCA, one among the most widely used cognitive screening tests for PD. Analysis of our follow-up data will through light on the rate of decline of cognitive functions in patients with PD

[1]. Krishnan S, Justus S, Meluveetil R, Menon RN, Sarma SP, Kishore A. Validity of Montreal Cognitive Assessment in Non-English-speaking patients with Parkinson's disease. Neurol India. 2015 Jan-Feb;63(1):63-7.


10. Publications: (1) Krishnan S, Justus S, Meluveetil R, Menon RN, Sarma SP, Kishore A. Validity of Montreal Cognitive Assessment in Non-English-speaking patients with Parkinson's disease. Neurol India. 2015 Jan-Feb;63(1):63-7.

Presentation in International Conference:

Syam Krishnan, Remya Ramesh, Gangadhara Sarma S, Ramshekhar N Menon, Asha Kishore. Mild Cognitive Impairment in Parkinson's disease in South Indian population – Development of a test battery and assessment of prevalence and characteristics. Presented in the International Congress of Parkinson's disease and Movement disorders, Nice, France, September 22- 26, 2019.

Date: 26/3/2020

Signature


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