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Short Comunication

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Utility of a Screening Test (MoCa) to Predict Amyloid Physiopathology in Mild Cognitive Impairment

María Florencia Clarens[1], Ismael Calandri[1], María Belen Helou[1], María Eugenia Martín[1], Patricio Chrem Méndez[1] & Lucía Crivelli[1]

[1] FLENI. Buenos Aires (Argentina)

Abstract

Introduction: The MoCa (Montreal Cognitive Assessment) Screening test has become relevant in recent years in the screening of patients with Mild Cognitive Impairment (MCI). It is important to seek and study simple and reliable tools in clinical practices that correlate with biological markers that have been used to predict conversion from MCI to AD. Objective: To analyze the MOCA and its cognitive sub-scores and the relationship with Amyloid pathophysiology in Alzheimer's Disease. Methodology: 32 patients with MCI were studied, they were separated according positive (n: 20) and negative (n: 12) underlying amyloid pathology. The patients performed a extensive cognitive assessment that included MoCa Test. Results: MoCa Total Scores showed significantly different results between groups ($p < 0.001$) as well as the Memory Score (MoCa MIS), the Executive (MoCa EIS), the Attentional Score (MoCa AIS)) ($p < 0.001$) and the Orientation Score (MoCa OIS)) ($p < 0.05$) with worse performance of patients with amyloid pathophysiology. Score of MoCa a cut-off point of < 24 was established, since the diagnostic sensitivity at this point was 83% and the specificity 70%. Conclusions: The MoCa is a useful tool to differentiate biomarker status in MCI. Future studies should study this tool in the prodromal phases of the disease.

Keywords*:* Neuropsychology; dementia; mild cognitive impairment; Alzheimer's disease; amyloid

Utilidad de un test de Screening (MoCa) para predecir Fisiopatología Amiloide en Deterioro Cognitivo Leve

Resumen

Introducción: El MoCa (Montreal Cognitive Assesment) ha cobrado relevancia en los últimos años en el cribaje de pacientes con Deterioro Cognitivo Leve (DCL). El uso de herramientas clinicas simples y confiables con alta capacidad de predicción de la conversion del DCL a Enfermedad de Alzheimer (EA) es de gran importancia. Objetivo: Analizar la capacidad del MoCa y sus sub-scores cognitivos para la detección de fisiopatología amiloide en un grupo de pacientes con DCL. Metodología: Se estudiaron 32 pacientes con DCL, se los separó según fisiopatología amiloide subyacente positiva (n:20) y negativa (n:12). Los pacientes realizaron una extensa evaluación cognitiva que incluyó en MoCA. Resultados: El Score Total del MoCa arrojó resultados significativamente diferentes entre grupos ($p < 0.001$) así como el Score de Memoria (MoCa MIS), el Ejecutivo (MoCa EIS), el Score Atencional (MoCa AIS)) ($p < 0.001$) y el de Orientación (MoCa OIS)) ($p < 0.05$) obteniendo un peor desempeño los pacientes con fisiopatología amiloide. Se establecio un punto de corte de < 24 para el Score Total del MoCa, ya que la sensibilidad en este punto fue de 83% y la especificidad de 70%. Conclusiones: El MoCa es una herramienta útil para utilizar en pacientes con Deterioro Cognitivo Leve debido a Enfermedad de Alzheimer. Futuros estudios deberían estudiar esta herramienta en las fases prodrómicas de la enfermedad.

Palabras clave: Neuropsicología; demencia; deterioro cognitivo leve; enfermedad de Alzheimer; amiloide

Correspondence:

María Florencia Clarens
FLENI. Buenos Aires (Argentina)
E mail: fclarens@fleni.org.ar

Introduction

Mild Cognitive Impairment (MCI) (Petersen et al, 1999) is a stage between normal aging and early dementia. The identification of subjects with MCI at risk of conversion to Alzheimer's Disease (AD) is very important not only for clinicians, but for patients and their families. The MoCa Screening Test (Montreal Cognitive Assessment) is a very well-known 10-minute cognitive screening test for detection of MCI. It is widely known to have a high sensitivity (90%) and specificity (87%) in the detection of MCI and the distinction from normal cognition (Nasreddine et al, 2005). In 2017, the UDS 3 (Uniform Data Set) (Weintraub et al., 2018) of the ADC program (Alzheimer's Disease Centers) of the National Institute of Aging included it as part of its neuropsychological evaluation as a screening test (Besser et al., 2018). It has been translated into more than 37 languages, and is a simple, fast and economic tool that is being used to detect cognitive changes in prodromal stages of neurodenegerative diseases. It is important to provide simple and reliable tools in clinical practices, besides biological markers that have been used to predict conversion from MCI to AD.

Sub scores from MoCa have already been used to predict conversion to AD in individuals with MCI , establishing cut off scores from MoCa Total Score and MoCa Memory Index (MIS) (Julayanont, Brousseau, Chertkow, Phillips & Nasreddine, 2014). The MoCa MIS is calculated by adding the number of words remembered in free delayed recall, category-cued recall, and multiple choice–cued recall multiplied by 3, 2 and 1, respectively, with a score ranging from 0 to 15 to get better information from a probable memory deficit. The Executive Index Score (EIS) is calculated by adding raw scores for the modified Trail-Making Test Part B, clock drawing, digit span forward and backward, letter A tap- ping, serial-7 subtraction, letter fluency, and abstraction, with a score ranging from 0 to 13. The Visuospatial Index Score (VIS) is determined by adding the raw scores of the cube copy, clock drawing, and naming, with a score from 0 to 7. The Language Index Score (LIS) is obtained by adding the raw scores for naming, sentence repetition, and letter fluency, with a score ranging from of 0 to 6. The Attention Index Score (AIS) is obtained by adding the raw scores for digit span forward and backward, letter A tapping, serial-7 subtraction, sentence repetition, and the words recalled in both immediate recall trials, with a score ranging from 0 to 18. The Orientation Index Score (OIS) is the sum of points for the orientation section, with a score ranging from 0 to 6.

The objective of this study is to analyze the MoCa and its cognitive sub-scores and its accuracy to identify amyloid physiopathology underlying AD in a South American cohort of MCI patients.

Methods

32 patients with MCI were studied. Inclusion criteria for this study were those included in the Alzheimer's Disease Neuroimaging Initiative (ADNI) criteria: presence of a subjective memory concern reported by the study subject, a partner, or their attending clinician; age between 55 and 85 years, at least 6 years of formal education and at least one study companion spending 10 or more hours a week with the participant; absence of visual or auditory deficits which could affect cognitive test performance; Hachinski Ischemic Score (HIS) (Hachinsk et al., 1975) less than or equal to 4; score of 6 points or less on the Geriatric Depression Scale (GDS); no concomitant neurological

or psychiatric diseases, or contraindications for lumbar puncture, brain MRI, or PET brain imaging. Furthermore, for MCI criteria, following specific criteria were used: MMSE (Folstein, Folstein & McHugh, 1975) scores between 24–30 (inclusive), a Clinical Dementia Rating (CDR) (Hugues, Romey, Duval, Vincent & Lazdunski, 1982) of 0.5, absence of significant levels of impairment in other cognitive domains, essentially preserved activities of daily living, and an absence of dementia.

Patients were assessed with an extensive cognitive evaluation that included MoCa test. For the purpose of this study, MMSE test was the only test analyzed with the MoCa, in order to study the relationship of another screening measure to amyloid pathology. All study subjects with MCI were grouped according to Aß biomarker results (i.e. positive or negative). Aß biomarker results were studied through Amyloid PET scans (11C-Pittsburgh compound B) using fluorodeoxyglucose (FDG) and 11C-Pittsburgh compound-B (PIB-PET) or Cerebrospinal fluid (CSF) samples using enzyme-linked immunosorbent assay (ELISA) kits (Innogenetics; Ghent, Belgium) following ADNI Quality Control Program guidelines.

Results

Table 1 shows the comparison between the groups of patients with MCI separated according to the presence of amyloid physiopathology identified with a positive PET PIB biomarker or low level of Aß42 in the CSF.

MoCa Total Score yielded significantly different results between groups ($p < 0.001$) as well as the Memory Score (MoCa MIS), the Executive (MoCa EIS), the Attention Score (MoCa AIS) ($p < 0.001$) and the Orientation score. (MoCa OIS) ($p < 0.05$). Patients with amyloid physiopathology had worse performance in these scores (Table 1). MMSE (Mini mental State Examination) showed significant differences between groups as well.

Table 1.
Demographic and Neuropsychological Characteristics

	MCI amyloid negative	MCI amyloid negative	p
Age	69,2 ± 8	71,4 ± 4,8	ns
MMSE	28 ± 3,3	24,7 ± 4,2	p < 0.01
Moce Subscores			
Total Score Moca	25,2 ± 3	2,0 ± 4,3	p < 0.001
MocCa MIS	8,3 ± 3,6	4,3 ± 3,6	p < 0.001
MoCa EIS	11,8 ± 1,6	9,6 ± 2,2	p < 0.001
Moca VIS	6,3 ± 0,9	5,7 ± 1,3	ns
MoCa LIS	5,6 ± 0,7	5,1 ± 1	ns
MoCa AIS	17,2 ± 1,1	13,4 ± 3,6	p < 0.001
MoCa OIS	6 ± 0	5,2 ± 1,2	p < 0.5

Note: Results described in Mean and Standard Desviation. MMSE: Mini Mental State Examination. MoCa MIS: MoCa Memory Index Score, MoCa EIS: MoCa Executive Index Score, MoCa VIS: Visuoespatial Index Score, MoCa LIS: MoCa Language Index Score, MoCA AIS: MoCA Attentional Index Score, MoCa OIS: MoCa Orientation Index Score. Ns: non significant.

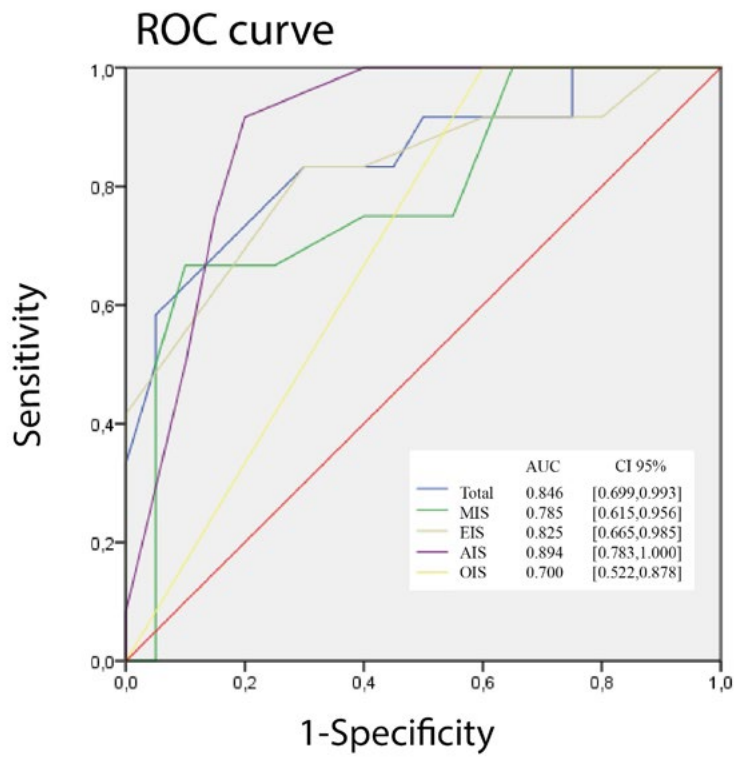

Figure 1. ROC Curves for MMSE and MoCa Sub scores.
Source: Authors.

ROC analysis was performed to calculate the cutoff score and diagnostic value to detect amyloid physiopathology. ROC CURVES were made for each of these scores. MMSE, MoCa AIS, MoCa EIS and MoCa Total Score presented the largest area under the curve (Figure 1). For the total Score of MoCa a cut-off point of < 24 was established, since the diagnostic sensitivity at this point was 83% and the specificity 70%.

Discussion and Conclusions

This study was designed to test the capacity of the MoCA to differentiate groups of patients with MCI according to their biomarker status. Results showed that MoCa Total Score and subscores (MoCa Ais, EIS) showed greater sensitivity and specificity than a commonly used screening test as MMSE, to differentiate groups of patients with MCI with and without amyloid physiopathology.

Cost effectiveness and accessibility of neuropsychological tests in the primary care setting, compared to neuroimaging studies or other biomarker assays, make them an appealing and useful tool for AD detection, particularly in developing countries were biomarkers technology is not available and resources are scarce. The results from this study add to previous results obtained from a South American Cohort were cut off scores from a memory test, the AVLT (Auditory Verbal Learning Test) were provided to predict AD presence (Clarens et al., 2020).

The MoCa total score and the subsequent analysis of its subscores is a useful tool to be used in the detection of patients with MCI due to Alzheimer's disease.

References

Besser, L., Kukull, W., Knopman, D. S., Chui, H., Galasko, D., Weintraub, S., Jicha, G., Carlsson, C., Burns, J., Quinn, J., Sweet, R. A., Rascovsky, K., Teylan, M., Beekly, D., Thomas, G., Bollenbeck, M., Monsell, S., Mock, C., Hua, X., Thomas, N., Robichaud, E., Dean, M., Hubbard, J., Jacka, M., Schwabe-Fry, K., Wu, J., Phelps, C. & Morris, J. C. (2018). Version 3 of the National Alzheimer's Coordinating Center's Uniform Data Set. *Alzheimer disease and associated disorders*, 32(4), 351–358. https://doi.org/10.1097/WAD.0000000000000279

Clarens, M. F., Crivelli, L., Calandri, I., Chrem, P., Martin, M. E., Russo, M. J., Campos, J., Surace, E., Vásquez, S., Sevlever, G. & Allegri, R. F. (2020). Neuropsychological profile of Alzheimer's disease based on amyloid biomarker findings results from a South American cohort. *Applied Neuropsychology: Adult*, 1–6. https://doi.org/10.1080/23279095.2020.1756816

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, 12(3), 189–198. https://doi.org/10.1016/0022-3956(75)90026-6

Hachinski, V. C., Iliff, L. D., Zilhka, E., Du Boulay, G. H., McAllister, V. L., Marshall, J., Rusell, R. W. & Symon, L. (1975). Cerebral blood flow in dementia. *Archives of neurology*, 32(9), 632–637. https://doi.org/10.1001/archneur.1975.00490510088009

Hugues, M., Romey, G., Duval, D., Vincent, J. P. & Lazdunski, M. (1982). Apamin as a selective blocker of the calcium-dependent potassium channel in neuroblastoma cells: voltage-clamp and biochemical characterization of the toxin receptor. *Proceedings of the National Academy of Sciences*, 79(4), 1308–1312. https://doi.org/10.1073/pnas.79.4.1308

Julayanont, P., Brousseau, M., Chertkow, H., Phillips, N. & Nasreddine, Z. S. (2014). Montreal Cognitive Assessment Memory Index Score (MoCa-MIS) as a Predictor of Conversion from Mild Cognitive Impairment to Alzheimer's Disease. *Journal of the American Geriatrics Society*, 62(4), 679–684. https://doi.org/10.1111/jgs.12742

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCa: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G. & Kokmen, E. (1999). Mild cognitive impairment: clinical characterization and outcome. *Archives of neurology*, 56(3), 303–308. https://doi.org/10.1001/archneur.56.3.303

Weintraub, S., Besser, L., Dodge, H. H., Teylan, M., Ferris, S., Goldstein, F. C., Kramer, J., Loewenstein, D., Marson, D., Mungas, D., Salmon, D., Welsh-Bohmer, K., Zhou, X.-H., Shirk, S. D., Atri, A., Kukull, W. A., Phelps, C. & Morris, J. C. (2018). Version 3 of the Alzheimer Disease Centers' neuropsychological test battery in the Uniform Data Set (UDS). *Alzheimer disease and associated disorders*, 32(1), 10–17. https://doi.org/10.1097/WAD.0000000000000223

Maria Florencia Clarens: PHD in Psychology.

Ismael Calandri: Neurologist.

María Belen Helou: Psychologist.

María Eugenia Martín: Psychologist.

Patricio Chrem Méndez: Neurologist.

Lucia Crivelli: PHD in Psychology.