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CSIS: Proposal for a New Combined Screening Interpretation Score for Patients with Mild Cognitive Impairment

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ABSTRACT

Introduction: It is essential to have sensitive, economical and quick cognitive screening tools for early detection of Mild Cognitive Impairment (MCI). The objective of the present study was to assess a new way of interpreting widely used screening tests, generating a new score: the CSIS (Combined Screening Interpretation Score). The CSIS considers the performance in various routine screening tests (MMSE, Clock drawing test, Short form of the Boston naming test, Phonological and Semantic fluency tests and the Frontal Assessment Battery) by summing up their gross scores in one general score.

Methods: We calculated the CSIS of 90 Hispanic older adults without dementia (40 controls and 50 patients with a diagnosis of MCI). The differences of the CSIS between the groups, and the discriminative capacity of the CSIS and each separate test were analyzed.

Results: Significant differences in the CSIS were observed between the groups, as a higher discriminative capacity of the CSIS compared to the other screening tests. A score of 86 points in the CSIS discriminates the groups with 84% sensitivity and 90% specificity.

Conclusion: It is concluded that the CSIS is a useful, simple and brief tool to assess the cognitive performance of subjects with MCI.

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Introduction

Population aging is associated with an increased prevalence of cognitive impairment, both mild cognitive impairment (MCI) and dementia (Calvo-Perxas et al., 2015; Panza et al., 2005). It is an important public health concern as the cost of this pathology represents an important burden for the healthcare system. MCI is a borderline concept between normal aging (or age-related cognitive impairment) and major cognitive impairment (or dementias). Dementias, for example Alzheimer's Disease (AD), are a group of slow and progressive disorders that do not present a fixed event that define their onset. Therefore, it is crucial (though difficult) for the clinicians to identify possible transition points from MCI to dementia, and to detect patients before they present a symptomatic phase (Albert et al., 2011).

Albert et al. (2011) define four cognitive and clinical criteria for MCI that include: concern regarding a change in the patient's condition, objective impairment in one or more cognitive domains, preservation of independence in functional abilities and absence of dementia. MCI is often the precursor of a dementia, but as the authors state "*sharp demarcations between*

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normal cognition and MCI, and between MCI and dementia are difficult, and clinical judgment must be used to make these distinctions" (p. 271). Neuropsychological assessment is an optimal way to study objectively the cognitive performance and the degree of cognitive impairment of an individual. Thus, neuropsychological screening tools for the identification of MCI not only would collaborate with the diagnosis, but would also aid to estimate globally the prevalence, incidence, risk and associated morbidity of this pathology. Although there is no scientific evidence of a specific pharmacological treatment for MCI to prevent its progression to dementia (Cooper, Li, Lyketsos, & Livingston, 2013; Li, Dai, Zhao, Liu, & Li, 2018) identifying dementia prodromes is crucial for future treatment efforts. Therefore, it is vital to study an effective, brief and sensitive screening score, feasible to be applied by health professionals in a context of primary care for the detection of cognitive impairment in older adults, considering both the extension in life expectancy in the elderly and the impact that these pathologies have on a family and economic level (Mías, Sassi, Masih, Querejeta, & Krawchik, 2007).

The Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) is a screening test widely used worldwide to detect cognitive impairment that has been used in various cognitive assessment studies throughout the last decades. However, the MMSE was not designed to identify MCI specifically, and for that reason the creation of sensitive tools to detect this pathology is particularly useful. Some tools have been proposed for MCI screening, such as the Montreal Cognitive Assessment (Ciesielska et al., 2016; Nasreddine et al., 2005), the Mini Cognitive Scale (Fage et al., 2015) or the combined use of different classic screening tests (Fage et al., 2015; Li et al., 2018; Milian et al., 2012; Xu, Meyer, Thornby, Chowdhury, & Quach, 2002). A meta-analysis (Ciesielska et al., 2016) studied the diagnostic reliability of the MMSE and the Montreal Cognitive Assessment concluding the latter (AUC =.85) was better than the former (AUC = .74) for MCI detection. This conclusion lines up with a prior study (Mitchell, 2009) that stated that the MMSE's accuracy may be weaker when detecting MCI, suggesting that it should be used combining it with other tests. Another recent meta-analysis (Breton, Casey, & Arnaoutoglou, 2019) studied the diagnostic accuracy of several cognitive tests to detect MCI, and stated that the Montreal Cognitive Assessment, the Memory Alteration Test and the Addenbrooke's Cognitive Examination-Revised had higher sensitivity (though not specificity) than the MMSE for MCI. Bondi et al. (2014) affirm that an actuarial approach based in the interpretation of several neuropsychological tests is better when characterizing MCI than the conventional criteria, and that patients detected this way tend to remain as MCI or progress to dementia, rather than revert to a cognitively normal status. Furthermore, Edmonds et al. (2015) conclude that the conventional clinical criteria may present flaws when detecting MCI as this traditional diagnostic method is more susceptible to false-positive errors. This study also shows the utility of studying MCI (diagnosis and progression) from an actuarial approach, considering that the sum of several indicators (neuropsychological scores, biomarkers, etc.) is more specific than considering just an individual criterion.

The objective of this work was to assess an actuarial method that quantifies overall impairment and can replace the clinical judgment often used for diagnosis following the administration of neuropsychological tests. By means of the proposed actuarial method for cognitive screening and early detection of MCI, it was proposed: I) To calculate a new score (Combined Screening Interpretation Score, hereinafter, CSIS) that would consider the performance of the subjects assessed in various routine screening tests, and II) To compare the specificity and sensitivity of this new score with the screening tests used separately, as they are currently used in the clinical setting. The new proposal of the CSIS would be useful to

operationalize a more efficient clinical cognitive screening, saving time and resources, and favoring an early and sensitive detection of cognitive decline for subsequent patient follow-up.

Materials and Methods

Participants

The sample consisted of 90 Hispanic subjects from the City of Buenos Aires without dementia between 60 and 85 years (40 controls and 50 patients with a diagnosis of MCI). Sex, age and educational level did not significantly differ between groups. All participants included were native Spanish Speakers. A convenience sampling was conducted, and participants were recruited from the neurology department at Hospital Español of Buenos Aires, via leaflets as well as from community centers for pensioners. The sociodemographic characteristics of the sample are summarized in Table 1.

The diagnosis of patients with MCI was done following the criteria proposed by Petersen et al. (1999) and the International Working Group on Mild Cognitive Impairment (Albert et al., 2011), namely: 1- Subjective complaints of patient memory and corroborated by an informant; 2- Cognitive deterioration objectified through specific neuropsychological tests; 3- Conservation of other cognitive functions; 4- Normal performance in activities of daily living and conservation of autonomy; 5- Absence of dementia criteria. Participants were selected ensuring that the sociodemographic characteristics (age, sex and educational level) of the controls were similar with respect to the group of patients. Those subjects without functional independence in their daily life activities, people with a history of neurological and psychiatric diseases, and visual or auditory decline (not compensated by glasses or hearing aids) were excluded from the study.

Instruments

All participants were examined with screening tests widely used in clinical neuropsychology. The versions and punctuation guidelines of the instruments used in the present study, as well as their psychometric properties, are described below:

- The *MMSE* (Allegri et al., 1999; 2011; Butman et al., 2001; Folstein, Folstein and McHugh, 1975; Lobo et al., 1999) is a short and quick test used for initial cognitive screening. The literature on cognitive assessment in geriatrics patients suggests a sensitivity of .89 and a specificity of .75 when a 24/30 cutoff point is used.
- The *Short form of the Boston naming test* (Kaplan, Goodglass, & Weintraub, 1983; Serrano et al., 2001) is an abridged version of the full form of the Boston naming test, used to detect semantic memory and language impairments associated with dementia.

Table 1. Sociodemographic characteristics of the sample.

	Control group N = 40	MCI group N = 50			
Age	76.33 ± 6.18	75.74 ± 6.38	$t = -.44$	$df = 88$	$p = .66$
Educational level (in years)	9.35 ± 3.87	8.62 ± 2.99	$t = -1.01$	$df = 88$	$p = .32$
Sex (% male)	15%	28%	$X^2 = 2.17$	$df = 1$	$p = .14$

The 12-item version used in the present study reports a sensitivity of .85 and a specificity of .94 when a 9/12 cutoff point is used.

- The *Semantic and Phonological verbal fluency tests* (Butman, Allegri, Harris, & Drake, 2000; Carnero-Pardo & Lendínez-González, 1999) assess categorial evocation, detecting semantic memory and cognitive flexibility impairments associated with demential signs. When using a cutoff score of 10, verbal fluency tests report a sensitivity of .90 and a specificity of .94.
- The *Clock Drawing Test* (Cacho, García-García, Arcaya, Vicente, & Lantada, 1999; López, Allegri, & Soto-Añari, 2014; Sunderland et al., 1999) is a quick and sensitive test used to rapidly evaluate cognitive deterioration. With a cutoff score of 6 the reported sensitivity is of .84 and the specificity of .92.
- The *Frontal Assessment Battery – FAB* (Dubois, Slachevsky, Litvan, & Pillon, 2000; Rodriguez- del Álamo, Catalán-Alonso and Carrasco-Marín, 2003) is a screening tool that explores executive functions, and the literature reports an acceptable internal consistency (Cronbach's alpha = .78) and an ability to discriminate patients and controls of .89.

Procedure

The participants were verbally informed of the research purposes and then were offered the written version of this information in a printed document, which they had to read, accept and sign. In this way, all participants gave their verbal and written consent for inclusion in the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Ethical approval for the study was obtained from the Ethics Committee of Spanish Hospital of Buenos Aires and all participants provided informed consent as previously mentioned. The group of patients with MCI had been previously diagnosed by a consultant neurologist and a neuropsychologist after applying a specialized neuropsychological battery and following the guidelines of Petersen et al. (1999) and the International Working Group on Mild Cognitive Impairment (Albert et al., 2011). The assessment of all participants was carried out in a session of approximately one hour and included the previously described instruments (MMSE, Phonological and Semantic fluency tests, Short form of the Boston naming test, Clock drawing test and FAB) and a brief interview. Each test was administered and scored according to the guidelines proposed by their respective authors (see Instruments section), and then the Combined Screening Interpretation Score (CSIS) was calculated considering the sum of the gross scores obtained in each test. The administration and calculation of the CSIS itself lasts approximately 30–45 minutes.

Statistical Analysis

For the statistical analysis, a mean differences study of the evaluated variables (Student's t) was carried out to analyze the differences in the performance of the CSIS and of the screening tests considered separately between the control group and the group with MCI. In cases where the differences were significant between the groups, the effect size (Cohen's d) was analyzed to conclude the magnitude of these differences. Subsequently, the areas under the curve (AUC) of the CSIS and each screening test were calculated to compare the discriminative capacity of each score. To study if there were statistical differences between the AUC of the CSIS and the MMSE, the DeLong method was used. Finally, the different

cutoff points for the CSIS were calculated based on the sensitivity and specificity observed in the discrimination of the control group and the group with MCI. The statistical packages SPSS v21.0, G*Power v.3.1.9.2. and MedCalc were used for general statistical analysis, for size of the effect analysis and for the DeLong method analysis, respectively.

Results

There were no statistically significant differences in the sociodemographic composition of the groups (see Table 1), although significant differences were observed between the groups in terms of performance in cognitive screening tests. The control group obtained higher scores than the group with MCI in all tests, as well as a clear statistically significant difference in the CSIS between both groups, always in favor of the control group. The analysis of the effect sizes for the differences that were significant evidenced very strong powers in all screening tests, but the score that obtained greater statistical power when describing the differences in the performance of the participants was the CSIS (d = 1.39). These results are summarized in Table 2.

Subsequently, the areas under the curve (AUC) were calculated for each screening test considered separately and for the gross sum of all of their scores, represented by the CSIS. Significant AUC values were observed in all screening tests (AUC ≤ .89; $p < .001$) but the AUC that showed the highest discriminatory capacity was the CSIS (AUC≤ .93; $p < .001$). Figure 1 shows the AUC of each screening test considered separately and the CSIS, showing the contrast between the tests. Table 3 presents the values obtained for this analysis according to the screening tests and in the CSIS.

Although the CSIS showed a greater AUC than the MMSE, the DeLong method for comparing ROC curves revealed no significant difference between both AUC (p= .24).

Finally, the best cutoff points were analyzed, prioritizing the specificity and sensitivity of the gross sum obtained in the CSIS score for discrimination between groups. It was observed that with a CSIS cutoff score of 86 the sensitivity was .84 and the specificity of .90, while with a cutoff score of 88 the sensitivity climbs to .88 but the specificity drops to .75.

Discussion

The objective of this study was to present an actuarial method that quantifies overall impairment and can replace the clinical judgment to rule-out MCI in a brief time and with easily accessible materials for the healthcare team. As a screening tool, the CSIS can be administered by trained sanitary agents and nurses, those who usually have the first contact to the patient in

Table 2. Cognitive performance between groups.

	MCI group N = 50		Control group N = 40		t	df	p	d
	Mean	SD	Mean	SD				
MMSE	25.06	2.98	28.7	1.26	−7.81	69.16	.001	1.22
Boston naming test (short version)	8.44	2.76	10.75	1.33	−5.2	73.85	.001	0.92
FAB	13.06	3.18	15.93	1.61	−5.54	75.55	.001	0.97
Clock drawing test	7.53	2.25	9.37	.99	−5.19	70.69	.001	0.91
Phonological fluency test	9.86	3.38	14.2	4.85	−4.8	67.16	.001	0.94
Semantic fluency test	10.42	3.72	16.48	3.97	−7.4	81.18	.001	1.24
CSIS	74.37	12.37	95.43	8.99	−9.34	87.27	.001	1.39

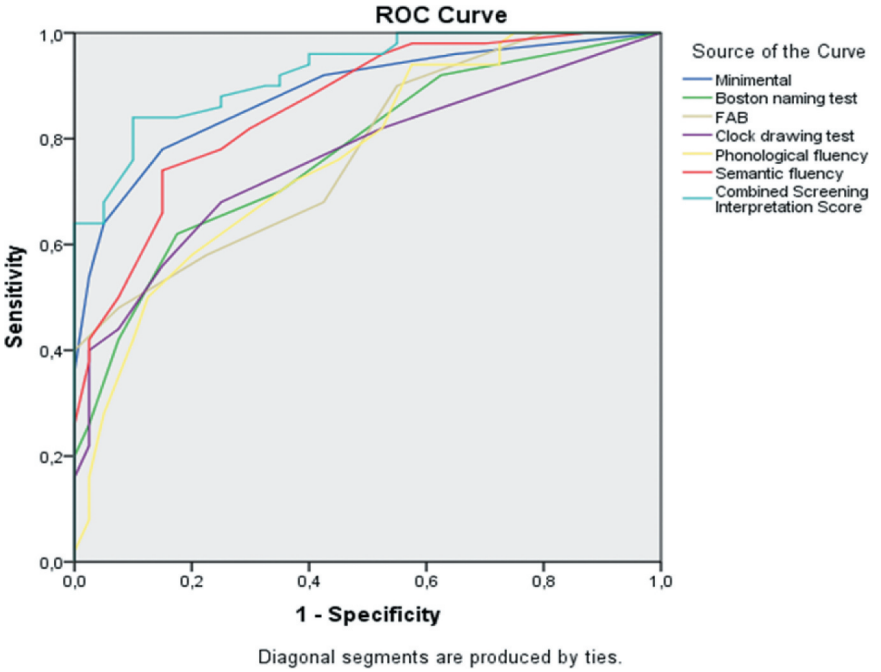

Figure 1. AUC analysis of the screening tests and the CSIS.

Table 3. AUC analysis of the screening tests and the CSIS.

	AUC	p	CI 95%
MMSE	.89	.001	.82-.95
Boston naming test (short version)	.77	.001	.68-.87
FAB	.78	.001	.68-.87
Clock drawing test	.76	.001	.67-.86
Phonological fluency test	.77	.001	.67–86
Semantic fluency test	.86	.001	.79-.93
CSIS	.93	.001	.87-.98

the public health system, offering a comprehensive outlook of several cognitive functions status. The CSIS is composed of a global score that considers the performance in various screening tests widely used for cognitive deficits detection. The analysis of the CSIS profiles obtained in the control group and the group with MCI show the additional value provided by this score in contrast to the separate scores of traditional screening tests. The calculation of the CSIS does not take time, it does not require administering additional tests or generating complex formulas, since it is obtained through a simple sum of the gross scores of the tests that compose it. However, this step achieves a more sensitive global score useful to operationalize in the daily practice to rule-out or confirm cognitive impairment in an evaluated patient. The CSIS is a promising tool that may have a greater discriminatory capacity than the MMSE, although this difference was not significant enough to propose the CSIS as a replacement of other screening tools. Nevertheless, the CSIS, in comparison to taking different separate scales, has a clear advantage: it objectively informs general cognitive status as it considers different tests (therefore, cognitive functions) that may allow the clinician to base the interpretation in

a cutoff point rather than a subjective judgment that synthesizes multiple different pieces of information. This score allows to infer preserved cognitive functions differentiating them from compromised domains, which is essential to guide further assessment and prognosis, as well as to orient the design of a neurorehabilitation plan. This valuable additional information cannot be obtained with the MMSE by itself, while the CSIS provides it with minimal additional time. Actuarial approaches as the CSIS have shown in the past to be better for MCI diagnosis and its progression to dementia (Bondi et al., 2014; Edmonds et al., 2015).

It is relevant to highlight that the present study included a unique sample of healthy controls and MCI patients, which were Hispanic (nonwhite), Spanish speakers (non-English) and with low educational levels, samples which are frequently understudied and highly needed to be characterized. It is also relevant the inclusion of non-demented patients in this analysis, and it can be hypothesized that in patients with dementia (for example, with dementia due to AD) the CSIS findings would be greater. However, the decision of including patients with MCI in the analysis was due to the risk they have to progress toward dementia, and the importance of the early detection of cognitive disfunction.

As other authors, we support the idea that an early and effective detection of cognitive impairment in patients with MCI is essential and should be a priority for health professionals (Bondi et al., 2014; Edmonds et al., 2015; Li et al., 2018; Mías et al., 2007; Ryals, O'Neil, Mesulam, Weintraub, & Voss, 2018). With this objective, the development of the CSIS and the analysis of its performance in patients with MCI and in controls contributed toward a holistic score, providing a useful tool to health professionals who work in primary care of older adults.

The CSIS calculation may differ with educational level, so future works with larger samples may replicate this study and corroborate if these results are similar in older adults with different educational exposures. Likewise, a next step in this strand of research would be to generate differential profiles of the CSIS based on the subtypes of MCI (amnesic and non-amnesic) considering the inclusion and analysis of more memory tasks. Finally, we anticipate further research studying the prediction capacity of CSIS for progression from MCI to dementia with a longitudinal design.

Disclosure statement

No potential conflict of interest was reported by the authors.

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