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Artículo de investigación

Is the Mattis Dementia Rating Scale appropriate to detect Mild Cognitive Impairment?

¿Es la Escala de Demencia de Mattis adecuada para detectar Deterioro Cognitivo Leve?

Anabel Belaus ^{1*}, Luis A. Fernández ^{2,3,4}, Yamila Farías-Sarquis ^{5,6}, Adrián M. Bueno M. ^{2,7}

1 Laboratorio de Psicología Cognitiva, Facultad de Psicología, Universidad Nacional de Córdoba. Córdoba, Argentina.

2 Carrera de Psicología, Facultad de Filosofía y Humanidades, Universidad Católica de Córdoba. Córdoba, Argentina

3 Universidad Nacional de Córdoba. Córdoba, Argentina

4 Fundación Cortex. Córdoba, Argentina

5 Servicio de Psiquiatría y Psicología. Hospital Privado. Córdoba, Argentina.

6 Laboratorio de Neuropsicología Clínica, Facultad de Psicología, Universidad Nacional de Córdoba. Córdoba, Argentina.

7 Laboratorio de Psicología, Facultad de Psicología, Universidad Nacional de Córdoba. Córdoba, Argentina.

Resumen

Algunos estudios han intentado evaluar la capacidad de la Escala de Demencia de Mattis (MDRS) para detectar demencia incipiente o Deterioro Cognitivo Leve (DCL), pero los resultados no son claros. El objetivo de este estudio fue evaluar la sensibilidad y especificidad de la MDRS para detectar DCL, y localizar el puntaje de corte más adecuado para la población local. *Metodología.* Una batería neuropsicológica que incluyó la MDRS fue aplicada a 60 adultos mayores de ambos sexos (edad media=68.38, DE=6.80) en Córdoba, Argentina, quienes fueron clasificados según su estado cognitivo en "Normales" (34 casos) o "DCL" (26 casos) según su desempeño en la batería neuropsicológica administrada, excluyendo la puntuación en la MDRS. El criterio empleado fue el de la Sociedad Española de Neurología. Se realizaron comparaciones de medias y un análisis de regresión logística para evaluar la capacidad del MDRS para diferenciar ambos grupos y localizar el puntaje de corte. *Resultados.* Aunque la MDRS diferenció ambos grupos a partir de la media ($p=.004$), la precisión diagnóstica fue sólo del 63% al utilizar un puntaje de corte total de 133. La sensibilidad fue del 42% y la especificidad fue del 79%. *Conclusiones.* El MDRS no parece ser una herramienta útil para detectar DCL, ya que presenta numerosos casos mal clasificados. El desarrollo de herramientas más adecuado para detectar DCL resulta fundamental.

Palabras clave: deterioro cognitivo leve, Escala de Demencia de Mattis, detección, test de cribado

Abstract

Some studies have tried to assess the Mattis Dementia Rating Scale (MDRS) capability to detect incipient dementia or Mild Cognitive Impairment (MCI), but the results are not clear. The aim of this research was to evaluate the sensitivity and specificity of the MDRS, and to localize the optimal cutoff score for MCI. *Methodology.* A neuropsychological battery that included the MDRS was administered to 60 older adults of both genders (Mean age=68.38, SD=6.80) in Córdoba, Argentina, who were then classified as "Control" (34 cases) or "MCI" (26 cases) according to performance in the neuropsychological evaluation, excluding the MDRS. The criteria used were those stated by the Sociedad Española de Neurología. We performed mean comparisons in order to evaluate if the MDRS was able to detect the group differences. Then, a logistic regression with the MDRS total score as the predictor variable and the group as the criterion variable was performed to determine the cutoff score. *Results.* Even though the mean comparisons showed a significant difference in the MDRS ($p=.004$), the diagnostic accuracy was only 63% with a 133 points cutoff score. The sensitivity was 42% and the specificity was 79%. *Conclusions.* The MDRS does not seem to be a useful tool to detect MCI since it generates numerous misclassified cases. The development of more accurate tools becomes fundamental in order to detect MCI.

Keywords: mild cognitive impairment, Mattis Dementia Rating Scale, detection, screening tests

Introduction

According to the World Health Organization, in 2010 there were 35.6 million people suffering some kind of dementia, and that number is predicted to almost double every 20 years (World Health Organization [WHO], 2012). Therefore, there has been increasing interest in detecting the early stages of dementia.

The Mild Cognitive Impairment (MCI) is a nosological entity considered as the intermediate stage in the continuum between normal aging and dementia (Alberti Ros, 2007). The index of evolution to dementia of MCI people is about 8-15%, while only the 1-2% of normal aged people develop this kind of illness (Allegri, Laurent, Thomas-Anterion & Serrano, 2005). Also, according to Sánchez-Rodríguez & Torrellas-Morales (2011), the prevalence of MCI fluctuates between 3 and 53%, being the variability in

* Correspondencia: belaus.anabel@gmail.com. Laboratorio de Psicología Cognitiva, Facultad de Psicología, UNC. Enrique Barros esq. Enfermera Gordillo, Ciudad Universitaria, Córdoba (X5000), Argentina. Tel.: 00-54-3514606557.

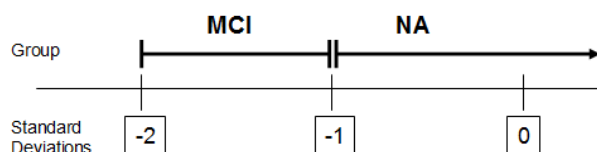


Figure 1. Group division. *Group 1.* Mild Cognitive Impairment (MCI) was integrated by those participants who got a score below 1 standard deviation below the mean but above 2 standard deviation below the mean (score between -1 and -2 SD) in at least two of the neuropsychological tests employed. Participants who obtained more than 2 tests below -2 SD, were excluded for being considered as possible demented. *Group 2.* Normal Aging (NA) was integrated by those participants who obtained a score above 1 standard deviation below the mean (-1 SD) according to age, gender and education in all the neuropsychological tests employed or those who obtained a score below 2 standard deviation below the mean (-2 SD) in just one of the neuropsychological tests, having a superior performance in the remaining tests.

these numbers being a reflection of the characteristics of the samples and diagnosis criterion in use.

Therefore, an accurate detection and diagnosis of MCI is fundamental. For that purpose it is indispensable to count with neuropsychological tests which are short and easy to apply. They must be appropriate to detect this particular pathology, especially to be used in the daily clinical practice.

The Mattis Dementia Rating Scale (MDRS) (Mattis, 1976, 1988) is a relatively short screening test, designed to evaluate and quantify the cognitive decline in demented subjects (Simone, Serrano & Allegrí, 2007). However, according to Busch & Smerz Chapin (2008), its use has been widened to include a wide range of diseases and to differentiate between neuropsychiatric disorders.

Comparing with other screening tests, the MDRS has the advantage of evaluating the cognitive functions with multiple items, thus providing estimative data of the contribution of each function to the global cognitive state (Chetelat, Eustache, Viader, De la Sayette, Pelerin, Mezenge, et al, 2005).

The test is divided into five subscales measuring attention, initiation and perseveration, visuospatial construction, conceptualization and memory. It sheds a global punctuation with a maximum of 144 points and partial values for each subscale (Simone et al., 2007).

Because of its wide utilization, some studies have shown interest in the capacity of the MDRS for differentiating MCI from other pathologies. In 1995, Green, Woodard and Green stated that the MDRS was useful in screening for MCI, reporting a cutoff of 133 that correctly classified 95% patients (n=22) and 100% control subjects (n=48). Nevertheless, this study presented some limitations to take into account. First, the patients group consisted in subjects with probable Alzheimer Disease (AD) or Vascular Dementia (VD) which is significantly different from MCI. Secondly, there was a disproportionate representation of older individuals in the impaired group, a feature which is known to affect cognitive performance (e.g. Pedraza, Lucas, Smith, Petersen, Graff-Radford, & Ivnik, 2010). Thirdly, they excluded patients with subtle cognitive impairment, which may bias the results as it is probably inapplicable to an unselected population. Fourthly and last, these authors did not provide enough information about the statistical analysis performed in order to find the cutoff score.

Later, there have been studies that reported significant mean differences of the MDRS score between MCI and other groups. For instance, Ivanouí, Adam, Van der Linden, Salmon, Juillerat, et al. (2005) found that the total and memory subscale score of the MDRS differentiate between healthy controls, MCI, and probable AD subjects. Wang, Saykin, Flashman, Wishart, Rabin, et al. (2005) found differences between MCI and AD patients through the MDRS total score. Similarly, Griffin, Netson, Harrel, Zamrini, Brockington & Marson (2006) reported that this screening instrument differentiates healthy control subjects from amnesic MCI (a-MCI) patients. Also, La Voie & Faulkner (2008) found mean differences between probable AD, a-MCI and healthy controls from the total score and most subscales except in construction scores. Matteau, Simard, Jean & Turgeon (2008) informed about mean differences between a-MCI, probable AD and healthy control subjects from both the total and the subscales score. But none of these studies tried to assess the validity of the MDRS for MCI, or to find a cutoff score.

However, in the recent years new attempts have emerged to validate the MDRS for MCI. Villeneuve, Rodrigues-Brazete, Joncas, Postuma, Latreille, & Gagnon (2011) informed about a cutoff of 138 for MCI in Parkinson Disease (PD-MCI) that correctly classified the 80% of cases with

0.72 sensitivity and 0.86 specificity. In the same study they found a cutoff of 141 for MCI in REM Behavior Disease with an 82% of cases correctly classified, and a sensitivity of 0.90 and specificity of 0.71. Meanwhile, Matteau, Dupre, Langlois, Provencher & Simard (2012) reported a cutoff score of 140 for PD-MCI which correctly classified 82% of cases, with a sensitivity of 0.86 and a specificity of 0.54, but they found no capacity to differentiate between PD-MCI and a-MCI. These authors also proposed an alternative cutoff score of 139 with a sensitivity of 0.80 and a specificity of 0.68. In the same study, they found that a cutoff of 132 correctly classified 100% of Demented PD patients when compared with healthy control subjects.

As noticeable results, from this background, we can say that there is no clear information about the validity of the MDRS to detect MCI. The few studies that tried to shed light about it focused only in a subtype of MCI or presented insufficient information. There are also evident differences between the cutoff scores that each of them reported. Therefore, the aim of this study was to evaluate the sensitivity and specificity of the MDRS to detect MCI, and also to localize the optimal cutoff score for the population of Córdoba.

Regarding the last objective, the only study about the validity of the MDRS in Argentina was performed by Fernandez & Scheffel (2003). In accordance to what Mattis proposed (1988), they found that 123 was the optimal cutoff for detecting Dementia, with a sensitivity of 0.83 and a specificity of 0.90. These authors found no difference by age, education or gender.

Methods

Subjects

There were 60 participants in the study. All of them were non clinical subjects who voluntarily attend a neuropsychological evaluation in a senior center located in Córdoba, Argentina. The mean age of the sample was 68.38 with a standard deviation of 6.80. A 21.66% had an educational level of 6 years or less, while 53.33% had 6 to 12 schooling years and 25% had more than 12 years of formal education. The female gender was overrepresented, conforming 88.33% of the participants. Criteria for inclusion were: being more than 50 years old, voluntary assistance to the evaluation centers, and signing a written consent where participants were informed about the nature of the study and the future use of the information collected. Criteria for exclusion were: diagnosed dementia, alcoholism, clinical diseases that could interfere with the cognitive performance, such as uncontrolled diabetes, liver or renal diseases, etc.; chronic consume of psychotropic substances or drugs that affect the central nervous system; history of neurologic diseases, stroke or trauma; history of psychiatric illness with cognitive affection; moderate or severe alteration of the daily life activities.

All participants included in the sample had a score of 2 or less in the Activities of daily living scale (ADLs) and absence of psychiatric symptoms which implied a score of 6 or less in de Geriatric Depression Scale (GDS), and 21 or less for women and 19 or less for men in the State-Trait Anxiety Inventory (STAI), according to the local adaptations. The Neuropsychiatric Inventory (NPI) was employed to exclude all participants who showed psychiatric symptoms with the following frequency: "Frequently", "Several times per week but less than daily" and "Very often, daily or constantly".

Table 1. Demographic characteristics of the sample.

| | NA | | MCI | | Total | |
|------------------|-------------|------------|-------------|------------|-------------|------------|
| | n | Percentage | n | Percentage | n | Percentage |
| Women | 33 | 97.05 | 20 | 76.92 | 53 | 88.33 |
| Men | 1 | 2.94 | 6 | 23.07 | 7 | 11.66 |
| Education | | | | | | |
| 6 years or less | 6 | 17.64 | 7 | 26.92 | 13 | 21.66 |
| 6 to 12 years | 17 | 50 | 15 | 57.69 | 32 | 53.33 |
| 12 years or more | 11 | 32.35 | 4 | 15.38 | 15 | 25 |
| Total group | 34 | | 26 | | 60 | |
| Age M(SD) | 67.29(6.01) | | 69.80(7.58) | | 68.38(6.80) | |

Note. M: Media, SD: Standar Desviation, NA: Normal Aging, MCI: Mild Cognitive Impairment.

Table 2. Mean comparison for NA and MCI participants.

| | Normal Aging Mean (SD) | MCI Mean (SD) | F fd(1,58) | p-value |
|-------------------------------------|---------------------------|------------------|------------|---------|
| MMSE | 29,26 (0,86) | 28,30 (1,28) | 2,38 | .050* |
| MDRS | 136,91 (5,05) | 132,34 (6,99) | 8,62 | .004* |
| Attention | 35,82 (1,40) | 34,53 (2,26) | 7,29 | .009* |
| Initiation-Perseveration | 35,38 (2,26) | 34,42 (3,07) | 1,93 | .169 |
| Construction | 5,79 (0,47) | 5,96 (0,19) | 2,81 | .098 |
| Conceptualization | 36,14 (2,72) | 34,11 (3,60) | 6,19 | .015* |
| Memory | 23,76 (1,59) | 23,38 (1,62) | 0,82 | .368 |
| Letter-Number Sequencing (WAIS-III) | 9 (3,02) | 8,03 (2,28) | 1,82 | .181 |
| RAVT immediate recall | 8,79 (2,38) | 6,53 (2,15) | 14,30 | .000* |
| RAVT delayed recall | 9,05 (2,71) | 6,73 (3,19) | 9,28 | .003* |
| Semantic Verbal Fluency | 20,5 (3,95) | 15,65 (3,69) | 23,37 | .000* |
| Phonological Verbal Fluency | 16,29 (4,86) | 11,69 (4,13) | 14,97 | .000* |
| TMT A | 53,05 (19,25) | 65,95 (20,23) | 6,33 | .014* |
| TMT B | 104,61 (47,02) | 186 (77,85) | 25,20 | .000* |
| Clock Test – Order | 8,80 (1,83) | 9,07 (1,21) | 0,41 | .521 |
| Clock Test – Copy | 9,45 (0,86) | 9,59 (0,93) | 0,36 | .550 |
| Symbol Search (WAIS-III) | 50,67 (13,21) | 38,19 (10,69) | 15,44 | .000* |

Note. NA: Normal Aging (n=34). MCI: Mild Cognitive Impairment (n=26). *Statistical differences at <.05.

The diagnosis criterion proposed by the Sociedad Española de Neurología for MCI is an alteration of one or more of the following cognitive areas: attention or executive functions, language, memory or visuospatial functions, and this alteration must be acquired, reported by the patient or an informant, have months or years of duration, objectified by neuropsychological evaluation (yield <1 or 1.5 standard deviations with respect to the group of the same age and educational level), the alteration minimally interferes or does not interfere with usual activities, and there is no level of consciousness disorder, acute confusional state, a focal neurobehavioral syndrome or dementia.

With the resulting sample, two groups were formed Mild Cognitive Impairment (MCI) and Normal Aging (NA) (see Figure 1). In every case the MDRS score was excluded in order to avoid result contamination. Groups did not differ on age $F(1,58)=2.04$, $p=.15$ nor educational level $\chi^2(2)=1.03$ $p=.59$. However, NA and MCI groups differ on gender $\chi^2(1)=5.79$ $p=.02$ with a woman over-representation. Table 1 shows the general characteristics of the groups.

Instruments

All patients were informed about the ethical aspects of the study and asked to provide their written consent to the use of the information gathered for research purposes. A socio-demographic profile was obtained through a semi-structured questionnaire.

The screening tests employed were: *Minimal State Examination* [MMSE] (Folstein & McHugh, 1975; adapted for the Argentinean population by Butman, et al., 2001) and *Mattis Dementia Rating Scale* [MDRS] (Mattis, 1988).

The comprehensive neuropsychological assessment was performed with the following tests: *Rey Auditory Verbal Learning Test* [RAVLT] (Rey, 1964; adapted for the Argentinean population by Burin, Ramenzoni & Arizaga, 2003), *Semantic Verbal Fluency Test* (Newcombe, 1969; adapted for the Argentinean population by Fernández, Marino & Alderete, 2004), *Phonologic Verbal Fluency Test* (Benton & Hansher, 1976; adapted for the Argentinean population by Butman, Allegri, Harris & Drake, 2000), *Trail Making Test* [TMT A y B] (Partington & Leiter, 1949; adapted for the Argentinean population by Fernández, Marino & Alderete, 2002), *Clock Test* (Freedman et al, 1994; adapted for the Hispanic population by Cacho, García-García, Arcaya, Vicente & Lantada, 1999), *Letter-Number Sequencing WAIS-III subtest* (Wechsler, 2002; Spanish version), *Symbol Search WAIS-III subtest* (Wechsler, 2002; Spanish version).

For psychiatric indicators we employed: *Geriatric Depression Scale* [GDS] (Yesavage, 1983; adapted for the Hispanic population by Aguado et al, 2000), *State-Trait Anxiety Inventory* [STAI] (Spielberger, Gorsuch & Lushene, 1982; adapted for the Argentinean population by Leibovich de Figueroa, 1991) and *Neuropsychiatric Inventory* [NPI] (Cummings, et al, 1994).

In order to evaluate the daily life activities we used the *Activities of daily living scale* [ADLs] (Lawton y Brody, 1969; Spanish adaptation by Kane & Kane, 1993).

Table 3. Subjects classification with 133 cutoff score.

| Observed | | Predicted (MDRS) | | |
|----------|-------|------------------|----|-------|
| | | MCI | NA | Total |
| Observed | MCI | 11 | 15 | 26 |
| | NA | 7 | 27 | 34 |
| | Total | 18 | 42 | 60 |

Note. MDRS: xxxxxx MCI: Mild Cognitive Impairment. NA: Normal Aging.

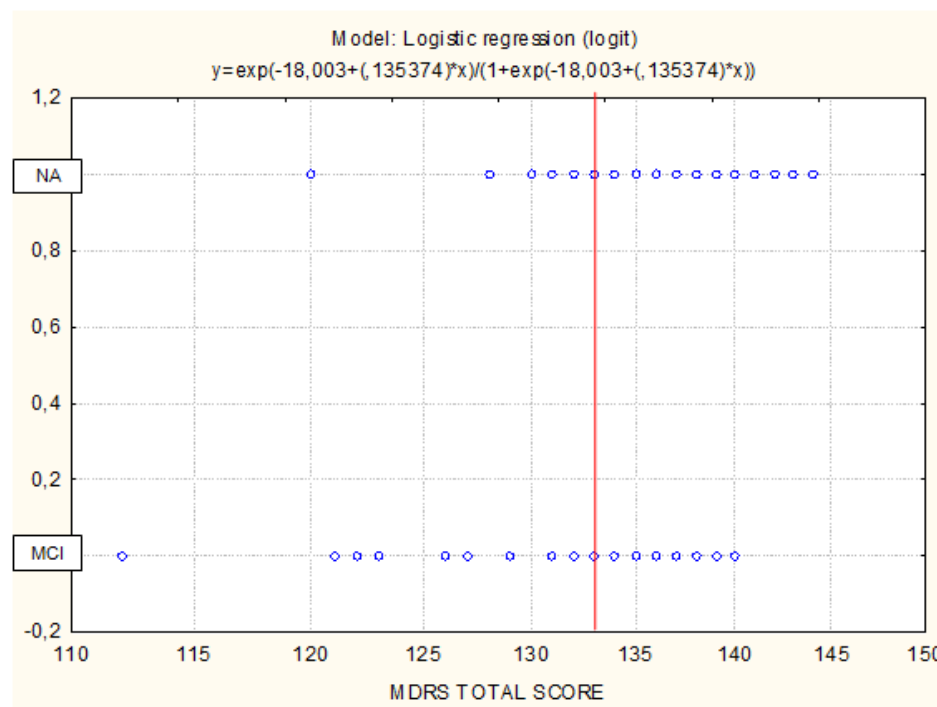


Figure 2. Logistic regression model. The red line sets the 133 points cutoff. Blue dots could represent more than one case simultaneously.

Statistical Analysis

In order to test out the differences between the groups a T-test was performed for each test employed. T-tests were also performed for the MDRS total score and subscales, to check if they differentiate both groups. To get the MDRS cutoff score for MCI detection, a logistic regression analysis was performed (see Wright, 1998) using the MDRS total score as the predictor variable and the group (NA or MCI) as the criterion variable. All the processes were conducted using the statistical software Statistica 7.0.

Results

Regarding the mean comparison, most tests show significant differences between the groups, except for the Clock Test and the Letter-Number Sequencing WAIS-III subtest. The MDRS total score showed differences between the groups, but only the Attention and Conceptualization subscales did so. The effect size was calculated through the Cohen's statistic, getting a value of 0.779, meanwhile, the power ($\beta-1$) was 0.852. All the mean comparisons results are shown in Table 2.

Regarding the logistic regression, the results are presented according to the suggestions of Wright (1998). The cutoff score considered by the model in order to classify the participants into NA or MCI was 133 points for the MDRS total score. The deviance (-2LL) was 73.79, while the likelihood ratio was $G=8.316$ ($p=.003$), calculated through Chi-square test.

As it can be seen in graphic 2, with a 133 points cutoff, a large number of MCI participants have similar punctuations as those classified as NA.

Table 3 shows the participants classification according to the model obtained through statistical analysis. Those values indicate that the Diagnostic Accuracy was 63%, with a Sensibility of 42% and a Specificity of 79%, having 7 false positives and 15 false negatives which add to a total of 22 cases misclassified. The Positive Predictive Value was 61% while the Negative Predictive Value was 64%.

Discussion

From the results obtained, we can confirm that the groups differ from one another, and those differences can be detected with neuropsychological tests. In our sample, most tests differentiate both groups significantly, except two (Clock Test, Letter-Number Sequencing-WAIS-III). Is relevant to note the large differences returned by the tests with limited time (Semantic and Phonological Verbal Fluency, TMT, Symbol Search-WAIS III), which can be interpreted as indicating a slower cognitive processing in the MCI group. There is also an important difference observed in both Verbal Fluency Tests, which have shown a good capability of detecting mild cognitive impairment (e.g. Nutter-Upham, Saykin, Rabin, Roth, Wishart, et al., 2008; Figueredo Balthazar, Cendes & Damasceno, 2007).

The MDRS total score also shown those differences, coincidentally with numerous studies mentioned above (Ivanou et al., 2005; Wang et al., 2005; Griffin et al., 2006; La Voie & Faulkner, 2008; Matteau et al., 2008). Regarding the subscales, only Attention and Conceptualization differentiate between NA and MCI. Those scales had been reported to be sensitive (La Voie & Faulkner; Matteau et al., 2011), however the MDRS subscales that usually show a higher power to differentiate those groups are Memory and Initiation-Perseveration (Ivanou et al., Griffin et al., Matteau et al., 2008). One possible explanation for this discordance is that in our sample, the Memory subscale did not show correlation with the RAVLT (RAVLT summation $r=.164$ $p=.208$, RAVLT deferred $r=.118$ $p=.367$) nor with any of the test employed, which could imply that the Memory subscale evaluates different aspects from those assessed by the RAVLT. In that way, Marson, Dymek, Duke, & Harrell (1997) found an important correlation between the MDRS Memory subscale and the Verbal Memory subtest of the WAIS III, both being oriented to assess the short term memory through evocation of sentences and recognition of figures, which evidently differ from learning a list of unrelated words and evaluating its long term recall as in the RAVLT. Meanwhile, the Initiation-Perseveration subscale showed significant correlations with the verbal fluency tests both semantic ($r=.272$ $p=.035$) and phonologic ($r=.268$ $p=.038$), in accordance with the results obtained by Marson et al., it also correlated significantly with the Letter-Number Sequencing WAIS-III subtest ($r=.254$ $p=.050$). Then, one could expect significant results in the Initiation-Perseveration subscale; however, it is important to take into account that this subscale has an important graphic component, which is an aspect that has not been deeply evaluated in this study. Finally, there is no study about the Construction subscale that reports differences between NA and MCI by its score, probably due to its narrow punctuation margin (0 to 6 points).

Regarding the MDRS capability to classify the participants as NA or MCI, the regression model determined a cutoff of 133 points. However, the diagnostic accuracy resulted moderated (63%), with an also moderated specificity (79%) and a low sensibility (42%). The found cutoff coincides with the one proposed by Green, Woodard & Green (1995) but the diagnostic accuracy is considerably different, a fact that may be explained by the limitations of their study (mentioned above). In regard to the studies of Villeneuve et al. (2011) and Matteau et al. (2012), it is difficult to perform comparisons because they examined the MCI associated with specific pathologies. Nonetheless, in accordance to Turner & Hinson (2013) we observed that the 138 score obtained by Villeneuve et al. corresponds to a cross-sectional age and education- corrected scale score equivalent to the 37th percentile, getting results that might not be acceptable for clinical practice. In fact, when they employed the Robust Age and Education Corrected Scale (RAECSS) Pedraza et al., 2010) the classification accuracy falls from 0.86 to 0.75 and the sensitivity from 0.72 to 0.50. The same situation can be observed in Matteau et al. (2012), who also proposed a cutoff of 138 points, but showed an important decrease on specificity and sensitivity when they employed the RAECSS. Anyway, if we look at the results that Matteau et al. (2012) highlighted, and contrary to their conclusions, the specificity obtained with their cross-sectional data (0.54) cannot be considered good enough to recommend the use of the MDRS in order to detect MCI in PD.

Even though Matteau et al. (2012) reported a higher diagnostic accuracy (82%) and an also higher sensitivity (0.86), the relation between sensitivity and specificity is not so different from the one we found in this study. We proposed a cutoff of 133 points with a low sensitivity (0.42) and a moderate specificity (0.79) while they proposed a cutoff score of 138 with a moderate sensitivity (0.80) and a low specificity (0.54). Therefore, we decided to evaluate the 138 cutoff in our sample. The result was a sensitivity of 0.73 and a specificity of 0.53. Those findings make the similarities in the results of both studies more evident.

At this point, it is important to make some considerations: On one hand, the significant results from the mean comparison showed that there is a real difference between NA and MCI groups for the MDRS total score. Also, taking into account the size effect of that comparison, we can say that the observed difference is substantial. But, according to Cohen (1988) this size effect implies that only approximately a 45% of the individual cases from both groups are not overlapping. This last observation means that there are about a 65% of cases actually overlapping, which becomes evident when looking at the logistic regression graphic (see figure 2). In other words, the distribution of the groups with respect to the MDRS cutoff score are so overlapped that it is not useful to know the individual score in order to distinguish them.

The poor classification capability found through the MDRS score, could be due to several reasons. On one hand, in the NA group the arith-

metic mean was 136 (SD = 5.05), the arithmetic median was 138 and the arithmetic mode was 140 points, which could be indicating a "ceiling effect" that masks the actual differences between the groups. On the other hand, even when the MDRS has been shown to be useful for several areas and pathologies, it is a screening test originally designed to assess dementia, which is characterized for showing notable differences in comparison with normal aging subjects. That implies this test may not have the capability to detect the subtle changes that characterized MCI and differentiates it from normal aging.

From these results we can conclude that, even when the MDRS can differentiate between NA and MCI when it is included in a neuropsychological battery, its diagnostic accuracy, together with its sensitivity and specificity, are not high enough to make this test recommendable in order to detect MCI in the clinical practice. Therefore, it is extremely important to develop screening tests specifically designed for mild cognitive impairment, in order to provide a useful tool for its detection.

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Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article. Universidad Católica de Córdoba did not have intervention in the study design, collection, analysis and interpretation of data, nor in the drafting of the report, or the submission of this paper for publication.

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