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Screening for Mild Cognitive Impairment Using the Dementia Rating Scale-2

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Abstract

This study examined the sensitivity and specificity of the Dementia Rating Scale-2 (DRS-2) to distinguish individuals with mild cognitive impairment (MCI) from both patients with Alzheimer's disease (AD) and healthy controls (HCs). A total of 50 HCs, 98 patients with MCI, and 49 patients with AD completed a neurological examination and battery of neuropsychological tests that included the DRS-2. Across almost all subscales of the DRS-2, patients with AD scored significantly worse than patients with MCI who in turn performed more poorly than the HCs. The only exception was the construction subscale where no significant difference was found between patients with MCI and the HCs. At a cutoff of 136, the sensitivity was 71% and specificity was 86% for distinguishing between patients with MCI and the HCs. Sensitivity was 82% and specificity was 78% for distinguishing between patients with MCI and patients with AD (cutoff score <124). For distinguishing between patients (with MCI and AD) and the HCs, sensitivity was 81% and specificity was 86% at a cutoff of 136. Our findings suggest the DRS-2 is a brief, easily administered cognitive test that appears to be useful in assisting with the detection of MCI.

Keywords

dementia, mild cognitive impairment, Alzheimer's disease, cognition, screening instruments

Mild cognitive impairment (MCI) is considered to be an intermediate state between normal aging and dementia, and those with MCI diagnoses have an increased risk of developing dementia compared to the general population.[1] It is becoming increasingly important to identify individuals with MCI, particularly as new treatment strategies for cognitive impairment are being identified and tested. A thorough neuropsychological and neurological assessment is often considered to be the gold standard for detecting cognitive impairment, but in some settings the administration of a thorough battery of tests may not be feasible. For example, patients may refuse additional workup or may lack access to specialists for financial reasons or because they live in rural areas, and being able to quickly and easily identify patients with cognitive impairments in these situations is important. In addition, brief cognitive screening measures are useful in research settings to quickly screen potential participants for clinical studies.

The Dementia Rating Scale-2 (DRS-2)[2] is a widely used cognitive screening test initially developed for assessment and follow-up of older adults with cognitive impairment. It consists of 5 subscales—attention, initiation/perseveration, construction, conceptualization, and memory, with lower scores indicating greater cognitive impairment (maximum score = 144). Administration of the DRS-2 takes as little as 10 to 15 minutes in cognitively healthy older adults and ranges up to 30 to 45 minutes in individuals with severe cognitive impairments. Several studies have supported the use of the DRS-2 to distinguish between individuals with dementia and cognitively healthy older adults.[3,4]

Fewer studies, however, have examined the ability of the DRS-2 to accurately identify patients with MCI. In an analysis designed to examine the ability of DRS-2 to distinguish between patients with mild cognitive impairment in Parkinson's disease (MCI-PD) and healthy controls (HCs), a normality cutoff of >140 was recommended (86% sensitivity, 54% specificity, and area under the curve [AUC] = 0.82).[5] This cutoff is similar to the cutoff proposed by Villeneuve and colleagues[6] who found a normality cutoff of >138 to have 72% sensitivity and 86% specificity in distinguishing patients with MCI-PD from patients with cognitively normal PD. Additionally, in a mixed sample of patients with amnestic MCI (aMCI) and patients with MCI-PD, Matteau et al[7] found a normality

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cutoff of >139 to have 80% sensitivity and 68% specificity in differentiating this mixed MCI group from healthy controls (AUC = 0.81).

Although these studies on PD suggest that DRS-2 may be useful in distinguishing individuals with MCI from HCs, only 1 study has examined this instrument within a sample of patients with primary memory disorder. In a small study of 28 HCs and 21 patients with aMCI included in a research database, Matteau et al[8] found a normality cutoff of >138 to be optimal in distinguishing the 2 groups (sensitivity = 0.71, specificity = 0.68, and AUC = 0.78). However, this study was limited by its small sample size and relatively incomplete description of participants.

The purpose of this study was to examine the performance of 3 groups—cognitively healthy older adults, individuals with MCI, and those with mild Alzheimer's disease (AD)—on the DRS-2 and its subscales. We sought to examine the sensitivity and specificity of the DRS-2 in distinguishing MCI from healthy aging as well as from AD.

Methods

Participants were 197 older adults aged 55 to 85 residing in the community and participating in an institutional review board–approved research study examining telephone-administered cognitive tests. In all, 98 of these individuals were diagnosed with MCI, 49 with possible/probable mild AD, and 50 were HCs. Patients with MCI and AD were recruited from a memory disorders center, and HCs were recruited through community advertising and solicitation of family members of memory clinic patients.

Patients were required to have an informant with whom they had at least 10 hours of contact per week, be taking stable doses (4 weeks) of dementia medications and/or antidepressants, completed neuroimaging to rule out structural changes that could be causing cognitive symptoms, and Hachinski scores <4 to rule out significant cerebrovascular disease.[9] Patients could not show evidence of current clinical depression (defined by a Cornell Scale for Depression in Dementia [CSDD][10] ≥8 or a current diagnosis of major depression), nor could they show a history of other neurologic or developmental disorders that could impact cognition.

Participants with MCI were required to have a memory complaint, objective memory loss (defined as scores falling at least 1.5 standard deviations below the age-adjusted mean on any aspect of the Hopkins Verbal Learning Test [HVLT]–Revised[11]), Clinical Dementia Rating Scale (CDR)[12] score of 0.5, and largely preserved activities of daily living. Participants with AD were required to have a CDR of 0.5 or 1.0 and meet National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association diagnostic criteria for possible or probable AD. Patient classifications were established through consensus conference with neuropsychologists, neurologists, and neuropathologists. All data available from patients' medical record, as well as measures from this study, were used to assign a diagnosis. Although the DRS-2 was included in the larger neuropsychological test battery used to guide the overall diagnostic process, determination of MCI versus AD status was primarily driven by the CDR and report of functional independence (eg, ability to manage medications and finances or drive).

To qualify as HCs, participants were required to have a Mini-Mental Status Examination (MMSE[13]) score within the normal range for their age and educational attainment,[14] no history of neurologic or developmental disorders that could impact cognition, no evidence of current depression, and no cognitive complaints. Controls were not required to have informants.

Procedure

After obtaining informed consent, all participants completed an office visit that included meeting with a neurologist to complete a neurological examination, CDR, MMSE, and CSDD as well as with a neuropsychologist or trained research assistant to complete a battery of cognitive tests, including the DRS-2. The complete neuropsychological evaluation was comprised of the American National Adult Reading Test,[15] Boston Naming Test,[16] Category Fluency (Animals), DRS-2,[2] HVLT-Revised,[11] Judgment of Line Orientation,[17] Rey-Osterrieth Complex Figure (copy condition, Boston Qualitative Scoring System[18]), Trail Making Test,[19] and Wechsler Adult Intelligence Scale–III Digit Symbol subtest.[20] Informants also completed the Lawton-Brody Activities of Daily Living Scale[21] for patients with MCI and AD.

Statistical Analyses

Analysis of variance was used to determine overall group differences in demographic characteristics and performance on the DRS-2. For 2-class diagnostic testing (eg, HC vs MCI), the receiver–operator characteristic (ROC) curves were used to evaluate overall classification accuracy. In this situation, the AUC within a unit square corresponds to the probability that 2 study participants, each one randomly drawn from the HC and MCI groups, will be correctly ordered in terms of their DRS-2 total scores (MCI < HC). Because the probability of obtaining such a correct ordering is 1/2 under the null hypothesis (no association between DRS-2 scores and cognitive impairment), AUC values greater than 0.50 are suggestive of marker informativeness and AUC values of 1.00 correspond to perfect classification.

For 3-class diagnostic tests, the extension of ROC methodology to 3 classes leads to volume under the surface (VUS) within a unit cube as the metric of classification accuracy.[22] This value corresponds to the probability that 3 participants, each one randomly drawn from the AD, MCI, and HC groups, will be correctly ordered in terms of their DRS-2 total score (AD < MCI < HC). Because the probability of obtaining such a correct ordering is 1/6 under the null hypothesis, VUS values above 0.17 are suggestive of marker informativeness and VUS values of 1.00 correspond to perfect discrimination.

Table 1. Demographic Characteristics.[a]

	HC, M (SD)	MCI, M (SD)	AD, M (SD)
Age[b]	70.28 (7.88)[c]	72.94 (6.76)[d]	73.92 (7.29)[d]
Education[e]	15.16 (2.57)[c]	13.31 (3.00)[d]	12.53 (2.93)[d]
% Female	72	57	57
% Caucasian	100	98	94

Abbreviations: AD, Alzheimer's disease; HC, healthy control; M, mean; MCI, mild cognitive impairment; SD, standard deviation.
[a] Means sharing the same superscript letters are not significantly different from each other.
[b] HC < MCI = AD, $P < .05$.
[e] HC > MCI = AD, $P < .001$.

Additionally, we used ordinal logistic regression to generate predicted probabilities for DRS-2 total scores using age and education as covariates. We then regenerated covariate-specific ROC curves to examine whether sensitivity or specificity improved after controlling for these demographic factors.

Finally, test informativeness was evaluated by calculating likelihood ratios (LRs) at specific DRS total score cutoffs. The positive LR (LR+) measures how much more likely a person with the disease is to score positive on a test compared to a person without the disease; it equals sensitivity/(1 − specificity), that is, true positives over false positives. The negative LR (LR−) measures how much more likely a person with the disease is to score negative on a test compared to a person without the disease; it equals (1 − sensitivity)/specificity, that is, false negatives over true negatives. Informative tests have LR+ above unity and LR− lower than unity. An advantage of LR-based measures over positive and negative predictive values is that they do not depend on disease prevalence and, hence, represent a yardstick that is equally valid for measuring test performance in a variety of settings. In contrast, predictive value calculations involve the prior odds of disease as well as the 2 LRs and can yield very different conclusions regarding test informativeness when applied to a family practice setting versus a specialist clinic at the hospital.[23]

Results

Group Differences

Demographic information for the 3 groups can be seen in Table 1. The HCs were significantly younger and had more education than participants with MCI and AD who did not differ from each other. Across all neuropsychological tests (Table 2), HCs significantly outperformed participants with MCI who in turn outperformed participants with AD. On the DRS-2, HCs performed significantly better than the MCI group on all subscales with the exception of construction subscale. Patients with AD performed significantly poorer than both HC and patients with MCI across all subtests (see Table 3). Group differences on the DRS-2 remained significant even after controlling for age and education, with the exception of the conceptualization subscale where the group difference between HCs and MCI groups was no longer significant ($P = .08$).

Table 2. Neuropsychological Test Scores for Each Group.[a]

	HC, M (SD)	MCI, M (SD)	AD, M (SD)
CDR	—	.50 (.00)	.85 (.23)
MMSE	29.40 (.83)	26.76 (2.55)	23.13 (2.57)
Digit Symbol Raw	60.54 (15.86)	42.97 (14.62)	24.71 (13.33)
Trails A, seconds	33.23 (12.81)	47.14 (20.62)	86.02 (52.42)
Trails B, seconds	84.69 (33.44)	158.11 (83.07)	274.73 (53.35)
Verbal Fluency–FAS	45.96 (16.57)	31.11 (11.33)	24.74 (9.86)
Verbal Fluency–Animals	19.82 (6.50)	13.34 (4.71)	9.31 (2.89)
Boston Naming Test	55.64 (3.40)	48.68 (8.54)	40.78 (11.48)
HVLT Total Learning	24.72 (4.41)	15.84 (4.98)	11.71 (3.25)
HVLT Delayed Recall	8.90 (2.47)	1.91 (2.23)	.60 (1.33)
ROCF Raw	16.90 (2.20)	15.49 (2.64)	12.35 (3.90)
ROCF Organization	5.50 (1.47)	4.48 (1.58)	3.63 (1.58)

Abbreviations: AD, Alzheimer's disease; CDR, Clinical Dementia Rating Scale; HC, healthy control; HVLT, Hopkins Verbal Learning Test; M, mean; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; ROCF, Rey-Osterrieth Complex Figure; SD, standard deviation.
[a] $P < .001$ for all post hoc group comparisons with the exception of the Trails A and ROCF copy comparisons between HC and MCI as well as the ROCF organization and FAS comparisons between MCI and AD (all Ps < .01).

Receiver–Operator Characteristics

The Youden index approach,[24] which maximizes the sum of correct classification probabilities to estimate optimal cutoff scores in our 3-class classification problem, suggested that individuals scoring above 136 on the DRS-2 be characterized as HCs (ie, a normality cutoff of >136) and those scoring below 123 be characterized as AD (ie, an AD cutoff of <123), with those scoring 123 to 136 inclusive characterized as MCI. This choice of total score cutoffs resulted in 76% of individuals with AD, 54% of individuals with MCI, and 86% of HCs being correctly classified. Overall classification accuracy was measured using the VUS criterion. Bootstrap simulation with 1000 replications and ties between observations broken at random produced a VUS estimate of 0.743, indicating the DRS-2 total score will correctly order randomly drawn triplets of participants with AD, MCI, and HCs almost 4.5 times more often than expected under the null hypothesis.

Although these cutoffs were derived in the context of a 3-class classification problem, we wanted to evaluate their performance in a 2-class setting as well, that is, comparing pairs of diagnostic classes against each other, with the remaining class excluded as a possible outcome.

The DRS-2 showed strong discriminatory power in distinguishing between HCs and participants with MCI, with an AUC of 0.87 (95% confidence interval [CI] = 0.82-0.93, $P < .001$). The 2-class Youden index was maximized at the same normality cutoff of >136 for which sensitivity was 71% and specificity was 86%, that is, LR+ = 5.07 and LR− = 0.34.

The DRS-2 also showed good ability to distinguish between participants with MCI and participants with AD, with an AUC of 0.87 (95% CI = 0.81-0.93, $P < .001$). With AD status as the disease state of interest, the 2-class Youden index was maximized at a slightly higher AD cutoff of <124 for which

Table 3. DRS-2 Scores for Each Group.[a]

	HC, M (SD)	MCI, M (SD)	AD, M (SD)	Cohen Effect Size (*d*)		
				HC-MCI	HC-AD	MCI-AD
Attention	36.52 (0.68)[b]	35.66 (1.35)[c]	34.29 (1.93)[d]	0.80	1.54	0.82
Initiation/Perseveration	36.30 (1.80)[b]	33.58 (4.48)[c]	28.55 (6.13)[d]	0.80	1.72	0.94
Construction	5.88 (0.48)[b]	5.81 (0.55)[c]	5.29 (1.12)[d]	0.14	0.68	0.59
Conceptualization	36.98 (2.41)[b]	35.64 (3.24)[c]	33.27 (3.85)[d]	0.47	1.16	0.67
Memory	23.98 (1.22)[b]	19.81 (3.39)[c]	15.02 (2.75)[d]	1.64	4.21	1.55
Total score	139.68 (3.32)[b]	130.67 (7.95)[c]	116.45 (9.34)[d]	1.48	3.31	1.64

Abbreviations: AD, Alzheimer's disease; HC, healthy control; M, mean; MCI, mild cognitive impairment; SD, standard deviation.
[a] Means sharing the same superscript letters are not significantly different from each other. $P \leq .001$ for all post hoc group comparisons with the exception of the construction comparison between HC and MCI (ns) and the conceptualization comparison between HC and MCI ($P < .05$). Cohen effect sizes are based on the pooled SD across all 3 groups.

sensitivity was 82% and specificity was 78%, that is, LR+ = 3.73 and LR− = 0.23.

Finally, an ROC analysis to examine the ability of the DRS-2 to distinguish between patient (either MCI or AD) and HC groups showed an AUC of 0.91 (95% CI = 0.87-0.95, $P < .001$). The 2-class Youden index was maximized at the same normality cutoff of >136, yielding sensitivity of 81% and specificity of 86%, that is, LR+ = 5.79 and LR− = 0.22.

Because significant differences in age and education were found between diagnostic groups, we reanalyzed data controlling for these variables in the ROC analyses and found only minimal changes in sensitivity and specificity. For example, sensitivity increased by 7% and specificity decreased by 3% in the distinction between HCs and MCI. As a result, we chose to present cutoff scores without age and education corrections in order to optimize ease of interpretation and use of cutoff scores.

Discussion

Overall, the results from this study suggest the DRS-2, a relatively brief cognitive screening instrument, is able to discriminate individuals with MCI from both HCs and those with AD. The HCs outperformed participants with MCI on all DRS-2 subscales except for construction subscale, and individuals with AD performed significantly worse than HC and MCI groups on all subscales.

The main goal of this study was to examine whether the DRS-2 could be utilized in screening for individuals with MCI who are at greater risk for the development of dementia than the general population. Although different sensitivity/specificity trade-offs were identified, sensitivity at the recommended normality cutoff of >136 for distinguishing the patient group (combined MCI and AD) from HCs was 81% and specificity was 86%. When the patient group was comprised only of patients with MCI, specificity remained the same by definition but sensitivity decreased to 71%. This decrease in sensitivity is to be expected, given that making the distinction between normal aging and MCI can be difficult even in an office setting following a thorough evaluation. Furthermore, our suggested cutoff score is comparable to the normality cutoff of 138 suggested by Matteau et al[8] in the only other study examining this issue within a population with primary memory disorders. Use of their suggested 138 cutoff in our sample resulted in a 16% increase in sensitivity but an 18% decrease in specificity compared to the values obtained using a normality cutoff of >136. The slight difference in suggested cutoff score between these 2 studies may be related to small differences in participant demographics and differences in the test batteries used to diagnose patients. The narrow range of scores allowed, particularly to be classified as normal, should be noted. Given the ease of items on the DRS-2, more than a small number of errors is potentially a cause for concern and suggests additional workup may be warranted. Additionally, we were able to replicate previous studies[3,4] demonstrating the ability of DRS-2 to accurately distinguish individuals with AD from individuals without dementia using a cutoff of 123.

Our obtained sensitivities and specificities for the MCI/HC distinction using the DRS-2 compare favorably with those obtained using other brief cognitive screening measures. For example, Benson et al[25] found the MMSE to have 57% sensitivity and 72% specificity in distinguishing patients with aMCI from healthy controls, and Abreu et al[26] found sensitivity and specificity values of 74% and 62%, respectively. Studies on the Montreal Cognitive Assessment,[27] a brief screening measure developed to address some of the MMSE's limitations, in screening for MCI have been more variable; although some researchers have found good sensitivity and specificity (90% and 87%, respectively),[27] other groups have shown poor specificity, ranging from 50% to 52%, particularly when MCI groups are comprised of non-aMCI patients.[28,29] Furthermore, the DRS-2 cutoffs displayed in Tables 4 to 6 could be adjusted to gain increased sensitivity or specificity based on the situation; for example, in clinical screening situations, one may want to reduce the risk of obtaining a false negative and adjust the suggested cutoff score accordingly.

This study has several limitations, including the use of self-report to classify controls as having no memory complaint without confirmation from an informant. Given the previous studies demonstrating that some individuals with MCI lack awareness of their cognitive deficits,[30,31] it is possible that some individuals with cognitive impairment were included in

Table 4. Sensitivity and Specificity of Select DRS-2 Total Score Cutoffs to Separate Participants With MCI From HC.[a]

Normality Cutoff >	Sensitivity	Specificity
132	0.54	0.96
133	0.58	0.96
134	0.60	0.92
135	0.66	0.90
136	**0.71**	**0.86**
137	0.79	0.78
138	0.87	0.68
139	0.93	0.60
140	0.94	0.50

Abbreviations: DRS-2, Dementia Rating Scale-2; HC, healthy control; MCI, mild cognitive impairment.
[a] Any score less than or equal to the cutoff is considered indicative of MCI.

Table 5. Sensitivity and Specificity of Select DRS-2 Total Score Cutoffs to Separate Participants With MCI From Participants With AD.[a]

AD Cutoff <	Sensitivity	Specificity
120	0.63	0.91
121	0.65	0.89
122	0.71	0.86
123	0.76	0.84
124	**0.78**	**0.83**
125	0.80	0.79
126	0.82	0.78
127	0.86	0.74
128	0.88	0.71
129	0.88	0.68
130	0.92	0.62

Abbreviations: AD, Alzheimer's disease; DRS-2, Dementia Rating Scale-2; HC, healthy control; MCI, mild cognitive impairment.
[a] Any score greater or equal to the cutoff is considered indicative of MCI.

Table 6. Sensitivity and Specificity of Select DRS-2 Total Score Cutoffs to Separate Participants With Cognitive Impairment (AD or MCI) From HC.[a]

Normality Cutoff >	Sensitivity	Specificity
132	0.68	0.96
133	0.71	0.96
134	0.73	0.92
135	0.77	0.90
136	**0.81**	**0.86**
137	0.86	0.78
138	0.91	0.68
139	0.95	0.60
140	0.96	0.50

Abbreviations: AD, Alzheimer's disease; DRS-2, Dementia Rating Scale-2; HC, healthy control; MCI, mild cognitive impairment.
[a] Any score less than or equal to the cutoff is considered indicative of AD or MCI.

the control group and potentially reduced the between-group differences, leading to decreased specificity. Only individuals with impairments on memory measures were included in the MCI group, so generalizability of findings to individuals with non-aMCI is unknown. In addition, this study is cross-sectional in nature and does not provide any information regarding the ability of DRS-2 to predict cognitive change over time. Although a criticism of the present study might be that the DRS-2 was one of the measures used in establishing diagnosis, it should be emphasized that this measure was not the sole determination of diagnosis. Furthermore, well-established DRS-2 cutoffs for MCI were not available to the consensus team when making their diagnosis, and patients were not selected based on impairment or lack of impairment on the DRS-2. Future studies should attempt to replicate these findings in an independent sample, investigate whether additional brief measures could be added to the DRS-2 to improve sensitivity and specificity, and examine the ability of DRS-2 to predict future cognitive change.

Despite these limitations, our findings suggest the DRS-2 is a brief, easily administered cognitive screening test that appears to be useful in assisting with the detection of MCI. As such, the DRS-2 may be helpful in screening older adults as a first step in identifying individuals who may be eligible for clinical trials and in order to identify individuals who may benefit from a referral for a more comprehensive clinical evaluation of their cognition.

Declaration of Conflicting Interests

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