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Diagnosis and Staging of Mild Cognitive Impairment, using a modification of the Clinical Dementia Rating Scale: the mCDR

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Abstract

Objective—To examine reliability and validity of the mCDR, a modified version of the Clinical Dementia Rating (CDR) scale.

Methods—The mCDR is an informant-based, technician-administered, structured interview with multiple choice responses, which does not include objective cognitive testing. Subjects (n=556) with no cognitive impairment (NCI), amnestic mild cognitive impairment (a-MCI), and Dementia were assessed with mCDR, CDR, and neuropsychological evaluation, while medial temporal atrophy (MTA) was measured on MRI scans. The mCDR and CDR were compared with respect to inter-rater reliability, validity, and ability to predict progression in cognitive diagnosis at 12 month follow-up.

Results—The mCDR can be administered in less than a third of the time required to administer the CDR (30 minutes). Inter-rater reliability (Cohen's weighted Kappa) was 0.86 for the mCDR,

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Key Points

- The modified Clinical Dementia Rating scale (mCDR) is an informant-based, technician-administered, structured interview with multiple choice responses.
- Subjects with no cognitive impairment, amnestic mild cognitive impairment, and dementia, were assessed with the mCDR, the CDR, and neuropsychological evaluation, while medial temporal atrophy (MTA) was measured on MRI scans.
- The mCDR, as compared to the CDR, is briefer, more reliable, and a valid measure of functional ability, among subjects with normal cognition, mild cognitive impairment and mild dementia.

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and 0.56 for the CDR. Ability to distinguish between NCI, a-MCI, and Dementia subjects, and correlations to memory and non-memory measures were marginally better for the CDR, in comparison to the mCDR. Correlations of mCDR and CDR scores to MTA scores did not differ. Baseline mCDR scores predicted transition from NCI to aMCI, whereas baseline CDR scores predicted transition from aMCI to Dementia.

Conclusions—The mCDR, as compared to the CDR, is briefer, more reliable, and a valid measure of functional ability, among subjects with normal cognition, mild cognitive impairment, and mild dementia. The mCDR should be particularly useful as a reliable and economical instrument for assessing change in functional abilities, especially in multi-center clinical trials and population studies of MCI and mild dementia.

Keywords

Dementia; Clinical Rating Scale; Mild Cognitive Impairment; Visual Rating; MRI

Introduction

The Clinical Dementia Rating (CDR) Scale (Morris, 1993; McCulla *et al.*, 1989; Morris, 1997; Fillenbaum *et al.*, 1977) that was developed to standardize staging of Alzheimer's disease (AD) and related disorders, is widely used in dementia research, epidemiological studies, and clinical trials (Petersen, 2000; Hanninen *et al.*, 2002; Li *et al.*, 2006) The CDR, which typically takes about 30 minutes to administer, was designed to be used primarily by experienced clinicians, to assist in the diagnosis and staging of functional severity in dementia. The CDR has also been used to diagnose mild cognitive impairment (MCI) and distinguish it from normal aging and dementia. Although the CDR is frequently used in multi-site research studies and has been found to have adequate reliability (e.g., Cohen's weighted Kappa =0.66) in normal and dementia cases, its reliability has been found to be suboptimal (Cohen's weighted Kappa =0.33) in very mild dementia cases (Rockwood *et al.*, 2000; Schafer *et al.*, 2004).

Currently, the earliest stages of Alzheimer's disease and other dementing disorders are being targeted for intervention, when treatments and secondary preventive measures are most likely to be effective (Fleisher et al., 2008). Instruments that are sensitive, reliable, valid, and brief are needed for measuring subtle functional deficits that occur during the earliest stages of dementia, and for studying the impact of interventions. Scoring the CDR requires reconciliation of information gleaned from an open-ended informant interview, with results of an objective cognitive assessment of the patient. However, objective cognitive scores and informant-based history may provide discrepant perspectives of the same subject, and guidelines have not been developed for performing this reconciliation in a consistent and reliable way, especially in cases of MCI and very mild dementia.

We have developed a modification of the CDR (mCDR), which uses a structured and focused informant interview that explores subtle changes in function, in the same six functional domains as the CDR. Unlike the open-ended response format of the CDR, the mCDR interview uses a multiple-choice response format, with each response reflecting severity of decline in functional ability from the subject's optimal level of functioning. Objective cognitive testing is not included in the mCDR, obviating the need to combine and reconcile a clinical impression from the informant interview with results of objective cognitive testing, to score each mCDR domain.

In this study, we evaluated performance of the mCDR and CDR and compared: (1) inter-rater reliabilities; (2) time required to administer each test; (3) ability to differentiate between subjects with normal cognition, amnestic MCI and dementia; (4) relationships to

neuropsychological test scores; (5) relationship to medial temporal atrophy (MTA) scores evaluated on brain MRI scans; (6) ability to predict cognitive change from baseline scores.

Methods

Subjects

Evaluations were completed for 556 participants enrolled in the Florida Alzheimer's Disease Research Center Clinical Core (FADRC-CC), who were at least 65 years of age, had six or more years of education, and a reliable informant who could provide a detailed history. These individuals were recruited from numerous sources such as community advertisements, free memory disorders screenings, and outpatient memory disorders clinics. Primary targets of recruitment were subjects with normal cognition and MCI, although those with mild dementia (MMSE> 20; Perneczky, Wagenpfeil, et al., 2006) were also enrolled. Subjects were evaluated with all measures of the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS; Beekly et al., 2007), which includes questionnaires assessing demographic information, risk factors for cognitive impairment, medical history, neurological and psychiatric history. Other measures used were standardized clinical rating scales including the CDR, neuropsychological tests, standardized consensus diagnosis procedure, and a diagnostic classification scheme. Measures included the mCDR interview (described below), and additional neuropsychological tests assessing memory, language, visuospatial skills and executive function, and standard laboratory tests used in the work-up of dementia. All patients received MRI brain scans that included a 3-D, inversion recovery acquisition sequence in the coronal plane.

Clinical Dementia Rating (CDR) Scale

The CDR was scored for each subject on the basis of a detailed history and clinical examination by a physician who was certified in administering the test. The physician was provided with MMSE scores and subscores for each subject, but not results of neuropsychological evaluations. Scoring of the CDR requires integration of the informant report with the results of objective cognitive performance (the MMSE), according to judgment of the examiner. The CDR has six domains (memory, orientation, judgment and problem-solving, home and hobbies, community affairs and personal care). Each domain is scored as follows: “0” (no impairment), “0.5” (questionable impairment), “1” (mild impairment), “2” (moderate impairment) and “3” (severe impairment). Scores for each of the six “box scores” are summed to provide a total box score (CDR-SB), as well as a global CDR scale, based on the standard CDR protocol (Morris, 1993).

Modified Clinical Dementia Rating Scale (mCDR)

The mCDR is a questionnaire that is administered as a structured interview to informants by a psychometrist or a nurse. In this study, the psychometrist was blind to clinical information about the subject. Each of the six domains of the mCDR, which are the same domains as those in the CDR, is assessed by six questions, prefaced as follows: “Compared to his/her best performance in adult life, provide one of the following answers describing his/her current performance: 0= no change; 0.5= questionably worse; 1.0 = worse (but not requiring assistance); 2 = much worse (requiring assistance) and 99= Not applicable.” The sum of scores for the six questions in each domain provides the total domain score, and the sum of scores for the six domain scores provides the mCDR summed score (mCDR-SS).

Neuropsychological Measures and Diagnosis

Each subject in the study was administered a neuropsychological test battery in his/her native language (English or Spanish). The following neuropsychological tests were used: (1)

Memory: Total Recall of the Three-Trial Fuld Object Memory Evaluation (OME; Fuld, 1981; Loewenstein *et al.*, 2001), and Delayed Visual Reproduction of the Wechsler Memory Scale (Wechsler, 1987); (2) Language: Controlled Oral Word Association Test (Benton and Hamsher, 1989), and Category Fluency Test (Monsch *et al.*, 1992); (3) Visuospatial Skills: Block Design WAIS-III (Wechsler, 1997); (4) Problem-Solving/Executive Function: Trails B (Spreen and Strauss, 1998), and Similarities WAIS-III (Wechsler, 1997). Neuropsychological classification was achieved utilizing methods previously described (Loewenstein *et al.*, 2006), and cognitive subgroups were determined as follows: (a) amnestic MCI: subject had one or more memory tests scores that were 1.5 Standard Deviation (SD) or greater below expected normative values, and all non-memory tests were within normal limits; (b) non-amnestic MCI: all memory measures were less than 1.5 SD below expected normative values, but one or more non-memory measures were 1.5 SD or more below expected values; (c) multiple-domain MCI: one or more memory tests scores were 1.5 SD or more below expected normative values, and one or more non-memory tests scores were 1.5 SD or below expected values; amnestic and multiple domain-MCI groups with an amnestic component were combined to form one amnestic MCI group; (d) mild dementia: subject had one memory and at least one non-memory domain score 2.0 SD or more below expected normative values; (e) No Cognitive Impairment: majority of memory and non-memory tests were no more than 1.0 SD below expected levels, with no tests scoring 1.5 SD below normative values.

MRI Procedures

Brain MRI scans were obtained with a 1.5 Tesla MRI (Siemens, Symphony) using proprietary 3-D MP-RAGE protocol, or with a 3.0 Tesla (General Electric, Signa HDX)) using 3-D FSPGR protocol. MRI scans were acquired in the coronal plane, and contiguous slices with thickness at 1.5 mm or less were reconstructed perpendicular to the AC-PC line.

Visual Rating System (VRS)

Atrophy ratings were performed for hippocampus (HPC), entorhinal cortex (ERC) and perirhinal cortex (PRC) on a single coronal slice intersecting the mammillary bodies. An in-house visual rating system (VRS) provided drop-down reference images that delineate the outline of each anatomical region of interest, and provide exemplars for five degrees of atrophy (0-4 scale) in each structure. Total medial temporal atrophy (MTA) scores were calculated for the left (LMTA) and right hemisphere (RMTA) by summing HPC, ERC and PRC atrophy scores. High inter-rater and intra-rater reliability, and correlation of VRS scores to cognitive status in elderly subjects has been reported previously (Urs et al., 2008; Duara et al., 2008).

Longitudinal Evaluation Procedures

Data from annual re-evaluations including all initial evaluation procedures, except MRI brain scans and blood tests, were used for the consensus follow-up diagnoses. A total of 232 subjects were re-evaluated and re-diagnosed at the scheduled one year follow-up evaluation. Retention rate for follow-up after Year 1 was 91%.

Statistical Analyses

Inter-rater and intra-rater reliability was assessed using Cohens' weighted Kappas (Cohen and Cohen, 1983). Group comparisons of mCDR-SS and CDR-SB scores were analyzed using a series of one-way analyses of variance (ANOVA). Scheffe' post-hoc procedure was used to examine differences between means; Pearson Product Moment correlation coefficients evaluated strength of relationships between atrophy scores and cognitive measures. Area under the Receiver Operating Characteristics (AUC) was obtained for CDR-

SS, CDR-SB, and CDR-global scores, to evaluate overall strength in distinguishing between diagnostic groups. Sensitivities, specificities and optimal cut-points using the mCDR-SS and CDR-SB for distinguishing between diagnostic groups were obtained from the ROC curves. Probabilities were calculated for no difference between two ROC-AUCs, and between two correlation coefficients (Delong et al., 1988). Hazard ratios for specific predictors (mCDR-SS and CDR-SB) of transition from NCI to MCI, MCI to NCI, and MCI to Probable AD (endpoint), were calculated using a three-state Markov model (Chen *et al.*, 1996) in continuous time. The proportional intensity model was used to analyze effects of covariates on hazard ratios.

Results

Subjects were classified as NCI (n=313), amnestic MCI (n=102), and dementia (n = 141). There were statistically significant differences with respect to age [$F(2,528)= 7.37; p<.002$] between NCI and dementia groups. Post-hoc test using the Scheffe' procedure indicated on average, NCI subjects were younger in comparison to subjects in the dementia group (Table 1). There were statistically significant group differences with respect to educational attainment [$F (2,499)=5.83; p<.009$], with dementia subjects being less well educated than NCI subjects. MMSE scores [$F(2,527)= 203.24; p<.001$] differed among groups, as the post-hoc Scheffe' procedure indicated the dementia group had statistically lower scores, in comparison to subjects in the amnestic MCI group, who in turn had lower scores than subjects in the NCI group.

Inter-rater Reliability for two raters was assessed for the CDR and mCDR in a group of 15 subjects (NCI =5, MCI =5; Dementia =5). Cohen's weighted Kappa was 0.56 (fair agreement) for the CDR, and 0.86 (excellent agreement) for the mCDR. For a group of 10 subjects, the average time taken to administer the CDR was 31 minutes (range: 29 minutes to 34 minutes), and for the mCDR it was 7.4 minutes (range: 5 minutes18 seconds to 9 minutes 45 seconds).

Both mCDR-SS and CDR–SB distinguished NCI from aMCI, and aMCI from dementia (Table 2). Each domain of the mCDR (except for “personal care”) separated the three diagnostic groups. Area under ROC curves (AUC) estimate for mCDR-SS, CDR-SB and CDR global scores were plotted against the following dichotomous diagnostic classifications: amnestic MCI versus normal, dementia versus normal, and dementia versus MCI (Table 3). Probabilities for testing differences between AUCs (mCDR versus CDR) were generally high, especially for the Dementia versus NCI comparison (Table 3). The only statistically significant differences between the CDR-SB and mCDR-SS AUCs were for the Dementia versus NCI contrast.

Associations between mCDR-SS, CDR-SB, specific neuropsychological scores, and measures of medial temporal atrophy (MTA) were calculated (Table 4). CDR-SB and mCDR-SS scores are most highly correlated to the FOME, a measure of episodic memory, followed by the Category Fluency test, a non-amnestic cognitive measure, and MTA scores. Correlation coefficients were highly significant overall; these were higher for Fuld and Category Fluency score for the mCDR-SS while MTA scores were equivalent for CDR-SB and mCDR-SS.

mCDR means, standard deviations, item correlation with mCDR total subscale score, and frequencies of response for the total sample were tabulated (Table 5). Interclass correlation coefficients were high between items comprising a subscale and total subscale score. An exception was the item concerned with control of bowels and the personal care subscale of

the mCDR, which only had an item-total scale correlation of 0.47. It should be noted that the vast majority of subjects in the sample were not impaired on this subscale.

mCDR and CDR scores in the Prediction of Transition in Diagnosis at One Year Follow-up

In predicting transition from NCI to aMCI, accounting for effects of age, education and gender, the hazard ratio (HR) was non-significant for CDR, while for mCDR, the HR was 3.25 (CI = 1.28 – 8.37; p = 0.01). In predicting transition from aMCI to Dementia, accounting for effects of age, education and gender, the HR was non-significant for mCDR, while for CDR it was 1.87 (1.06 - 3.31) (p = 0.03).

Discussion

The mCDR was designed to be used in clinical research studies as an efficient and reliable alternative to the CDR. The mCDR has excellent inter-rater reliability and can be completed in well under 10 minutes. In comparison, the CDR has only fair to good inter-rater reliability, and requires 30 minutes or more to complete. Although no cognitive tests are included in the mCDR, its validity is almost equivalent to the CDR. This is demonstrated by the mCDR's performance in distinguishing NCI, aMCI, and dementia (Table 2), and its correlation to neuropsychological test results (Table 3). A slight advantage of the CDR may be likely related to inclusion of objective cognitive testing. However, most if not all research studies of MCI and the earliest stages of dementia require separate standardized cognitive tests, thus obviating a need for including them in the mCDR.

Subtle changes in functional abilities, commonly seen in the MCI stages of dementing disorders, are often only recognized when the examiner provides informants with specific examples of functional decline (Lim *et al.*, 2007). When history is elicited in an open-ended format, the informant often provides a lengthy and unfocused response, requiring a seasoned clinician to extract desired information efficiently and judiciously, in order to score individual CDR domains (Morris, 1993). Especially among subjects with purely subjective cognitive complaints, MCI, or very mild dementia, there is frequently a lack of correspondence between results of objective cognitive testing and information provided by an informant, regarding the subject's functional status (Galvin *et al.*, 2007; Tabert *et al.*, 2002). When judgment is used to reconcile discrepant information, resulting diagnoses are likely to be affected by the examiner's clinical and experiential bias. From a research perspective, inclusion of cognitive testing in the CDR increases the time necessary to complete assessment, introduces a cognitive test that lacks normative and reliability data, and requires a clinician's judgment to combine results of functional assessment with cognitive testing into a single domain score.

We have shown that mCDR and CDR scores are strongly correlated to MTA ratings, and may predict progression from NCI to aMCI, and aMCI to dementia, after a 12 month follow-up. Severity of MTA in MRI brain scans has been shown to be strongly correlated with severity of medial temporal degenerative pathology at autopsy (Bobinski *et al.*, 1996; Jack *et al.*, 2002). Structural MRI studies in subjects diagnosed with mild cognitive impairment (MCI) and AD consistently display atrophy in the entorhinal cortex (ERC) and hippocampus (HPC; Killiany *et al.*, Rusinek *et al.*, 2004). It has been shown that severity of MTA on MRI scans predicts rate of transition from amnestic MCI to dementia (Duara *et al.*, 2008; Rusinek *et al.*, 2004). Our findings of a strong correlation between mCDR scores and MTA ratings, suggest mCDR scores reflect the biological severity of underlying degenerative disease that in most cases, is likely to be AD.

The CDR is extensively used in clinical research trials and epidemiological studies, primarily as a measure of function in distinguishing individuals with no cognitive

impairment from subjects with MCI, and in distinguishing individuals with MCI from subjects with dementia (McCulla *et al.*, 1989; Morris, 1997; Fillenbaum *et al.*, 1996; Petersen, 2000; Hanninen *et al.*, 2002; Li *et al*, 2006; Rockwood *et al.*, 2000; Schafer *et al.*, 2004). As previously reported, the CDR shows relatively low inter-rater reliability during the early stages of dementing disorders (Rockwood *et al.*, 2000; Schafer *et al.*, 2004), and in comparison to the mCDR, the CDR necessitates a higher level of training and greater time to administer. Key factors accounting for the relative brevity and reliability of mCDR include a structured interview and multiple-choice response format, and the avoidance of cognitive testing. These features render unnecessary a reconciliation of cognitive tests and informant-based reports of functional ability.

Transition from NCI to MCI was predicted by mCDR scores, whereas CDR scores predicted transition from MCI to dementia. These findings suggest mCDR is more accurate than the CDR in quantifying functional changes during the earliest stages of dementing disorders, prior to the manifestation of objective cognitive deficits. As such, the mCDR is an independent measure of functional abilities that can be combined with neuropsychological measures, or used independently to diagnose MCI and dementia in a transparent, well-defined and repeatable paradigm for research studies. For purposes of categorizing cognitive-functional status of subjects in cross-sectional and longitudinal research studies, scores from specific cognitive tests could be combined with the scores of the mCDR, in a defined and transparent algorithm, expressed either as a continuous interval-level score, akin to the body mass index (Keys et al., 1972), and/or as specific diagnostic entities (e.g., amnestic or non-amnestic MCI). A limitation of this study is we have not examined utility of the mCDR in evaluating specific etiologies of cognitive impairment, such as Alzheimer's disease, vascular dementia, Lewy body dementia, or frontotemporal lobar dementia.

Conclusion

The mCDR is an efficient, reliable and valid instrument for discriminating between subjects with no functional impairment, aMCI and mild dementia, in five of the six domains of the traditional CDR scale. The mCDR is brief and reliable in comparison to the CDR, and the mCDR better predicts the transition from NCI to aMCI, whereas the CDR better predicts the transition from aMCI to mild dementia. The mCDR could be a particularly useful and economical instrument for assessing change in functional abilities, in multi-center clinical trials, and population studies of MCI and dementia, especially in combination with standard neuropsychological testing.

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References

Beekly DL, Ramos EM, Lee WW, Deitrich WD, Jacka ME, Wu J, Hubbard JL, Koepsell TD, Morris JC, Kukull WA. NIA Alzheimer's Disease Centers. The National Alzheimer's Coordinating Center (NACC) Database: the Uniform Data Set. Alzheimer Dis Assoc Disord. 2007; 21:249–58. [PubMed: 17804958]

Benton, AL.; Hamsher, K. Multilingual Aphasia Examination: Manual of Instructions. 2nd. AJA Associates; Iowa City: 1989.

Bobinski M, Wegiel J, Wisniewski HM, Tarnawski M, Bobinski M, Reisberg B, De Leon MJ, Miller DC. Neurofibrillary pathology - correlation with hippocampal formation atrophy in Alzheimer disease. Neurobiol Aging. 1996; 17:909–919. [PubMed: 9363803]

Chen HH, Duffy SW, Tabar L. A Markov chain method to estimate the tumor progression rate from preclinical to clinical phase, sensitivity and positive predictive value for mammography in breast cancer screening. The Statistician. 1996; 45:307–317.

Cohen, J.; Cohen, P. Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences. Lawrence Erlbaum Assoc; Hillsdale, New York: 1983.

Delong ER, Delong DM, Clarke-Pearson DL. Comparing the Areas under Two or More Correlated Receiver Operating Characteristic Curves: A Nonparametric Approach. Biometrics. 1988; 44:837–845. [PubMed: 3203132]

Duara R, Loewenstein DA, Potter E, Appel J, Greig MT, Urs R, Shen Q, Raj A, Small B, Barker WW, Schofield E, Wu Y, Potter H. Neurology. 2008; 71:1986–1992. [PubMed: 19064880]

Fillenbaum GG, Peterson B, Morris JC. Estimating the validity of the clinical Dementia Rating Scale: the CERAD experience. Consortium to Establish a Registry for Alzheimer's Disease. Aging (Milano). 1996; 8:379–385. [PubMed: 9061124]

Fleisher AS, Raman R, Siemers ER, Becerra L, Clark CM, Dean RA, Farlow MR, Galvin JE, Peskind ER, Quinn JF, Sherzai A, Sowell BB, Alsen PS, Thal LJ. Phase 2 safety trial targeting amyloid beta production with a gamma secretase inhibitor in Alzheimer's disease. Arch Neurol. 2008; 65:1031–1038. [PubMed: 18695053]

Fuld, PA. Fuld Object-Memory Evaluation. Stoelting Company; Woodale, IL: 1981.

Galvin JE, Roe CM, Morris JC. Evaluation of Cognitive Impairment in Older Adults Combining Brief Informant and Performance Measures. Arch Neurol. 2007; 64:718–724. [PubMed: 17502471]

Hanninen T, Hallikainen M, Tuomainen S, Vanhanen M, Soininen H. Prevalence of mild cognitive impairment: a population-based study in elderly subjects. Acta Neurologica Scandinavica. 2002; 106:148–154. [PubMed: 12174174]

Jack CR, Dickson DW, Parisi JE, Xu YC, Cha RH, O'Brien PC, Edland SD, Smith GE, Boeve BF, Tangalos EG, Kokmen E, Petersen RC. Antemortem MRI findings correlate with hippocampal neuropathology in typical aging and dementia. Neurology. 2002; 58:750–757. [PubMed: 11889239]

Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. J Chron Dis. 1972; 25:329–43. [PubMed: 4650929]

Killiany RJ, Hyman BT, Gomez-Isla T, Moss MB, Kikinis R, Jolesz F, Tanzi R, Jones K, Albert MS. MRI measures of entorhinal cortex versus hippocampus in preclinical AD. Neurology. 2002; 58:1188–1196. [PubMed: 11971085]

Li M, Ng TP, Kua EH, Ko SM. Brief informant screening test for mild cognitive impairment and early Alzheimer's disease. Dementia and Geriatric Cognitive Disorders. 2006; 21:392–402. [PubMed: 16645272]

Lim WS, Chong MS, Sahadevan S. Review: Utility of the Clinical Dementia Rating in Asian Populations. Clinical Medicine & Research. 2007; 5:61–70. [PubMed: 17456836]

Loewenstein DA, Argüelles T, Barker WW, Schram L, Ownby R, Acevedo A, Mogosky B, White G, Duara R. The utility of a modified object memory test in distinguishing between three different age groups of Alzheimer's disease patients and normal controls. J Mental Health Aging. 2001; 7:317–324.

Loewenstein DA, Acevedo A, Agron J, Issacson R, Strauman S, Crocco E, Barker WW, Duara R. Cognitive profiles in Alzheimer's disease and in mild cognitive impairment of different etiologies. Dementia and Geriatric Cognitive Disorders. 2006; 21:309–315. [PubMed: 16490966]

McCulla MM, Coats M, Van Fleet N, Duchek J, Grant E, Morris JC. Reliability of clinical nurse specialists in the staging of dementia. Arch Neurol. 1989; 46:1210–1211. [PubMed: 2818255]

Monsch AU, Bondi MW, Butter N, Salmon DP, Katzman R, Thal LJ. Comparisons of verbal fluency tasks in the detection of dementia of the Alzheimer type. Arch Neurology. 1992; 49:1253–1258.

Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. Neurology. 1993; 43:2412–2414. [PubMed: 8232972]

Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Intl Psychogeriatrics. 1997; (Supp 1):173–176.

Perneczky R, Wagenpfeil S, Komossa K, Grimmer T, Diehl J, Kurz A. Mapping scores onto stages: Mini-Mental State Examination and clinical dementia rating. Am J Geriatr Psychiatry. 14:139–144. [PubMed: 16473978]

Petersen RC. Mild Cognitive Impairment or Questionable Dementia? Arch Neurol. 2000; 57:643–644. [PubMed: 10815128]

Rockwood K, Strang D, MacKnight C, Downer R, Morris JC. Interrater reliability of the Clinical Dementia Rating in a multicenter trial. J Am Geriatrics Soc. 2000; 48:558–559.

Rusinek H, Endo Y, De Santi S, Frid D, Tsui WH, Segal S, Convit A, de Leon MJ. Atrophy rate in medial temporal lobe during progression of Alzheimer disease. Neurology. 2004; 63:2354–2359. [PubMed: 15623699]

Schafer KA, Tractenberg RE, Sano M, Mackell JA, Thomas RG, Gamst A, Thal LJ, Morris JC. Alzheimer's Disease Cooperative Study. Reliability of monitoring the clinical dementia rating in multicenter clinical trials. Alzheimer's Disease and Related Disorders. 2004; 18:219–222.

Spreen, O.; Strauss, E. A compendium of neuropsychological tests: administration, norms, and commentary. 2nd. Oxford University Press; New York: 1998.

Tabert MH, Albert SM, Borukhova-Milov L, Camacho Y, Pelton G, Liu X, Stern Y, Devanand DP. Functional Deficits in Patients with Mild Cognitive Impairment: Prediction of Alzheimer's Disease. Neurology. 2002; 58:758–764. [PubMed: 11889240]

Urs R, Potter E, Barker W, Appel J, Loewenstein DA, Zhao W, Duara D. Visual Rating System (VRS) for Assessing Magnetic Resonance Images (MRIs): A tool in the diagnosis of MCI and Alzheimer's Disease. J Comput Assist Tomogr. 2009; 33:73–78. [PubMed: 19188789]

Wechsler, D. The Wechsler Memory Scale, revised. The Psychological Corporation; San Antonio: 1987.

Wechsler, D. The Wechsler Adult Intelligence Scale. 3rd. The Psychological Corporation; San Antonio: 1997.

Table 1
Demographic Characteristics of the Sample [Means and (SDs)]

	Normal	AmMCI	Dementia
Sample Size	n = 313	n = 102	n = 141
Age (yrs)	73.2 (6.7)	75.1 (6.3)	75.7 (6.7)
Education (yrs)	14.5 (3.6)	13.9 (3.1)	13.4 (3.4)
MMSE	28.8 (1.3)	27.0 (2.6)	23.7 (3.8)
Lang (%Spanish)	21.2%	27.3%	17.8%
Gender (%Female)	63.5%	51.6%	54.3%

Table 2

Mean mCDR scores for Domains and Diagnostic Groups

	NCI	A-MCI	Dementia	F-Value	n
mCDR-SS	0.43 (0.53)^{A}	1.20 (0.99)^{B}	2.46 (1.94)^{C}	156.77***	556
CDR-SB	0.42 (0.64)^{A}	1.73 (1.56)^{B}	3.86 (2.79)^{C}	216.71***	556
mCDR Memory	0.21 (0.24)^{A}	0.44 (0.29)^{B}	0.68 (0.40)^{C}	124.10***	556
mCDR Orientation	0.06 (0.11)^{A}	0.20 (0.22)^{B}	0.50 (0.49)^{C}	122.78***	556
mCDR Judgment	0.04 (0.10)^{A}	0.20 (0.28)^{B}	0.48 (0.47)^{C}	125.58***	556
mCDR Community Affairs	0.07 (0.14)^{A}	0.17 (0.22)^{B}	0.31 (0.31)^{C}	62.33***	556
mCDR Home & Hobbies	0.02 (0.06)^{A}	0.13 (0.19)^{B}	0.36 (0.39)^{C}	119.95***	556
mCDR Personal Care	0.02 (0.06)^{A}	0.06 (0.12)^{A}	0.13 (0.23)^{C}	30.82***	556

Note: Means with different alphabetic superscripts are statistically significant utilizing the Scheffe' Procedure

*** p<.001

Table 3

mCDR sum, CDR-SOB and CDR-global in the Prediction of Neuropsychological Diagnosis (AUC[a] of ROC[b])

	mCDR-SS	CDR-SB	CDR (global)	p-value
AmMCI vs Normal	0.770	0.805	0.748	0.132
Dementia vs Normal	0.897	0.932	0.887	0.014
Dementia vs AmMCI	0.729	0.757	0.713	0.211

Note: p-value applies to comparative areas under the ROC curve for mCDR sum of domain scores and CDR sum of box scores; P-value is for mCDR-SS and CDR-SB Comparisons

[a] Area Undr the Curve

[b] Receiver Operating Characteristics

Table 4

Correlations Between mCDR and CDR scores versus Neuropsychological scores and Medial Temporal Atrophy (MTA) (all patients)

	mCDR-Sum of Domains	CDR Sum of Boxes	P-value	
Fuld OME	-0.69	-0.75	0.0036	(n=392)
Category Fluency	-0.58	-0.62	0.0108	(n=395)
Right MTA	0.56	0.59	0.423	(n=257)
Left MTA	0.60	0.63	0.101	(n=256)

Table 5

Item Characteristics of the mCDR for 556 Subjects

mCDR Memory	Mean	SD	Item/Scale Corr	Proportion of Responses				
				0	.5	1.0	2.0	NA
Memory Recent Events	.45	.56	.82***	8.4%	23.4%	21.1%	6.1%	1.1%
Completion of Tasks When Interrupted	.34	.48	.79***	7.6%	22.7%	15.5%	3.2%	1.0%
Memory Names	.21	.35	.55***	69.6%	18.3%	11.3%	0.2%	0.5%
Memory for Words In Conversation	.32	.44	.60***	56.8%	27.0%	13.1%	2.3%	0.7%
Memory for Possessions	.46	.51	.79***	43.9%	28.4%	22.7%	4.3%	0.7%
Memory for Responsibilities	.42	.52	.85***	47.8%	29.1%	17.3%	5.0%	0.7%
mCDR Orientation								
Relationships Between Events	.34	.50	.85***	57.6%	22.1%	14.4%	4.1%	1.8%
Find Places in Neighborhoods	.11	.33	.70***	85.1%	6.7%	5.4%	1.3%	1.6%
Find Places Outside of Neighborhood	.29	.53	.82***	67.1%	14.0%	11.2%	5.2%	2.5%
Memory for Day	.21	.43	.87***	73.4%	14.2%	8.5%	2.7%	1.3%
Memory for Month	.11	.36	.84***	87.2%	5.6%	4.0%	2.2%	1.1%
Memory for Year	.07	.30	.78***	91.4%	3.8%	2.2%	1.6%	1.1%
mCDR Judgment and Problem-Solving								
Insight into Errors	.21	.38	.77***	70.9%	17.6%	9.4%	1.3%	0.9%
Appropriate Caution	.13	.35	.72***	84.2%	7.6%	5.4%	1.6%	1.3%
Planning & Organizing	.23	.50	.87***	76.4%	7.4%	9.4%	4.5%	2.3%
Change for Purchase	.12	.36	.78***	84.4%	7.0%	4.5%	2.0%	2.2%
Manage Financial Affairs	.26	.54	.88***	71.4%	8.6%	9.4%	5.8%	4.9%
Judging Purchases	.13	.36	.79***	80.8%	8.3%	4.3%	1.8%	4.9%
mCDR Community Affairs				0	.5	1.0	2.0	NA
Community Activities	.18	.38	.69***	75.4%	14.0%	7.9%	1.6%	1.1%
Personal Hygiene	.09	.31	.63***	87.9%	6.3%	3.6%	1.3%	0.9%
Impulsivity	.18	.36	.59***	74.5%	16.9%	6.7%	1.3%	0.7%
Lack of Interest	.15	.38	.74***	80.9%	9.0%	7.6%	1.6%	0.9%
Consideration of Others	.12	.29	.64***	82.9%	9.9%	5.9%	0.4%	0.9%

mCDR Memory	Mean	SD	Item/Scale Corr	Proportion of Responses				
Reactions in Social Situations	.14	.35	.73***	80.0%	12.2%	5.2%	1.4%	1.1%
mCDR Home and Hobbies								
Household Chores	.05	.23	.66***	56.7%	2.9%	1.1%	0.4%	39.0%
Use Appliances	.18	.39	.83***	48.4%	7.0%	5.9%	0.9%	37.8%
Complex Routine Tasks	.20	.46	.82***	47.5%	6.8%	4.3%	2.3%	39.0%
Complex Non-Routine Tasks	.20	.45	.80***	71.4%	10.3%	6.8%	3.1%	8.5%
Understand and Follow Written or Televised Media	.16	.40	.81***	77.9%	8.6%	7.0%	2.2%	4.3%
Participate in Games & Hobbies	.14	.38	.77***	73.2%	7.4%	5.4%	1.8%	12.2%
mCDR Personal Care								
Control of Urine	.15	.32	.69***	77.9%	13.7%	6.5%	0.5%	1.4%
Control of Bowels	.03	.16	.47***	93.9%	2.7%	1.1%	0.2%	2.2%
Dressing/Choosing Clothes	.05	.24	.73***	91.5%	4.7%	1.3%	0.9%	1.6%
Groom	.03	.18	.65***	95.3%	2.2%	0.5%	0.5%	1.4%
Use Eating Utensils	.03	.18	.55***	95.9%	1.1%	0.9%	0.5%	1.6%