Journal of Alzheimer's Disease 22 (2010) 889–896
DOI 10.3233/JAD-2010-101182
IOS Press

Does the Combination of the MMSE and Clock Drawing Test (Mini-Clock) Improve the Detection of Mild Alzheimer's Disease and Mild Cognitive Impairment?

Jesús Cacho[a], Julián Benito-León[b,c,*], Ricardo García-García[d], Bernardino Fernández-Calvo[e], José Luis Vicente-Villardón[f] and Alex J. Mitchell[g]
[a]*Department of Neurology* (*Dr. Cacho*), *University Hospital of Salamanca, University of Salamanca, Salamanca, Spain*
[b]*Department of Neurology* (*Dr. Benito-León*), *University Hospital "12 de Octubre", Madrid, Spain*
[c]*Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas* (*CIBERNED*), *Madrid, Spain*
[d]*Department of Basic Psychology and Psychobiology* (*Dr. García-García*), *University of Salamanca, Salamanca, Spain*
[e]*Department of Psychology* (*Dr. Fernández-Calvo*), *Federal University of Paraíba, Brazil*
[f]*Department of Statistics* (*Dr. Vicente-Villardón*), *University Hospital of Salamanca, University of Salamanca, Salamanca, Spain*
[g]*Department of Liaison Psychiatry* (*Dr. Mitchell*), *Leicestershire Partnership Trust and University of Leicester, Leicester, UK*

Accepted 26 July 2010

Abstract. There is currently a need to develop tools to identify patients with mild AD and mild cognitive impairment (MCI). We determined the validity and reliability of a brief, easily administered cognitive screening battery consisting of fusion of two well-known brief tests (Mini-Mental Status Examination [MMSE] and Clock Drawing Test [CDT]) (Mini-clock) to differentiate between patients with mild AD, MCI, and healthy control subjects. 66 consecutive patients with mild AD, 21 with MCI, and 66 healthy controls seen in a memory clinic setting were compared. Receiver operating characteristic (ROC) curve analysis was used to calculate the cut-off value permitting discrimination between mild AD, MCI, and healthy control subjects. Interrater and test-retest reliability were also assessed. Mean cognitive scores for patients with AD, MCI, and control subjects on all two individual tests were significantly different (for each, $p < 0.001$). The mean area under the ROC curve for Mini-clock was higher than that obtained with MMSE or CDT in differentiating mild AD from controls (0.973 vs. 0.952 and 0.881, respectively) and MCI from controls (0.855 vs. 0.821 and 0.779, respectively). Test-retest reliability for the Mini-clock was 0.99, meanwhile interrater reliability was 0.87. The mean time to complete the test for all subjects was 8 min and 50 s. The Mini-clock is highly sensitive and specific in the detection of mild AD and reasonably accurate when attempting to separate MCI from health controls. It has a high interrater and test-retest reliability, can be quickly administered, and does not require major training.

Keywords: Alzheimer's disease, diagnosis, screening

INTRODUCTION

The increasing prevalence and incidence of Alzheimer's disease (AD) and development of new disease-modifying treatments has fueled the research into de-

*Correspondence to: Dr. Julián Benito-León, Avda. de la Constitución 73, portal 3, 7° Izquierda, E-28821 Coslada, Madrid, Spain. E-mail: jbenitol@meditex.es.

ISSN 1387-2877/10/$27.50

velopment of accurate and easily administered screening instruments for AD [1,2]. However, there is currently a need to develop tools to identify patients with mild AD. Among the most widely used screening tests for dementia are the Mini-Mental State Examination (MMSE) and the clock drawing test (CDT).

The MMSE was published more than 30 years ago in 1975 as a practical method of grading cognitive impairment [3]. The MMSE has 19 individual tests of 11 domains covering orientation, registration, attention or calculation (serial sevens or spelling), recall, naming, repetition, comprehension (verbal and written), writing, and construction [3]. Several surveys of health professionals show that it has become the most commonly applied cognitive test, used by approximately 9 out of 10 specialists [4–6]. It is also often used by non-specialists although many in primary care consider it too time consuming to administer [7,8]. Opinion is divided about how useful the MMSE is in diagnosing dementia, whether it is suitable for primary and specialist settings and regarding the optimal cut-off threshold [9,10]. Nevertheless the MMSE has been the most extensively studied screening instrument for cognitive impairment [11,12]. A recent meta-analysis of MMSE accuracy suggested a modest sensitivity of 77% and a specificity of 90% for application in high prevalence specialist settings and a sensitivity of 81% and a specificity of 87%, respectively for application in low prevalence primary care settings [11]. The MMSE therefore appears to be only modestly accurate method of detecting dementia.

On the other hand, the CDT has been widely used particularly as a quick cognitive to screen for dementia especially in primary care [13]. The CDT is a pre-drawn clock face with the request to add numbers and setting a specific time. It usually takes about 2 min to complete. Although it is a very simple task auditory and visual comprehension, concentration and planning are needed [13]. Its application in memory clinic settings is rare (Table 2) [14–18]. Simple pooling of these CDT studies suggests a sensitivity of approximately 74% and a specificity of 80%, which may not be adequate when used alone [14–18].

The goals of this study were: 1) To know if the combination of the MMSE and the CDT ("*Mini-clock*") increases sensitivity and specificity with respect to the separated use of both tests. 2) To assess if the Mini-clock improves discrimination between patients with mild Alzheimer's disease (AD), mild cognitive impairment (MCI), and healthy individuals.

METHODS

Study population

Patients with mild AD, MCI, and healthy individuals were recruited from the Memory and Dementing Disorders Clinic at University Hospital of Salamanca, Spain, between January 2005 and June 2005, by a neurologist with expertise in dementing disorders (J.C.). The patients with mild AD and MCI represented consecutive referrals to the clinic. Dementia was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] criteria [19]. The patients with MCI met the diagnosis criteria of MCI by Petersen et al. [20]. These criteria include: 1) the presence of a subjective memory complaint, 2) preserved general intellectual functioning as estimated by performance on a vocabulary test, 3) demonstration of a memory impairment by cognitive testing, 4) intact ability to perform activities of daily living, and 5) absence of dementia. The patients with AD had to score one (i.e., mild dementia) on the Clinical Dementia Rating [21]. AD was diagnosed with the National Institute of Neurological Disorders and Stroke–Alzheimer's Disease and Related Disorders Association diagnostic criteria [22] based on 1) neurological, medical, psychiatric, and/or social examinations; 2) standard laboratory studies; 3) computed tomographic scans or magnetic resonance imaging; 4) neuropsychological evaluations; and 5) history from a caregiver indicating at least a 1-year history of progressive cognitive decline. To ensure more the diagnosis, every mild AD patient was followed at least 5 years to confirm the diagnosis of AD. Results from the Mini-clock did not contribute to the diagnosis of mild AD and MCI.

Healthy controls were recruited from the spouses of patients in the Memory and Dementing Disorders Clinic at University Hospital of Salamanca, Spain. A medical history was obtained from each subject, including current medication use, stroke, mental illness, mental retardation, or life-threatening illness. Subjects with a history of psychiatric or neurological diseases or alcoholism were excluded, as were those subjected to psychopharmacological treatment. All claimed to be independent in activities of daily living, including shopping, transportation, and managing finances.

This study was approved by the research ethics board at Salamanca University Hospital. Signed consent was obtained for all participants.

Table 1
Previous studies of clock drawing test and clock drawing test plus mini-mental state examination in specialist clinic settings

Name	Gold standard	Methodology	Sensitivity	Specificity	PPV	NPV
Heinik et al. [14]	DSM-IV	Specialist outpatient psychogeriatric clinic assessed using MMSE, CAMCOG and CDT. CDT results shown.	0.85	0.89	0.963	0.637
Heinik et al. [14]	DSM-IV	As above CDT + MMSE shown.	1.00	0.91	0.974	1.00
Aprahamian et al. [15]	DSM-IV and NINCDS-ADRDA for AD	Sample was heterogeneous educational levels from a geriatric outpatient clinic that completed the CAMDEX	0.742	0.899	0.90	0.74
Aprahamian et al. [15]	DSM-IV and NINCDS-ADRDA	As above but with CDT plus MMSE.	0.90	0.727	0.801	0.856
Lin et al. [16]	DSM-IV and NINCDS-ADRDA	Subjects were administered Chinese version of CASI and CDR rating given.	0.67	0.75	0.60	0.80
Lessig et al. [17]	DSM-IV and NINCDS-ADRDA for AD	Memory clinic study with attempt to optimize CDT and Mini-Cog. Excluding those with less than 5 years of education and /or mild cognitive impairment.	0.71	0.88	0.90	0.65
Schmidtke et al. [18]	Expert Diagnosis	Memory clinic study. Mild cognitive impairment excluded from this analysis.	0.86	0.78	0.92	0.64

AD = Alzheimer's disease; CAMCOG = Cambridge Cognitive Examination; CAMDEX = Cambridge Examination for Mental Disorders of the Elderly; CASI = Cognitive Abilities Screening Instrument; CDR = Clinical Dementia Rating; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria. MMSE = Mini-Mental State Examination; NINCDS-ADRDA = National Institute of Neurological Disorders and Stroke¤CAlzheimer's Disease and Related Disorders Association diagnostic criteria. NPV = Negative predictive value. PPV = Positive predictive value.

Neuropsychological assessment

Every enrolled subject (patients and controls) underwent detailed baseline neurologic examination including evaluation of cognitive deficits with the Mattis Dementia Rating Scale (MDRS) [23]. The Mini-clock and the MDRS was administered and scored by three experienced neuropsychologist blinded to the diagnosis (Y.C.-E., S. G.-N. and L. G.-L., see acknowledgments).

The MMSE was performed according to Folstein and colleagues [3] and translated into Spanish from the original version following criteria previously published by a Spanish group [24]. When the subject had completed item 11, copying the overlapping pentagons, the CDT was performed on verbal command following these instruction: "I want you to draw a clock with all the numbers on it. Make it large and draw the hands set at ten after eleven." The CDT was scored on a 0–10 scale according to the criteria previously published by our group [25]. Thus range of possible Mini-clock scores is 0–40, with lower totals reflecting greater cognitive impairment.

Statistical analyses

Analyses were performed in SPSS (version 18.0). Gender and educational level of patients and healthy subjects were compared using chi-square tests. Age and every one of the neuropsychological tests scores, except for MDRS, was not normally distributed (Kolmogorov-Smirnov, $p < 0.05$). Therefore, age and scores were compared using a non-parametric approach (Kruskal-Wallis test), meanwhile MDRS scores were compared using one-way analysis of variance (ANOVA). Receiver Operating Characteristic (ROC) curve analysis was performed in order to assess the significance of the relationship between the neuropsychological test (MMSE, CDT and Mini-clock) and the diagnosis (patient vs. healthy control). The sensitivity and specificity were established in order to use the potential cut-off values and thereby facilitate discrimination between patients with mild AD and healthy controls; patients with MCI and healthy controls; and patients with mild AD and the combination of patients with MCI and healthy controls. In the ROC curve for each neuropsychological test (MMSE, CDT and Mini-clock), the size of the area under the ROC curve indicated the degree of relationship between the scores and the diagnosis of the participant. The closer to 1, the stronger the relation was; the closer to 0.5, the weaker the relation was. In discerning patient versus healthy control, the desirable cut-off value should have high true-positive and low false-positive rates. Test-retest reliability was evaluated in 30 randomly selected patients with mild AD and 30 randomly selected control subjects by re-administering the Mini-clock 1 to 2 months after initial

Table 2
Baseline characteristics of patients with mild Alzheimer's disease (AD) patients, with mild cognitive impairment (MCI) and healthy controls

Characteristics	Patients with mild AD (N = 66)	Patients with MCI (N = 21)	Healthy controls (N = 66)	p value
Gender (female)	46 (69.7%)	14 (66.7%)	37 (56.1%)	0.252[a]
Age	73.8 (74.5) ± 4.3	73.8 (75.0) ± 5.0	72.1 (71.0) ± 5.7	0.081[a]
Educational level				
Can read and write	44 (66.7%)	8 (38.1%)	37 (56.1%)	0.226[a]
Primary school	20 (30.3%)	12 (57.1%)	26 (39.4%)	
Secondary school or higher	2 (3.0%)	1 (4.8%)	3 (4.5%)	
Mini-Mental State Examination score	21.8 (22.0) ± 2.8	24.6 (24.0) ± 2.7	27.8 (28.0) ± 1.8	< 0.0001[b]
Clock drawing test	6.3 (7.0) ± 1.9	7.2 (8.0) ± 2.0	8.8 (9.0) ± 1.2	< 0.0001[b]
Mattis Dementia Rating Scale score	115.4 (117.0) ± 9.6	123.6 (125.0) ± 12.0	135.2 (138.0) ± 14.2	< 0.0001[c]
Mini-clock score	28.1 (28.0) ± 3.6	31.8 (31.0) ± 3.9	36.6 (37.0) ± 2.2	< 0.0001[b]

Mean (median) ± standard deviation and frequency (%) are reported. [a]Chi-square test. [b]Kruskal-Wallis test. [c]One-way analysis of variance test.

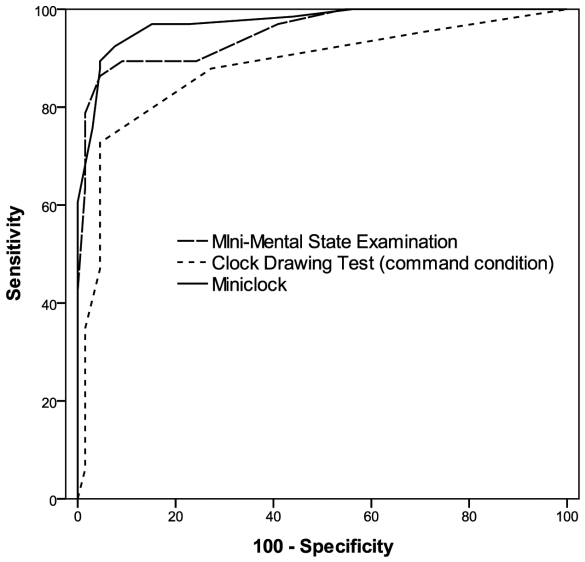

Fig. 1. Receiver operating characteristic curves for patients with mild Alzheimer's disease versus controls.

administration. Interrater reliability was accomplished by having 3 raters score the same testing session for 30 randomly selected patients with mild AD and 30 randomly selected control subjects.

RESULTS

We recruited 66 patients with mild AD, 21 with MCI, and 66 healthy controls. There were no differences in mean age, education and gender between patients with mild AD, MCI, and control subjects (Table 2). Mean cognitive scores for patients with mild AD and control subjects on all tests were significantly different (for each, $p < 0.001$) (Table 2).

The mean time to complete the test for all subjects was 8 min and 50 s (range, 7 min and 10 s to 11 min and 20 s). Patients with mild AD took longer than control subjects, with a mean of 9 minutes and 49 s (range, 7 min and 45 s to 11 min and 40 s). The control subjects took a mean of 7 min and 51 s (range, 6 min and 37 s to 9 min and 23 s).

Patients with mild AD versus healthy controls

The areas under the ROC curve were 0.973 (confidence interval [CI] = 0.646–1) for the Mini-clock ($p < 0.001$), 0.952 (CI = 0.639–1) for the MMSE ($p < 0.001$) and 0.881 (CI = 0.611–1) for the CDT ($p < 0.001$) (Fig. 1). A cut-off of 23v24 for the MMSE (sensitivity 86.4%, specificity 95.5%), 6v7 for the CDT (sensitivity 72.7%, specificity 97.0%), and 30v31 for the Mini-clock (sensitivity 89.4%, specificity 95.4%) best discriminated patients versus healthy controls (Table 3).

Test-retest reliabilities for MMSE and CDT were 0.99 and 0.98, respectively. Test-retest reliability for the Mini-clock was 0.99, meanwhile interrater reliability was 0.87.

Patients with mild AD versus healthy controls or MCI

The areas under the ROC curve were 0.918 (CI = 0.645 to 1) for the Mini-clock ($p < 0.001$), 0.903 (95% CI = 0.639 to 1) for the MMSE ($p < 0.001$) and 0.825 (95% CI = 0.604 to 1) for the CDT ($p < 0.001$) (Fig. 2). A cut-off of 23v24 for the MMSE (sensitivity 86.4%, specificity 83.9%), 7v8 for the CDT (sensitivity 72.7%, specificity 87.3%), and 31v32 for the Mini-clock (sensitivity 89.4%, specificity 83.9%) best discriminated patients with AD versus healthy controls or patients with MCI (Table 4).

Table 3
Statistical comparison of mini-mental state examination versus clock drawing test versus mini-clock for Alzheimer's disease versus healthy controls

Characteristics	Mini-mental state examination alone	Clock drawing test alone	Mini-clock
Suggested Cut-Off	23v24	6v7	30v31
Sensitivity	86.4% (75.7 to 93.6)	72.7% (60.4 to 83.0)	89.4% (79.4 to 95.6)
Specificity	95.4% (87.3 to 99.0)	97.0% (89.5 to 99.6)	95.4% (87.3 to 99.0)
Positive Predictive Value	95.0% (86.0 to 99.0)	96.0% (86.3 to 99.5)	92.4% (83.2 to 97.5)
Negative Predictive Value	87.5% (77.6 to 94.1)	78.0% (67.5 to 86.4)	92.4% (83,2 to 97.5)
Area under Curve	0.952 (95% CI = 0.639 to 1)	0.881 (95% CI = 0.611 to 1)	0.973 (95% CI = 0.646 to 1)
Clinical Utility (case-finding)	0.82 (excellent)	0.70 (good)	0.83 (excellent)
Clinical Utility (screening)	0.84 (excellent)	0.76 (good)	0.89 (excellent)

Clinical Utility (case-finding) = sensitivity x positive predictive value. Clinical Utility (screening) = specificity x positive predictive value. CI = confidence interval.

Table 4
Statistical comparison of mini-mental state examination versus clock drawing test versus mini-clock for Alzheimer's disease versus controls and mild cognitive impairment

Characteristics	Mini-mental state examination alone	Clock drawing test alone	Mini-clock
Suggested Cut-Off	23v24	7v8	31v32
Sensitivity	86.4% (75.7 to 93.6)	72.7% (60.4 to 83.0)	89.4% (79.4 to 95.6)
Specificity	83.9% (74.5 to 90.9)	87.4% (78.5 to 93.5)	83.9% (74.5 to 90.9)
Positive Predictive Value	43.8% (34,8 to 53,1)	40.3% (31.4 to 49.7)	45.4% (36.6 to 54.3)
Negative Predictive Value	59.4% (40.6 to 76.3)	47.1% (29.8 to 64.9)	69.6% (47.1 to 86.8)
Area under Curve	0.903 (95% CI = 0.639 to 1)	0.825 (95% CI = 0.605 to 1)	0.918 (95% CI = 0.645 to 1)
Clinical Utility (case-finding)	0.38 (poor)	0.29 (poor)	0.41 (poor)
Clinical Utility (screening)	0.50 (average)	0.41 (poor)	0.58 (average)

Clinical Utility (case-finding) = sensitivity x positive predictive value. Clinical Utility (screening) = specificity x positive predictive value. CI = confidence interval.

Patients with MCI versus healthy controls

The areas under the ROC curve were 0.855 (95% CI = 0.487 to 1) for the Mini-clock ($p < 0.001$), 0.821 (95% CI = 0.484 to 1) for the MMSE ($p < 0.001$) and 0.779 (95% CI = 0.473 to 1) for the CDT ($p < 0.001$) (Fig. 3). This suggests that the Mini-Clock was the optimal test, although the MMSE also performed well in a screening capacity. A cut-off of 24v25 for the MMSE (sensitivity 52.4%, specificity 95.4%), 8v9 for the CDT (sensitivity 76.2%, specificity 69.7%) and 35v36 for the Mini-clock (sensitivity 76.2% specificity 77.3% best discriminated patients with MCI versus healthy controls (Table 5).

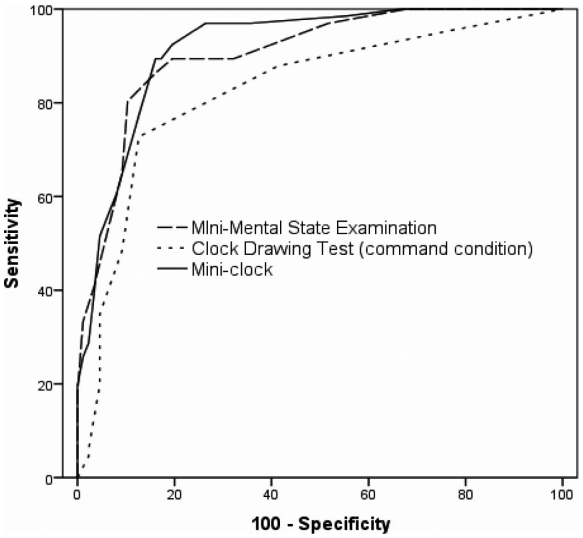

Fig. 2. Receiver operating characteristic curves for patients with mild Alzheimer's disease versus patients with cognitive impairment and controls.

DISCUSSION

We compared the MMSE alone and the CDT alone with the MMSE-CDT (Mini-clock) combination to detect mild AD and MCI. In this study, the Mini-clock was highly sensitive and specific in the detection of mild AD. It was less accurate in the detection of MCI but nevertheless performed well in a screening capacity to rule out those without MCI.

The MMSE has been found to have modest value

Table 5
Statistical comparison of mini-mental state examination versus clock drawing test versus mini-clock for mild cognitive impairment versus controls

Characteristics	Mini-mental state examination alone	Clock drawing test alone	Mini-clock
Suggested Cut-Off	24v25	8v9	35v36
Sensitivity	52.4% (29.8 to 74.3)	76.2% (52.8 to 91.8)	76.2% (52.8 to 91.8)
Specificity	95.4% (87.3 to 99.0)	69.7% (57.1 to 80.4)	77.3% (65.3 to 86.7)
Positive Predictive Value	81.3% (54.3 to 95.9)	85.7% (57.2 to 98.2)	57.1% (39.3 to 73.7)
Negative Predictive Value	88.7% (79.0 to 95.0)	87.7% (77.9 to 94.2)	98.1% (89.7 to 99.9)
Area under Curve	0.821 (95% CI = 0.484 to 1)	0.779 (95% CI = 0.473 to 1)	0.855 (95% CI = 0.487 to 1)
Clinical Utility (case-finding)	0.43 (poor)	0.65 (good)	0.44 (poor)
Clinical Utility (screening)	0.85 (excellent)	0.61 (average)	0.76 (good)

Clinical Utility (case-finding) = sensitivity x positive predictive value. Clinical Utility (screening) = specificity x positive predictive value. CI = confidence interval.

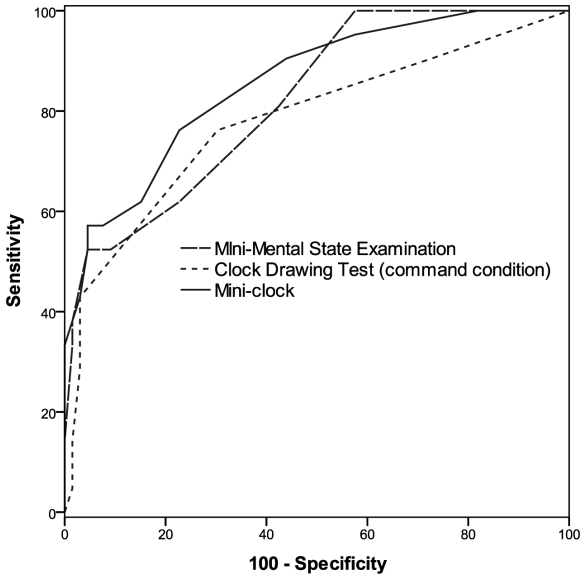

Fig. 3. Receiver operating characteristic curves for patients with mild cognitive impairment versus controls.

in specialist settings with a sensitivity of 77% and a specificity of 90% in AD, according to a recent meta-analysis [11] although studies in mild dementia were lacking. We found somewhat better performance of the MMSE here of 86% sensitivity and 95% specificity. This may mean that the MMSE could indeed be considered for use in memory clinics to detect mild AD if time were limited. Compared with the MMSE we found that the CDT lacks sensitivity and negative predictive value. Thus the CDT alone would not be ideally suited to use as an initial screening tool followed by more definitive testing if necessary. From our data the optimal test was the Mini-clock which had excellent case-finding and excellent screening properties for detection of AD versus controls. Furthermore it can be employed simply and with minimal additional time. For detection of MCI no test could be relied upon alone, but the Mini-clock had high negative predictive value and may be used as a first step in screening out those without MCI. However in this group, more advanced second stage testing is advised.

Brodaty and Moore (1997) were one of the first to show that the CDT can be better than the MMSE in a memory clinic [26]. Early studies demonstrated that there is also a potential advantage when both tests are applied concomitantly [27] in the detection of dementia. Few have looked specifically at probable AD. Schramm and collaborators (2002) studied 123 consecutive patients (79 dementia patients, 44 controls) at a memory clinic, and the combination between the two tests enhanced the accuracy [28]. They found that combining the CDT with the MMSE, respectively, improved sensitivity but specificity was not fully reported [28]. Heinik et al. (2003) showed that the CDT plus MMSE combined improved both sensitivity and specificity compared with the CDT alone [14]. Further this combination was better than the CAMCOG (the cognitive and self-contained part of the Cambridge Examination for Mental Disorders of the Elderly) itself, a much longer test [14]. Recently, Aprahamian and coworkers (2010) found that the addition of the MMSE to the CDT increased sensitivity and reduced specificity but with only a slight gain in overall accuracy [15]. Our results suggest that the combination of CDT and MMSE improves sensitivity but with a modest loss of specificity. Likewise it improves negative predictive value but with a slight decrement in positive predictive value. However, case-finding and screening functions remain excellent.

Several questions remain however. A recent review of nine CDT studies for MCI found poor utility of this test in MCI [29]. We also acknowledge that we had only modest sample size, especially for MCI. We recommend replication of our results in a larger sample. We also cannot be certain how the Mini-clock would perform in a primary care or community setting. Fi-

nally we acknowledge we had no access to pathological verification. However, we followed-up the patients with probable mild AD for at least 5 years to ensure the diagnosis of AD was correct.

In conclusion for interested in using simple tools for screening or mild AD cases-finding, we recommend that the CDT is combined with the well established MMSE. This combination appears to improve case-finding and screening accuracy without undue increase in length over the MMSE alone.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the vital help of Yamisel Chong-Espino, Silvia Gamazo-Navarro and Laura Gomez-Liz who performed the neuropsychological testing of the study subjects. Dr. Benito-León is supported by NIH R01 NS024859 from the National Institutes of Health, Bethesda, MD, USA.

Authors' disclosures available online (http://www.j-alz.com/disclosures/view.php?id=556).

REFERENCES

[1] Bermejo-Pareja F, Benito-León J, Vega S, Olazarán J, de Toledo M, Díaz-Guzmán J, Sánchez-Sánchez F, Morales-González JM, Trincado R, Portera-Sánchez A, Román GC (2009) Consistency of Clinical Diagnosis of Dementia in NEDICES: A Population-Based Longitudinal Study in Spain. *J Geriatr Psychiatry Neurol* **22**, 246-255.

[2] Bermejo-Pareja F, Benito-León J, Vega S, Medrano MJ, Román GC; Neurological Disorders in Central Spain (NEDICES) Study Group (2008) Incidence and subtypes of dementia in three elderly populations of central Spain. *J Neurol Sci* **264**, 63-72.

[3] Folstein MF, Folstein SE, McHugh PR (1975) Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J *Psychiatr Res* **12**, 189-198.

[4] Davey RJ, Jamieson S (2004) The validity of using the mini mental state examination in NICE dementia guidelines. *J Neurol Neurosurg Psychiatry* **75**, 343-344.

[5] Shulman KI, Herrmann N, Brodaty H, Chiu H, Lawlor B, Ritchie K, Scanlan JM (2006) IPA survey of brief cognitive screening instruments. *Int Psychogeriatr* **18**, 281-294.

[6] Reilly S, Challis D, Burns A, Hughes J (2004) The use of assessment scales in Old Age Psychiatry Services in England and Northern Ireland. *Aging Ment Health* **8**, 249-255.

[7] Glasser M (1993) Alzheimer's disease and dementing disorders: practices and experiences of rural physicians. *Am J Alzheimers Care Rel Disord Res* **8**, 28-35.

[8] Brodaty H, Howarth GC, Mant A, Kurrle SE (1994) General practice and dementia. A national survey of Australian GPs. *Med J Aust* **160**, 10-14.

[9] Tombaugh TN, McIntyre NJ (1992) The mini-mental state examination: a comprehensive review. *J Am Geriatr Soc* **40**, 922-935.

[10] Mossello E, Boncinelli M (2006) Mini-mental state examination: a 30-year story. *Aging Clin Exp Res* **18**, 271-273.

[11] Mitchell AJ (2009) A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. *J Psychiatr Res* **43**, 411-431.

[12] Mitchell AJ, Malladi S (2010) Screening and case finding tools for the detection of dementia Part II. Evidence based meta-analysis of single domain tests. *Am J Gen Psychiatry*, in press.

[13] Shulman K I (2000) Clock-drawing: Is it the ideal cognitive screening test? *Int J Geriatr Psychiatry* **15**, 548-561.

[14] Heinik J, Solomesh I, Bleich A, Berkman P (2003) Are the clock-drawing test and the MMSE combined interchangeable with CAMCOG as a dementia evaluation instrument in a specialized outpatient setting? *J Geriatr Psychiatry Neurol* **16**, 74-79.

[15] Aprahamian I, Martinelli JE, Neri AL, Yassuda MS (2010) The accuracy of the Clock Drawing Test compared to that of standard screening tests for Alzheimer's disease: results from a study of Brazilian elderly with heterogeneous educational backgrounds. *Int Psychogeriatr* **22**, 64-71.

[16] Lin KN, Wang PN, Chen C, Chiu YH, Kuo CC, Chuang YY, Liu HC (2003) The Three-item clock drawing test: a simplified screening for Alzheimer's disease. *Eur Neurol* **49**, 53-58.

[17] Lessig MC, Scanlan JM, Nazemi H, Borson S (2008) Time that tells: critical clock-drawing errors for dementia screening. *Int Psychogeriatr* **20**, 459-470.

[18] Schmidtke K, Olbrich S (2007) The Clock Reading Test: validation of an instrument for the diagnosis of dementia and disorders of visuo-spatial cognition. *Int Psychogeriatr* **19**, 307-321.

[19] American Psychiatric Association. DSM-IV. Diagnostic and Statistical Manual of Mental Disorders. Washington DC: American Psychiatric Association; 1994.

[20] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG (1997) Aging, memory, and mild cognitive impairment. *Int Psychogeriatr* **9**(Suppl 1), 65-69.

[21] Morris JC (1993) The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* **43**, 2412-2414.

[22] McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM (1984) Clinical diagnosis of Alzheimer's disease. Report of the NINCDS ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology* **34**, 939-944.

[23] Schmidt R, Freidl W, Fazekas F, Reinhart B, Grieshofer P, Koch M, Eber B, Schumacher M, Polmin K, Lechner H (1994) The Mattis Dementia Rating Scale: normative data from 1,001 healthy volunteers. *Neurology* **44**, 964-966.

[24] Blesa R, Pujol M, Aguilar M, Santacruz P, Bertran-Serra I, Hernández G, Sol JM, Peña-Casanova J; NORMACODEM Group (2001) NORMAlisation of Cognitive And Functional Instruments for DEMentia.Clinical validity of the 'mini-mental state' for Spanish speaking communities. *Neuropsychologia* **39**, 1150-1157.

[25] Cacho J, García-García R, Fernández-Calvo B, Gamazo S, Rodríguez-Pérez R, Almeida A, Contador I (2005) Improvement pattern in the clock drawing test in early Alzheimer's disease. *Eur Neurol* **53**, 140-145.

[26] Brodaty H, Moore CM (1997) The clock drawing test for dementia of the Alzheimer's type: a comparison of three scoring methods in a memory disorders clinic. *Int J Geriatr Psychiatry* **12**, 619-627.

[27] Ferrucci L, Cecchi F, Guralnik JM, Giampaoli S, Lo Noce C, Salani B, Bandinelli S, Baroni A. The FINE Study Group.

Finland, Italy, The Netherlands Elderly (1996) Does the clock drawing test predict cognitive decline in older persons independent of the Mini-mental State Examination? *J Am Geriatr Soc* **44**, 1326-1331.

[28] Schramm U, Berger G, Müller R, Kratzsch T, Peters J, Frölich L (2002) Psychometric properties of Clock Drawing Test and MMSE or Short Performance Test (SKT) in dementia screening in a memory clinic population. *Int J Geriatr Psychiatry* **17**, 254-260.

[29] Ehreke L, Luppa M, König HH, Riedel-Heller SG (2010) Is the Clock Drawing Test a screening tool for the diagnosis of mild cognitive impairment? A systematic review. *Int Psychogeriatr* **22**, 56-63.