

The Short Cognitive Evaluation Battery in Cognitive Disorders of the Elderly – Italian Version

Nicola Girtler^a Andrea Brugnolo^a Claudio Campus^{a,b}
Fabrizio De Carli^c Francesco Famà^a Lucio Ghio^d Philippe Robert^f
Maria Paola Barbieri^a Marta Delmonte^a Stefano Venuti^d
Filippo Gabrielli^d Guido Rodriguez^e Flavio Nobili^a

^aClinical Neurophysiology, Department of Neuroscience, Ophthalmology and Genetics, IRCCS San Martino – IST University Hospital, University of Genoa, ^bItalian Institute of Technology, ^cInstitute of Bioimaging and Molecular Physiology, Genoa Unit, National Research Council, ^dPsychiatry Section, IRCCS San Martino – IST University Hospital, ^eUniversity of Genoa, Genoa, Italy; ^fMemory Center EA CoBTeK, University of Nice Sophia Antipolis, Nice, France

Key Words

Short Cognitive Evaluation Battery · Cognitive screening · Alzheimer's disease · Mild cognitive impairment · Depression

Abstract

Aims: To validate the Italian version of the Short Cognitive Evaluation Battery (SCEB), consisting of 4 tests (temporal orientation, five words, clock drawing and verbal fluency) in healthy controls (CONT), patients with mild Alzheimer's disease (AD), mild cognitive impairment (MCI), and major depressive disorder (DEP). **Methods:** Twenty-nine AD patients (mean Mini-Mental State Examination, MMSE, score: 22.1 ± 3.1), 27 MCI patients (mean MMSE score: 26.5 ± 2.0), 27 depressed patients (mean MMSE score: 26.9 ± 2.8), and 48 controls (mean MMSE score: 29.7 ± 0.5) were enrolled. **Results:** MANCOVA showed highly significant ($p < 0.0001$) difference among groups. As for total SCEB score, AD were separated from CONT with high accuracy (93%; with sensitivity 93%, specificity 92%, area under ROC curve, AUC, 0.96) and from DEP with satisfying accuracy (84%; with sensitivity 76%,

specificity 93%, AUC 0.84). Results in MCI versus CONT comparison yielded more moderate accuracy (80%; with sensitivity 70%, specificity 87%, AUC 0.80), which increased in the subgroup of MCI patients who later converted to AD (85%; with sensitivity 75%, specificity 83%, AUC 0.86). The direct comparison between MCI converters and nonconverters did not yield accurate results. **Conclusion:** The Italian version of the SCEB is a short (between 6 min in CONT and 12 min in DEP) screening tool in cognitive disorders of the elderly, and is potentially useful in clinical practice.

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Introduction

One of the current challenges in Alzheimer's disease (AD) is to identify cognitive changes that occur during the prodromal stage that precedes the manifestation of the overt dementia syndrome. The ability to identify cognitive decline prior to overt dementia has led to the adoption of the designation mild cognitive impairment (MCI) [1–4] for those with impaired performance on ob-

jective memory tests, or another cognitive domain, but with intact general cognition and daily functioning. MCI classification into the amnestic (amnestic MCI, aMCI) and nonamnestic (nonamnestic MCI, naMCI) types has been defined for objective impairment in either memory or non-memory cognitive domains, respectively. Multiple deficit may coexist, either including memory or not (multi-domain aMCI or naMCI).

Some studies suggest that subtle declines in episodic memory in the older adult presage the development of the dementia syndrome associated with AD [5–9], while other studies indicated that prodromal AD is characterized by subtle deficits in a broad range of neuropsychological domains, particularly in learning and memory, executive functioning, processing speed, attention, and semantic knowledge [10]. A cognitive screening will become increasingly important as part of routine in primary care of the elderly because dementia prevalence dramatically increases with age [11]. The Mini-Mental State Examination (MMSE) [12] is the most widely used instrument for the mental state examination, but it has been criticized both for its limited sensitivity [13, 14] and the influence that education has on performance [15, 16]. Moreover, the 3-item recall, the most important subtest to detect MCI and AD, seems to be poorly sensitive [17].

Other well-established, valid instruments for a brief screening for dementia are available, such as the Mini-Cog test [18], the Memory Impairment Screen [19], the General Practitioner Assessment of Cognition [20, 21], the Addenbrooke's Cognitive Examination Revised validated in main languages [22–26], the 7-Minute Screen [27] and the Short Cognitive Evaluation Battery (SCEB) [28]. The SCEB includes four tests representing four cognitive areas typically and early compromised in AD: (1) memory, (2) verbal fluency, (3) visuospatial and visuoconstruction and (4) orientation in time.

The memory subtest derived from Enhanced Cued Recall [29] has been shown to distinguish between benign forgetfulness of aging on the one hand and patients with AD, MCI, or depression [30, 31] on the other hand. Also, the category verbal fluency test seems accurate to distinguish between AD, MCI and normal control subjects [32]. Orientation in time is a good measure of cognitive status in AD [33] and it is included both in the MMSE and the Alzheimer Disease Assessment Scale-Cognitive [34] that are largely used in assessment of AD. Visuoconstructive deficits are common in patients with AD, and the clock drawing test is among the simplest and most sensitive visuoconstructive tasks even in MCI [35].

The SCEB has not been translated into Italian and validated yet, while it has already been validated in French [28]. The aim of this study was to validate an Italian version of the SCEB in order to improve the discrimination among patients with AD, depression and healthy controls (CONT). As compared to the original French version, we also included a group of patients with MCI.

Methods

Patients

The study population included consecutive Caucasian outpatients with mild AD, MCI, or major depressive disorder (DEP). A group of age-matched healthy volunteers was also enrolled. The study was conducted in two outpatient facilities (a neurologic one for AD, MCI and controls, a psychiatric one for depressed patients) of the same University Hospital. Both SCEB and MMSE [12] were administered by a skilled neuropsychologist. All MCI and AD patients were at their first ever neurological evaluation, whereas depressed patients were regularly followed as outpatients by the psychiatric unit. All of them gave their consent to participate in the study.

AD Group

The inclusion criteria were mild AD, as defined by an MMSE score between 17 and 27 (included). There were 29 patients (22 women and 7 men; mean age: 79.8 ± 6 years) who also underwent the ADAS-cog. The diagnosis of AD followed the NINCDS-ADRDA [36] and the DSM-IV criteria [37], and the presence of at least two cognitive deficits was documented by a wide neuropsychological battery, including standard tests for attention, language, verbal and spatial memory, visuoconstruction, and executive functions. The Clinical Dementia Rating Scale (CDR) was 1 in 21 patients and 2 in 8 patients. Subjects were not included if they were receiving treatment with acetylcholinesterase inhibitors or memantine.

Dementia with Lewy bodies, frontotemporal dementia and vascular dementia were ruled out according to current criteria [38–40]. Both secondary and mixed dementias were ruled out in all patients by a complete diagnostic protocol including general and neurological examinations, brain magnetic resonance imaging (MRI) or computed tomography in the case MRI was unfeasible due to contraindications, complete blood count, urinalysis, liver and kidney function tests, thyroid hormone assay, HIV antibodies, Venereal Disease Research Laboratory slide test, B₁₂ and folic acid assay. Patients with MRI/CT signs of stroke or large lesions of any kind were excluded, while the presence of leukoaraiosis and/or small white matter hyperintensities was not an exclusion criterion. Presence of illiteracy, major vision disturbances, psychiatric illnesses, confusion, epilepsy, major head trauma, Parkinsonism, previous stroke or TIA and brain masses were other exclusion criteria. Presence of severe and uncontrolled arterial hypertension, diabetes mellitus, renal, hepatic or respiratory failure, anemia (Hb level <10 mg/dl) or malignancies were other exclusion criteria. A mild depressive trait, i.e.

with a score lower than 6 on the 15-item Geriatric Depression Scale [41], was not an exclusion criterion. Neuropsychiatric symptoms were assessed by interviewing the informant with the neuropsychiatric inventory (NPI) [42]. Patients scoring higher than 0 on the delusion and the hallucination NPI items were excluded. Consistent with the diagnosis of AD, all patients scored lower than 4 on the modified Hachinski ischemic scale.

MCI Group

The inclusion criteria were the presence of an objective deficit in memory and/or other cognitive domains, with reference to age-matched healthy population, taking education into account. A wide neuropsychological test battery, including standard tests for attention, language, verbal and spatial memory, visuoconstruction, and executive functions was administered, according to the protocol described in detail elsewhere [43]. Both single-domain and multi-domain MCI, according to the Petersen criteria [1], were considered for enrolment. Dementia was excluded on the basis of clinical interview with the patient and caregiver, using the MMSE [12] for general cognition, questionnaires for the activities of daily living (ADL) [44] and instrumental ADL [45]. The CDR scale was 0.5 in all patients. Nine patients were on selective-serotonin reuptake inhibitor (SSRI) therapy and 3 took low-dose benzodiazepines or a hypnotic at bedtime.

The other inclusion/exclusion criteria were the same as in the AD group. There were 27 MCI patients (17 women, 10 men; mean age: 76.6 ± 6.6 years), including 15 patients with aMCI (mean age: 77.7 ± 6.6 ; mean MMSE score: 27.2 ± 1.8) and 12 patients with naMCI (mean age: 75.3 ± 3.8 ; mean MMSE score: 26.6 ± 2.3). MCI patients underwent clinical and neuropsychological follow-up on a yearly basis. Ten patients (8 with aMCI and 2 with naMCI, mean age at baseline: 78.1 ± 7.9 years; mean MMSE score at baseline: 25.7 ± 1.8) converted to AD dementia after a mean follow-up time of 58.2 ± 41.8 months. Fifteen patients (6 with aMCI and 9 with naMCI, mean age at baseline: 74.7 ± 3.6 ; mean MMSE score at baseline: 26.9 ± 2.2) remained substantially stable or improved after a mean follow-up time of 47.8 ± 46.6 months. The remaining 2 patients were lost at follow-up.

DEP Group

The inclusion criteria were a diagnosis of major depressive disorder according to the DSM-IV [37] criteria and a score higher than 17 on the Montgomery-Asberg Depression Rating Scale [46]. There were 27 patients, (20 women, 7 men; mean age: 73.0 ± 5.2 years; duration of symptoms since the diagnosis: 6–36 months, mean 16.2 ± 6.4). The other inclusion/exclusion criteria were the same as in the AD group. All patients were on treatment with antidepressants of the SSRI or the serotonin-norepinephrine reuptake inhibitor type. Moreover, 17 of them also received benzodiazepines, 4 anti-epileptic drugs, and ten low-dose anti-psychotics. No patients received tricyclic antidepressants. Drug dosage was stable for at least 2 weeks before patients were administered the SCEB. Dementia was excluded by means of the same protocol used in MCI patients. The CDR scale was 0 in all patients. All depressed patients were followed-up with clinical assessment, also including the CDR,

ADL and instrumental ADL scales for at least 2 years, during which none of them developed dementia.

CONT Group

Forty subjects contacted during University courses reserved to elderly people and 15 subjects contacted by the Italian Alpine Club were informed about the aim of the study and accepted to participate. They had their general medical histories carefully taken and underwent clinical examination. Exclusion criteria included previous or present neurological, psychiatric, metabolic or cardiovascular disorders, and current medication of any kind. Only subjects with an MMSE score higher than 28 and without mistakes in the 3-word delayed recall test were considered for this study. These criteria were fitted by 48 subjects (31 women, 17 men; mean age: 76.1 ± 6.0 years).

Demographic and main characteristics of the four groups of subjects are listed in table 1.

Short Cognitive Evaluation Battery

The SCEB consists of four tasks presented in the following order:

- a The temporal orientation test [47] assesses the patient's orientation in time, namely month, date, year, day of the week and time of the day. The test uses a graduated scoring system that reflects the degree of errors. Scores are given as follows: 5 points for each month of difference (maximum score 30), 1 point for each day of difference (maximum score 15), 10 points for each year of difference (maximum score 60), 1 point for each day of the week of difference (maximum score 3), 1 point every 30 min of difference (maximum score 5). The maximum error score is 113.
- b The 5-word test derived from the French short version [48] of the enhanced cued recall test. For the Italian version, we translated the French words (*museo*, *limonade*, *sauterelle*, *passoire* and *camion*) into Italian and used the words that have a similar frequency of use [49]. *Museo* and *camion* were unchanged. *Passoire*, *sauterelle* and *limonade* were replaced maintaining the same semantic category to *padella*, *farfalla* and *aranciata*. Thus, the Italian version of the 5-word test includes *museo*, *aranciata*, *farfalla*, *padella* and *camion* (for museum, orange juice, butterfly, pan and truck). Each participant was presented with a sheet of paper containing the list of 5 words to be recalled, each item belonging to a different category. The individual was asked to read the items aloud and then to identify and name each item when the assessor provided its semantic category cue. The list was then removed, and the individual was immediately asked to recall each item. For those items that were not spontaneously recalled by the subject, the semantic cue was provided. In case of error, the procedure could be repeated up to 3 times, because the objective was to ensure that all the 5 items were registered before evaluating long-term recall abilities. After a nonverbal interference task (clock drawing test), the individual was asked to recall the 5 items in any order. The category cues were then used to elicit cued recall of only those items that were not retrieved by free recall. The score in the SCEB was the sum of the free and cued delayed recall with a maximum score of 5.

Table 1. Age, gender, education and MMSE: characteristics in the four groups of subjects

	AD (n = 29)	MCI (n = 27)	DEP (n = 27)	CONT (n = 48)
Age, years	79.1±6.1	76.6±6.5	72±5.5	75.1±6
Range	61–88	66–94	61–84	65–92
Male/female	0.32 (7/22)	0.59 (10/17)	0.5 (9/18)	0.55 (17/31)
MMSE	22.1±3.1	26.5±2.0	26.9±2.8	29.7±0.5
Range	17–27	22–30	21–30	29–30
Years of full education	7.4±4.3	7.3±4.3	7.7±2.8	11.4±3.6
Range	3–18	1–17	5–13	4–18

MMSE = Raw MMSE scores. Values for age, MMSE and years of education are expressed as mean ± SD.

c In the clock drawing test [50], the subject had to draw a clock with all the numbers and to draw the clock hands at twenty minutes to four. The scoring procedure is the same as that used by Solomon et al. [27]. The score ranges from one (worst) to seven (best).

d In the semantic verbal fluency test [51], the subject was asked to generate as many words as possible from a given category, animals, in a fixed time period of 60 s. One point was given for each appropriate answer.

The total SCEB score was computed by summing up the score on each of the four tests, with negative sign for temporal orientation.

Statistical Analysis

Statistical analysis was performed by means of the 'R' software [52], and $p < 0.05$ was considered as the first level of statistical significance.

In a preliminary analysis, the MMSE scores, corrected for age and education according to Magni et al. [53], underwent ANOVA using group belonging (CONT, DEP, MCI, AD) as a factor. For descriptive purposes, the time taken to perform SCEB was also analyzed among groups by means of ANOVA. In both instances, post-hoc analyses were carried out between groups in the case of significant result for each ANOVA.

As a first step of SCEB analysis, SCEB data were evaluated by a multivariate analysis of covariance (MANCOVA) using the Wilks' lambda statistics. The scores on the four SCEB tests (temporal orientation, 5-word, clock drawing and semantic verbal fluency) were the dependent variables; group belonging was considered as a factor; age, gender and education were considered as confounding variables. In the case MANCOVA yielded significant results, multiple post-hoc comparisons were performed between groups by means of the unpaired t test. Comparability of variance among groups was tested by means of Levene's test. Then, to correct for multiple comparisons, either Bonferroni's (comparable variance among groups) or Tamhane's (variance not comparable among groups) correction was used.

As a second step, receiver operating characteristic (ROC) analysis was performed for each of the 4 test scores as well as

for the total SCEB score to show the relationship between sensitivity and specificity as a function of the cutoff value. To obtain the optimal cutoff for group discrimination, the distance between the point of maximum sensitivity and specificity (i.e. the upper left corner in fig. 1–5) and the ROC curve was computed, the best cutoff point being established at the minimum distance. The area under the curve (AUC) was also computed for the four tests and the total SCEB in each group comparison.

As a final step, multivariate logistic regression was applied to predict group membership (between pairs of groups labeled as 0 and 1) from the set of the four tests. The independent variables were the four tests, and the dependent variable was group belonging probability. For every 1-unit change in a given SCEB test, the odds ratio drawn from logistic regression coefficient provides an estimation of the relative rate of increase/decrease in probability of being in group 1 instead of group 0.

Results

MMSE Score (table 1)

A significant effect of group was found for age- and education-corrected MMSE score ($F_{3, 127} = 66.2$, $p < 0.0001$). Post-hoc comparisons showed that AD scored lower than the other groups ($p < 0.0001$), while CONT scored higher than the other groups ($p < 0.0001$). There was no significant difference between DEP and MCI groups. A significant correlation was found between the SCEB and the MMSE scores in all subjects ($r = 0.73$; $p < 0.0001$) as well as within the AD group ($r = 0.59$, $p < 0.01$).

Time Taken to Perform SCEB (table 2)

A significant effect was found for group ($F_{3, 127} = 18.9$, $p < 0.0001$). Post-hoc analysis showed that time was significantly shorter in CONT than in AD and DEP ($p < 0.0001$), and was shorter in MCI than in DEP ($p < 0.001$).

Table 2. Administration time and mean scores (\pm SD) of the four tests in the four patient groups

	AD (n = 29)	MCI (n = 27)	DEP (n = 27)	CONT (n = 48)
Administration time, min	10.3 \pm 3.0	8.0 \pm 2.6	12.5 \pm 6.9	6.1 \pm 1.7
Temporal orientation	40.6 \pm 33.2	3.1 \pm 7.0	3.1 \pm 5.3	0.1 \pm 0.4
5-word test	3.0 \pm 1.8	4.7 \pm 0.5	4.8 \pm 0.4	5.0 \pm 0
Clock drawing	1.9 \pm 1.7	4.2 \pm 2.1	3.2 \pm 2.2	6.1 \pm 0.9
Semantic verbal fluency	8.3 \pm 2.9	12.7 \pm 4.9	13.8 \pm 6.9	18.5 \pm 3.4

Table 3. Summary of diagnostic values for each of the four SCEB tests: CONT vs. AD groups

	Temporal orientation	5-word test	Clock drawing	Verbal fluency	Total SCEB test
Se, %	82.76	79.66	89.21	96.55	93.10
Sp, %	87.92	82.42	90.15	93.75	92.33
PPV, %	84.30	83.76	87.56	90.32	90.00
NPV, %	87.13	84.00	90.69	97.83	95.74
Accuracy, %	84.70	80.62	89.84	95.01	92.77
AUC	0.88	0.83	0.94	0.98	0.96
Cutoff point	1	3	4	14	2

Se = Sensitivity; Sp = specificity; PPV = positive predictive value; NPV = negative predictive value.

MANCOVA and post-hoc Analysis

Table 2 shows mean (\pm standard deviation) results of the four tests. MANCOVA showed a main effect of group ($F_{12, 297} = 18.2, p < 0.0001$), taking age and education into account; there was no effect of gender. At post-hoc comparisons, the AD group was significantly ($p < 0.0001$) impaired on temporal orientation as compared to the other groups. On the 5-word test, the AD group scored lower than the other groups ($p < 0.001$), while CONT scored higher ($p < 0.0001$) compared to DEP and MCI. No significant difference was found between MCI and DEP. On clock drawing, the AD group was significantly impaired compared to CONT ($p < 0.0001$), MCI ($p < 0.0001$) and DEP ($p < 0.05$), while CONT performed significantly better than the other groups ($p < 0.0001$), and DEP did not differ from MCI. As for semantic verbal fluency, CONT scored higher ($p < 0.0001$) than the other groups and AD scored lower ($p < 0.002$) than the other groups, whereas DEP and MCI did not differ from each other.

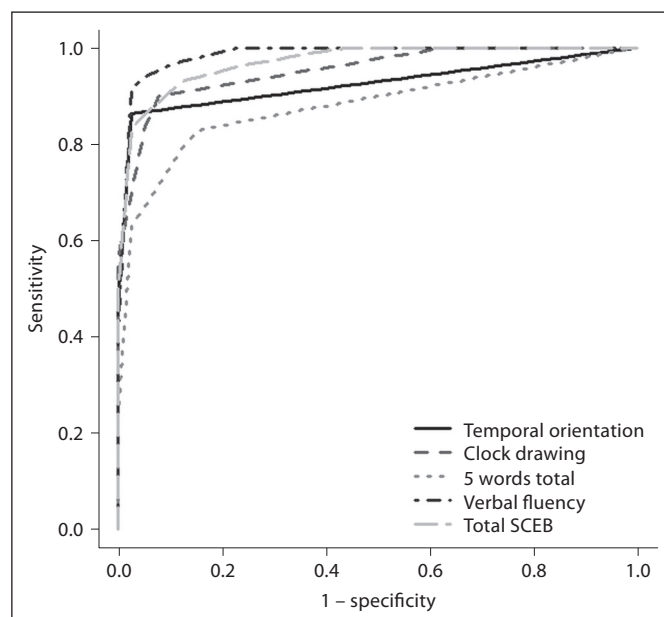


Fig. 1. ROC curves for the four tests and the SCEB total score in the comparison between AD patients and CONT. See ‘Results’ and table 3 for numerical details.

ROC Analysis and Multivariate Logistic Regression

AD versus CONT (table 3; fig. 1)

Accuracy of the total SCEB was 92.8%, with 93.1% sensitivity and 92.3% specificity, and the AUC was 0.96. All tests showed a high discriminant power between the two groups, with some differences. The highest accuracy was achieved by verbal fluency, followed by clock drawing, temporal orientation, and the 5-word test in this order. Both sensitivity and specificity were virtually always higher than 80%. Verbal fluency was more sensitive than specific, whereas temporal orientation was more specific than sensitive. Multivariate logistic regression showed the highest statistical significance for clock drawing (odds ratio 0.19; 95% confidence intervals, CI: 0.07–0.36; $p < 0.0001$) and verbal fluency (odds ratio 0.40; 95% CI: 0.21–0.57; $p < 0.0001$), followed by the 5-word test (odds ratio 0.15; 95% CI: 0.05–0.31; $p < 0.001$) and by temporal orientation (odds ratio 2.80; 95% CI: 1.46–12.60; $p < 0.01$).

AD versus DEP (table 4; fig. 2)

Accuracy for the total SCEB was 84.5%, with 76.0% sensitivity and 92.6% specificity, and the AUC was 0.84. Temporal orientation and 5-word test showed a good accuracy (higher than 80%), the former being more spe-

Table 4. Summary of diagnostic values for each of the four SCEB tests: AD vs. DEP groups

	Temporal orientation	5-word test	Clock drawing	Verbal fluency	Total SCEB test
Se, %	75.86	82.76	72.41	80.51	76.01
Sp, %	88.89	76.25	62.96	66.67	92.59
PPV, %	88.00	81.05	67.74	72.73	91.67
NPV, %	77.42	81.48	68.00	78.26	78.12
Accuracy, %	83.06	80.96	68.07	74.99	84.46
AUC	0.87	0.88	0.67	0.79	0.84
Cutoff point	1	4	3	10	2

Table 5. Summary of diagnostic values for each of the four SCEB tests: MCI vs. CONT groups

	Temporal orientation	5-word test	Clock drawing	Verbal fluency	Total SCEB test
Se, %	33.33	35.27	62.83	82.50	70.11
Sp, %	97.92	85.42	74.85	77.08	87.50
PPV, %	90.00	86.25	58.60	68.51	75.30
NPV, %	72.31	69.49	76.95	88.10	82.35
Accuracy, %	74.71	60.82	71.58	78.74	80.15
AUC	0.66	0.60	0.70	0.83	0.80
Cutoff point	2	4	5	16	1

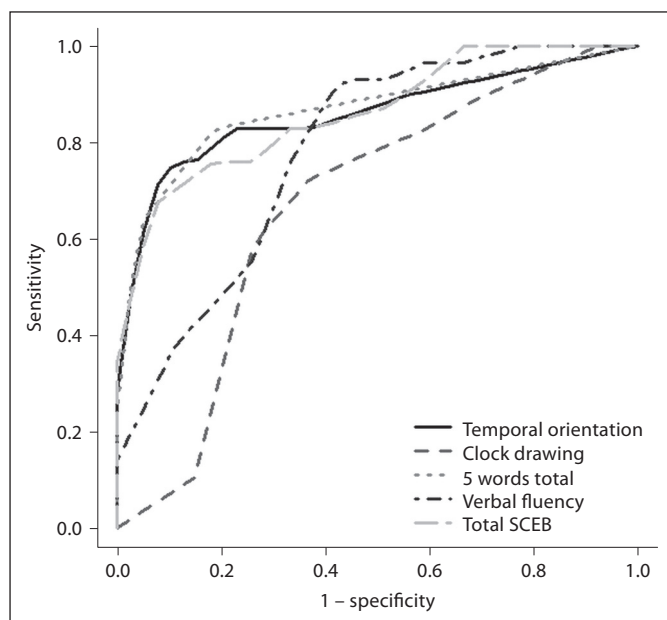


Fig. 2. ROC curves for the four tests and the SCEB total score in the comparison between AD patients and depressed patients. See 'Results' and table 4 for numerical details.

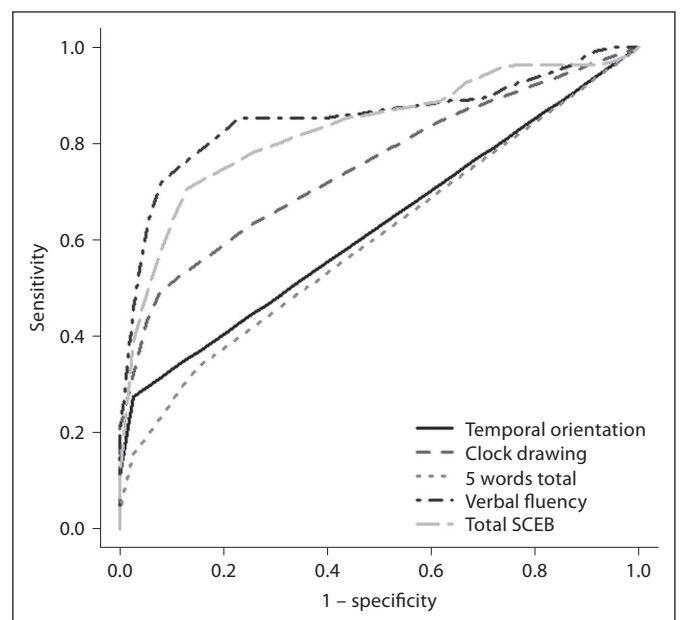


Fig. 3. ROC curves for the four tests and the SCEB total score in the comparison between patients with MCI and CONT. See 'Results' and table 5 for numerical details.

cific than sensitive and the latter more sensitive than specific. Clock drawing and verbal fluency showed only moderate accuracy (lower than 80%), and both were much more sensitive than specific. Multivariate logistic regression showed the highest statistical significance for verbal fluency (odds ratio 0.72; 95% CI: 0.57–0.85; $p < 0.001$) followed by the 5-word test (odds ratio 0.19; 95% CI: 0.06–0.43; $p < 0.001$), temporal orientation (odds ratio 1.17; 95% CI: 1.06–1.29; $p < 0.01$) and clock drawing (odds ratio 0.26; 95% CI: 0.12–0.54; $p < 0.05$).

MCI versus CONT (table 5; fig. 3)

Accuracy for the total SCEB was 80.1%, with 70.1% sensitivity and 87.5% specificity, and the AUC was 0.80. Verbal fluency reached the highest accuracy (78.7%), followed by temporal orientation, clock drawing and 5-word tests which showed moderate accuracy (between 61 and 75%). Verbal fluency was also the most sensitive (82.5%) while both temporal orientation and 5-word test were highly specific but very poorly sensitive (33 and 35%, respectively). Multivariate logistic regression showed the

Table 6. Summary of diagnostic values for each of the four SCEB tests: MCI converters vs. CONT groups

	Temporal orientation	5-word test	Clock drawing	Verbal fluency	Total SCEB test
Se, %	30.21	20.00	39.97	80.34	75.15
Sp, %	96.73	86.72	74.69	79.16	86.30
PPV, %	87.04	83.67	25.00	42.11	40.04
NPV, %	75.27	66.34	84.66	94.87	94.74
Accuracy, %	86.89	74.31	69.66	79.53	84.81
AUC	0.64	0.53	0.63	0.82	0.86
Cutoff point	3	3	4	15	3

Abbreviations as in tables 1 and 3.

highest statistical significance for verbal fluency (odds ratio 0.68; 95% CI: 0.55–0.80; $p < 0.0001$) followed by clock drawing (odds ratio 0.16; 95% CI: 0.08–0.45; $p < 0.001$), the 5-word test (odds ratio 0.15; 95% CI: 0.06; 0.47; $p < 0.01$) and temporal orientation (odds ratio 2.36; 95% CI: 1.22–7.89; $p = 0.06$).

MCI Subgroups

MCI population is heterogeneous because patients with prodromal AD are mixed with patients with a variety of other disorders. Thus, we also explored the SCEB data by dividing MCI patients into those who converted to AD dementia during the follow-up (MCI converters) and those who did not convert to dementia (nonconverters; see description above in ‘Methods’). We compared MCI converters with CONT to verify the SCEB diagnostic power even in prodromal AD, and MCI nonconverters with AD to assess the ‘specificity’ of the SCEB in identifying AD from other heterogeneous causes of cognitive impairment.

MCI Converters versus CONT (table 6; fig. 4)

Accuracy for the total SCEB was 84.8%, with 75.0% sensitivity and 86.3% specificity, and the AUC was 0.86. Temporal orientation reached the highest accuracy (86.9%), whereas verbal fluency, clock drawing and 5-word tests showed moderate accuracy (between 70 and 80%). Verbal fluency was again the most sensitive (80%), while both temporal orientation and 5-word test were highly specific but very poorly sensitive. Multivariate logistic regression showed a statistical significance just for verbal fluency (odds ratio 0.66; 95% CI: 0.48–0.84; $p < 0.01$).

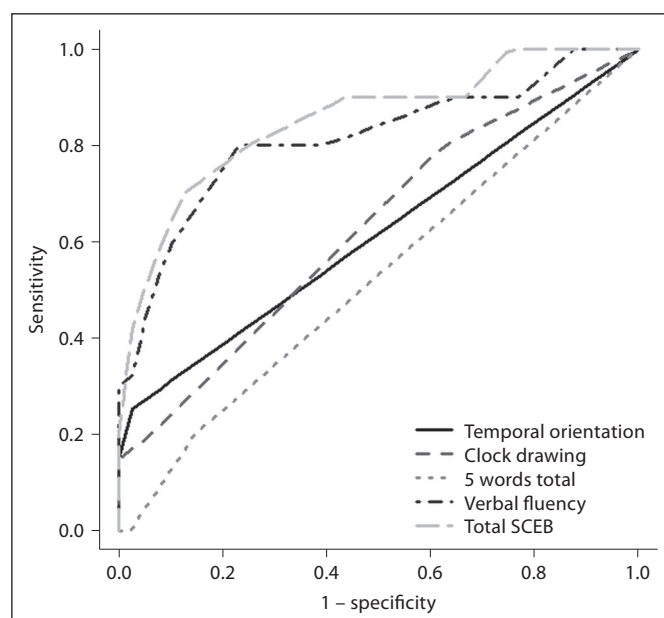


Fig. 4. ROC curves for the four tests and the SCEB total score in the comparison between patients with MCI who converted to AD dementia during the follow-up and CONT. See ‘Results’ and table 6 for numerical details.

Table 7. Summary of diagnostic values for each of the four SCEB tests: MCI non-converters vs. AD groups

	Temporal orientation	5-word test	Clock drawing	Verbal fluency	Total SCEB test
Se, %	79.31	57.14	58.62	82.11	82.29
Sp, %	85.71	82.64	92.86	74.58	87.57
PPV, %	80.42	61.54	52.00	64.29	68.75
NPV, %	92.00	80.23	94.44	84.37	87.51
Accuracy, %	81.85	74.62	70.47	77.46	83.51
AUC	0.85	0.78	0.76	0.74	0.81
Cutoff point	2	4	5	11	4

MCI Nonconverters versus AD (table 7; fig. 5)

Accuracy for the total SCEB was 83.5%, with 82% sensitivity and 88% specificity, and the AUC was 0.81. Temporal orientation reached the highest accuracy (82%), whereas the other tests showed moderate accuracy (between 70 and 77%). Temporal orientation showed both good sensitivity and specificity, whereas the 5-word test and clock drawing were rather specific but poorly sensitive, and verbal fluency showed the opposite figures.

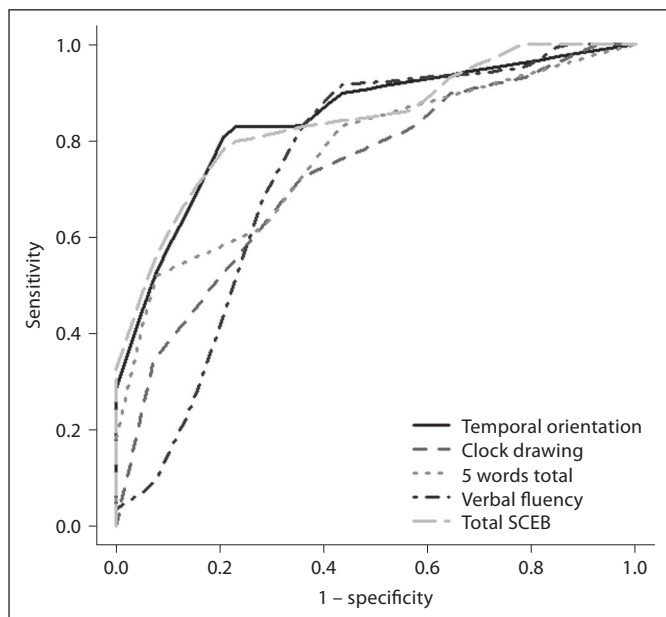


Fig. 5. ROC curves for the four tests and the SCEB total score in the comparison between patients with MCI who did not convert to AD dementia during the follow-up and AD patients. See 'Results' and table 7 for numerical details.

Multivariate logistic regression showed similar statistical significance for all tests: verbal fluency (odds ratio 0.76; 95% CI: 0.53–0.94; $p < 0.01$); clock drawing (odds ratio 0.63; 95% CI: 0.46–0.74; $p < 0.01$); 5-word test (odds ratio 0.49; 95% CI: 0.23–0.71; $p < 0.01$); temporal orientation (odds ratio 1.09; 95% CI: 0.82–1.47; $p < 0.05$).

MCI Nonconverters versus MCI Converters

Accuracy for the total SCEB was 58.3%, with 50.1% sensitivity and 64.3% specificity, and the AUC was 0.52. Verbal fluency reached the highest accuracy (75%), whereas the other tests showed little accuracy (between 54 and 71%). Multivariate logistic regression showed only a weak statistical significance for the clock drawing test (odds ratio 0.59; 95% CI: 0.32–0.95; $p < 0.05$).

Discussion

Accurate dementia screening tools in the primary care setting are of paramount importance. These instruments should be brief, easy to administer, acceptable to older persons, minimally affected by education, gender, age, and other factors unrelated to dementia, and having high sensitivity and specificity.

This study demonstrates that the Italian version of the SCEB is able to discriminate between patients with relatively mild AD (mean MMSE score of about 22) and normal elderly people with extremely high accuracy (93%) and in a mean administration time of 10 min in AD patients and 6 min in controls. This time is just in the range of the time needed to complete the MMSE. Among the SCEB tests, semantic verbal fluency showed the highest accuracy (95%), which is consistent with the original paper of Robert et al. [28] who found a sensitivity of 90%. The sensitivity of the total score was comparable to the French version (93.1% in the Italian version, 93.8% in the French one), whereas specificity was a bit higher in the Italian (92.3%) than in the French (85%) version.

The sensitivity and specificity in distinguishing between AD patients and controls were higher for the SCEB than what was reported for the MMSE in the literature. Mitchell [54] in a recent meta-analysis of 34 dementia studies and 5 MCI studies found that in memory clinic settings the MMSE had a pooled sensitivity of 79.8% and a specificity of 81.3%; in mixed specialist hospital settings, the sensitivity and specificity were 71.1 and 95.6%, respectively, and in nonclinical community settings the MMSE had a pooled sensitivity of 85.1% and a specificity of 85.5%. Several other studies [55–57] have emphasized that the sensitivity of the MMSE is lower when patients are examined in the early stages of dementia. Tombaugh and McIntyre [58] found that the sensitivity of the MMSE decreased to 44–68% in mild AD with an MMSE score above 20. It is worth emphasizing again that our sample was composed of individuals with relatively mild AD (mean MMSE score: 22.1 ± 3.1).

The Italian version of SCEB has also showed definitely higher sensitivity and specificity in distinguishing between demented patients and old controls, as compared with several other short screening scales. In the review article by Ismail et al. [59], the Mini-Cog test has been reported to have a sensitivity of 76% and a specificity of 89% in the identification of dementia from nondemented individuals. The Memory Impairment Screen was reported to have similar specificity (96%) as the Italian SCEB, but lower sensitivity (80%) in identifying dementia, and the General Practitioner Assessment of Cognition achieved values of 85 and 86% for sensitivity and specificity, respectively. It should be noted that the above results can be just roughly compared with the present ones because the Italian SCEB concerns the differentiation of mild AD from healthy controls, whereas the other studies refer to dementia more in general.

On the other hand, the 7-Minute Screen performed very similar to the Italian SCEB. The two batteries are composed of 4 sub-tests and differ only in memory task. The 7-Minute Screen is composed of pictures, whereas the 5-word test is composed of verbal items. In their validation study, Solomon et al. [27] obtained sensitivity and specificity of 92 and 96%, respectively, in separating AD patients from normal controls. In the 7-Minute Screen, administration time was a bit longer in controls but a bit shorter in AD patients than in the Italian SCEB. All these results are quite similar to those achieved by the Italian SCEB version, although the sample of AD patients in the study by Solomon et al. [27] was a bit more severely demented and with a wider heterogeneity (mean MMSE score: 21.0 ± 7.8) than the present sample (mean MMSE score: 22.1 ± 3.1).

A common confounder in clinical practice is depression and the so called 'pseudo-depressive' dementia syndrome. The Italian SCEB has shown satisfying accuracy (84.5%) in identifying AD patients and depressed patients, with higher specificity (92.6%) than sensitivity (76.0%). Compared to the French version, sensitivity was definitely higher (76.0 vs. 63.0%), while specificity was a bit lower (92.6 vs. 96%). Verbal fluency and temporal orientation were the tests reaching the highest total accuracy between AD and depressed patients, with verbal fluency and the 5-word test being the most sensitive. Sexton et al. [60] found that the depression group performed significantly worse in many cognitive domains, including episodic memory and language skills, in comparison with normal controls. Sheline et al. [61] reported that processing speed appears to be the most core cognitive deficit in late life depression, and this could explain the longest time taken to perform the SCEB. These impairments as well as the use of multiple drugs in depressed patients as compared to the MCI group could be the reason for the lack of accuracy of the SCEB in distinguishing between these two groups. However, extensive neuropsychological testing was not available in the DEP group, which could have confirmed MCI in these patients too, and this may be regarded as a limitation of this study. Moreover, one third of MCI patients were on therapy with low to medium dose of SSRI, which could represent a bias toward execution of the SCEB. However, this is a typical situation in an outpatient memory clinic, and reflects the naturalistic MCI population, a part of which is aware of cognitive impairment and may develop reactive depression. Alternatively, some patients who already are on the path to AD may have depression as a psychological symptom of their underlying neurodegenerative process.

The Italian SCEB (comparable data not available in the French version) showed a discrete (80.2%) accuracy even in identifying MCI from controls. However, while specificity was rather good (87.5%), sensitivity was too low (70.1%). By considering each test, verbal fluency was the most sensitive (82.5%), whereas temporal orientation was the most specific reaching 97.9%. This can be extremely useful information in clinical practice, suggesting that if a patient with subtle cognitive deficit scores low on temporal orientation, he/she is almost surely affected at least by the MCI syndrome. When we divided the MCI patients into MCI converters (10 patients only) and nonconverters (15 patients) and compared the MCI converters with healthy controls, the accuracy of the SCEB increased to 84.8%; verbal fluency and temporal orientation were again the most sensitive and specific, respectively. Thus, even at this stage of what is now defined as 'prodromal' AD (according to the new lexicon) [62], the Italian SCEB has shown some usefulness in differentiating patients from controls, taking into consideration that it is just a short screening battery, with obvious intrinsic limitations.

Interestingly, the accuracy was satisfying even in identifying nonconverter MCI patients from AD patients, reaching the 83.5%. The clock drawing test was the most specific (93%) among tests, thus suggesting that an MCI patient who draws a good clock is unlikely to be on the path of AD. However, the results achieved in the MCI subgroups should be regarded as preliminary findings and considered with caution, because the two subgroups were composed of a very limited number of subjects. Thus, the data in MCI subgroups need to be confirmed in larger samples of patients.

The direct comparison between MCI converters and MCI nonconverters yielded a very limited accuracy. Thus, it appeared that such a short screening battery has not enough power to identify these subgroups of MCI patients when their deficit is so mild. This issue cannot be solved by means of a short battery, and even a more extended neuropsychological evaluation is often inaccurate, leading to the use of biomarkers instead.

As far as the individual tests are concerned, all of them were almost equally accurate in the differentiation of AD patients from controls. However, verbal fluency and temporal orientation generally performed better than the 5-word test and clock drawing. In detail, temporal orientation was accurate in the comparison between AD and DEP as well as between AD and MCI nonconverters. Verbal fluency was accurate in distinguishing between MCI and controls as well as between MCI converters and

controls. As such, temporal orientation seems to be the key tool to identify AD, whereas verbal fluency seems to be the hallmark of MCI and possibly of prodromal AD (i.e. MCI converters). This impairment in categorical verbal fluency in MCI syndrome is in keeping with the finding that elderly patients with aMCI were impaired in generating lists of animals [63], while unimpaired in letter fluency [64].

In summary, it has been shown that the Italian version of the SCEB is very accurate in discriminating be-

tween patients with relatively mild AD and age-matched control subjects. It can be administered at a time that is similar to that needed to administer the MMSE, and the scoring system is easy. It can also be used to improve discrimination between AD and depressed patients, while in prodromal AD it can be of some use (i.e. 85% accuracy) and give interesting qualitative information. Its accuracy in identifying other dementing illnesses remains to be investigated.

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