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The Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI)

General description

The CANS-MCI was designed to measure all of the cognitive domains known to be most predictive of Alzheimer's disease (AD): immediate and delayed memory; attentional speed and flexibility; executive mental control; clock hand placement fluency; language fluency. A short form of the CANS-MCI is available that just measures attentional speed and flexibility; executive mental control; immediate memory; and delayed recall.

- Mental control is measured with a Stroop test (on which the user matches the ink color of word names rather than the name itself).
- Spatial abilities are evaluated with: a general reaction time test with minimal cognitive complexity (on which the user touches ascending numbers presented on a jumbled display); design-letter matching; word-to-picture matching; and a clock hand placement test (touching the hour and minute positions for a series of 10 digital times).
- Memory for 20 object names is measured with immediate and delayed free and guided recognition tests.
- Language fluency is tested with a picture naming test (on which 28 pictures are consecutively presented for the selection of 1 out of 4 2-letter word beginnings).
- The CANS-MCI also includes progressive questions about possible causes of cognitive abnormality (e.g. depression, alcohol abuse, head injury history, pain medication) and preventive **action** (e.g. years of physical exercise). Progressive questioning works by having the number of questions depend upon the symptom presence and severity detected by previous questions.

Usability

The CANS-MCI is a Windows native application, installed on medical facility computers that have internal or connected touch-enabled monitors. The touch screens must be of adequate size for geriatric reading and touching (11.3" to 19" integrated widescreen touchscreen capable of displaying 640 x 480 resolution with a preserved aspect ratio). The software is free and is located on the medical facility's testing computer.

The CANS-MCI does not require a response other than a finger touch or the presence, much less training, of a test administrator. Years of CANS-MCI usability research funded by the VA and SBIR grants from NIH resulted in its ability to be fully self-administered in a doctor's office by elderly people (even by those with MCI), regardless of computer experience, without causing anxiety-based cognitive interference during testing (Hill & Hammond, 2000).
When the tests are complete, the data are automatically sent to a central server where they are kept for longitudinal comparisons. Scoring and longitudinal comparison test analysis is performed by an independent neuropsychology-trained technician who does not know the identity of person tested. Software, installation, support and confidential data storage are free. A charge is made for each completed report, returned to the medical facility within an hour of test completion.

The CANS-MCI has been commended for its exceptional usability with geriatric patients (Wild et al, 2008). After any staff member enters the facility's patient's code number, their age, sex, and education, the staff member can leave the room. No other computer-assisted test battery accomplishes 100% of test administration without the presence of a staff member. Other tests that are administered online are too influenced by the testing environment to be valid or

reliable, unless administered in a controlled facility environment where a staff member can confirm appropriate testing conditions.

Emory Hill and Kenric Hammond. The Usability of Multimedia Automated Psychological Tests to Screen for Alzheimer's Disease. Proceedings of the American Medical Informatics Association Symposium 2000; 1030.

Wild, K., Howieson, D., Webbe, F., Seelye, A., Kaye, J. Status of computerized cognitive testing in aging: a systematic review. Alzheimer's & Dementia: Journal of the Alzheimer's Association, Volume 4, No. 6, 428-437, 2008.

Normative data

USA - A community sample of 400 elderly people was recruited through senior centers, American Legion halls, and retirement homes in four counties of Washington State. Exclusionary criteria were non-English language, significant hand tremor, inability to sustain a seated position for 45 minutes, recent surgery, cognitive side effects of drugs, indications of recent alcohol abuse, or inadequacies in visual acuity, reading ability, hearing, or dominant hand agility. The subjects were predominantly Caucasian (86%), female (65%), and had at least some college education (76%). Subject age ranged from 51–93 years, with the majority between 60–80 years of age (63%).

Brazil - Ninety-seven older adults (age range: 65 to 88 years) with moderate to high education (4 to 20 years of formal education) and predominantly female (71%), were selected to participate if they were at least 65 years of age. All participants were volunteers in a prospective study on cognitive aging, currently in course at the Institute of Psychiatry, University of São Paulo. The translated and culturally adapted version of the battery maintained all of its original psychometric characteristics. In spite of linguistic and cultural differences, the internal consistency reported for the Brazilian version of CANS-MCI was quite similar to the one reported by Tornatore et al (2005), and the tests were similarly stable over time.
The duration of test administration with AD subjects was described by Memoria et al as a deficiency of the CANS-MCI.* However, all individuals, including all with early AD, completed the tests and offered positive feedback.

Relevant publications:

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Mary E. McGann. Self-Administered Screening for Mild Cognitive Impairment: Validation of a Computerized Test Battery. Journal of Neuropsychiatry and Clinical Neurosciences, Volume 17, No. 1, 98-105, 2005.

Cláudia M. Memória, Mônica S. Yassuda, Eduardo Y. Nakano and Orestes V. Forlenza. Contributions of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) for the diagnosis of MCI in Brazil. International Psychogeriatrics, Volume 26 / Issue 09 / 1483-1491, 2014.

* The problem of lengthy administration time was eliminated in 2014, using early detection of speed limitations and omission of fluency tests, when necessary, to equalize the time between immediate and delayed memory tests for all patients. The most precise measurement of memory was thus improved for patients with impaired memory, at the expense of the less-predictive fluency tests.

Reliability and validity

Convergence with biomarkers

Memória *et al* (2014) evaluated the CANS-MCI's validity using diagnostic groups established according to their global cognitive state (normal controls, n = 41; MCI, n = 35; AD, n = 21). "These diagnoses were ascertained clinically at multidisciplinary consensus sessions, taking into account medical, neuropsychological, laboratorial, and neuroimaging data." However, the relative contribution of neuroimaging data to the cognitive state grouping was not reported.

Preliminary (2016) analysis of ongoing longitudinal data collection by Frederick A Schmitt, PhD Department of Neurology, Alzheimer's Disease Research Center, University of Kentucky Medical Center (Co-director of the Memory Disorders Clinic and Co-director of the Biostatistics and Data Management Core) had indicated significant relationships between CANS-MCI Memory and Executive Function Factors and imaging data. In the first 48 cases analyzed, the CANS-MCI memory factor score (CANS-MEM) and executive functioning factor score (CANS-EXEC) showed significant

declines in subjects who had initially tested as completely normal according to Uniform Data Set (UDS) criteria and numerous research oriented cognitive instruments but subsequently showed declines in research cognitive testing, but would not be officially classified as MCI or demented by UDS criteria. A subset of the Kentucky subjects (N=21) was also assessed with volumetric MRI, revealing that CANS-MEM was positively related to hippocampal brain volume (right hippocampus: r=.43, p<.05; left hippocampus: r=.38, p<.08). These provocative findings from the Kentucky data set indicated that the CANS-MEM and CANS-EXEC were sensitive to early cognitive changes which are "pre-clinical" in nature, occurring before any formal diagnosis of MCI or dementia is likely to occur, while the hippocampal imaging results suggested that CANS-MEM differences reflect differences in brain volume.

The Kentucky pilot studies were followed by a full study that examined cerebrospinal fluid (CSF), amyloid β 1-42 (Aβ), tau levels, and performance on the CANS-MC (Barber et al, 2018). Compared to the Aβ-Tau- group, the Aβ+Tau- and Aβ+Tau+ groups showed significant CANS-MCI performance deficits in memory, visuospatial, and executive domains. The Aβ+Tau+ group performed below the Aβ-Tau- group on the test of language fluency. They concluded that, "Performance on the CANS-MCI is sensitive to heightened Aβ and tau brain deposition." The CANS-MCI has established itself as the only test battery that can efficiently predict the need to perform expensive and invasive biomarker diagnostic tests.

Justin M. Barber, Brooke F. Beech, Gregory A. Jichaa, Allison Caban-Holt, Emory Hill, Fred Schmitt. CSF Markers of Preclinical Alzheimer's and Deficits on a Self-Administered Computerized Test Battery, the CANS-MCI. AAIC 2018, Chicago. Abstract ID: 25554.

Predictive validity

There is good agreement between the CANS-MCI measures and the results of well-known "gold standard" Mild Cognitive Impairment tests.

CORRELATIONS BETWEEN CONVENTIONAL TESTS WITH THE CANS-MCI SUBTESTS (MEMÓRIA ET AL, 2014)

COGNITIVE DOMAINS	STANDARDIZED (CANS-MCI) CANS-MCI SCORE†	CORRELATION TEST SCORE	COEFFICIENT	P-VALUE
Executive functions	Picture naming (latency)	Digit symbol	−0.61	<0.001∗
	Stroop (discordant latency)	Digit symbol	−0.49	<0.001∗
	Word-to-picture matching (latency)	Digit symbol	−0.44	<0.001∗
Immediate recall	Free recognition I	RAVLT – sum of words from A1 through A5	0.59	<0.001∗
Delayed recall	Free recognition II	Delayed recall of RAVLT – A7	0.50	<0.001∗
Composite memory score	Free recognition I & II	RAVLT – sum of words from A1 through A5	0.54	<0.001∗
		Delayed recall of RAVLT – A7	0.57	
Language/spatial fluency	Design Matching	Digit symbol	0.38	0.003
	Clock Hand Placement	Digit symbol	0.37	0.004
	General reaction time	Digit symbol	−0.65	<0.001∗
	Picture Naming	Semantic verbal fluency	0.49	<0.001∗
Total domains	All subtests	MoCA test	0.76	<0.001∗

†Based on z-score.

∗Correlation is significant at 0.01 level (2-tailed).

Cláudia M. Memória, Mônica S. Yassuda, Eduardo Y. Nakano and Orestes V. Forlenza. Contributions of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) for the diagnosis of MCI in Brazil. International Psychogeriatrics, Volume 26 / Issue 09 / 1483-1491, 2014.

CORRELATIONS OF CONVENTIONAL TESTS WITH CANS-MCI TESTS (TORNATORE ET AL, 2005)

Cognitive Domain (CANS-MCI)	CANS-MCI	Standardized Test Score	Correlation Coefficient	P
Executive Functions	General Reaction Time†	Digit Symbol	-0.530	0.001
	Design Matching	Digit Symbol	0.644	0.001
	Word-To-Picture Matching(Latency)†	Digit Symbol	-0.610	0.001
	Clock Hand Placement	Digit Symbol	0.502	0.001
	Stroop (Discordant Latency) †	Digit Symbol	-0.589	0.001
Immediate Recall	Free Recognition I	DRS Memory	0.506	0.001
	WMS LMS-I	0.563 0.001		
	Guided Recognition I Errors	DRS Memory	-0.567	0.001
	WMS LMS-I	-0.493 0.001		
Delayed Recall	Free Recognition II	DRS Memory	0.526	0.001
	WMS LMS-II	0.458 0.001		
Composite Memory Score	Free Recognition I & II	DRS Memory	0.553	0.001
	WMS LMS-I	0.519 0.001		
	WMS LMS-II	0.538 0.001		
Spatial Fluency	Clock Hand Placement	DRS Initiation	0.437	0.001
Language Fluency	Picture Naming	DRS Initiation	0.531	0.001

*All tests administered within the same testing sessions.
† Low latency scores mean faster response time.

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Mary E. McGann. Self-Administered Screening for Mild Cognitive Impairment: Validation of a Computerized Test Battery. Journal of Neuropsychiatry and Clinical Neurosciences, Volume 17, No. 1, 98-105, 2005.

Ahmed *et al.* (2012) compared the diagnostic accuracy of four cognitive screening tests in a sample of older adults; the CANS-MCI and the Montreal Cognitive Assessment (MoCA) more accurately differentiated cases of MCI from normal controls than did the Revised Addenbrook Cognitive Examination (ACE-R) or, to an even a greater extent, the Mini–Mental State Examination (MMSE).

Ahmed, S., de Jager, C. and Wilcock, G. (2012). A comparison of screening tools for the assessment of mild cognitive impairment: preliminary findings. *Neurocase*, 18, 336–351.

As an example of good agreement between the CANS-MCI measures and the results of "gold standard" cognitive tests for MCI, the CANS-MCI Memory factor alone appears as sensitive to dementia and MCI as full neuropsychological examination, while the full three factor CANS-MCI results may be even more sensitive than a conventional full neuropsychological examination. An optimal cognitive screen would be expected to detect all of the patients considered demented by the Dementia Rating Scale (DRS2) and the majority of those judged to be MCI by the Wechsler Immediate Memory (WMS1) and Wechsler Delayed Memory (WMS2). The percentage of patients considered to have "dementia", according to these measures, were found to be as follows:

CANS-MCI AND NEUROPSYCHOLOGICAL EXAM VS. COGNITIVE "GOLD STANDARDS" N=169 (SCANLAN ET AL, 2012)

	Neuropsych Examination	CANS-MCI Memory Memory Alone	CANS-MCI All 3 Factors
DRS2 Impairment (Initiation)	89%	93%	100%
Wechsler Impairment (WMS1 or WMS2)	79%	80%	95%

James M. Scanlan, Jo A. Laboff and Emory Hill. Self-reported memory fails to substitute for objective memory measures. Alzheimer's Association International Conference (AAIC) Vancouver, BC Canada. July 17, 2012.

Sensitivity and specificity

To determine the ability of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) to accurately screen for mild cognitive impairment (MCI) scores on the CANS-MCI were compared with the results of a full neuropsychological examination that was blind to the CANS-MCI results (Tornatore *et al*, 2003). Logistic regression models were used to predict the dichotomous outcomes of MCI vs. normal cognitive functioning (as determined by the neuropsychological exam). Because education can affect scores on measures of cognitive

impairment, samples were separated into individuals with a high school degree or less (N=26) and those with schooling beyond high school (N=57). Gender and age were included in the model. Receiver operating characteristic (ROC) analyses were performed to calculate the sensitivity and specificity of the CANS-MCI.

The regression model statistics were very strong indicating a good fit of the data to the model. The CANS-MCI has extremely high levels of sensitivity and specificity (100%) in classifying those with an education up to a high school degree. The optimum sensitivity and specificity for those with 13+ years of education is lower (100%; 85%) but still excellent. These findings indicate the CANS-MCI can be a useful screening measure to determine if a person needs to be intensively assessed for cognitive impairment.

CANS-MCI Logistic Regression (Tornatore et al, 2005)

EDUCATION	X^2	NAGELKERKE R^2	PREDICTED CLASSIFICATION % CORRECT
Less Than 13 Years	35.4	1.0	100
13 or More Years	50.3	.79	84.2

CANS-MCI ROC Analyses

EDUCATION	AREA UNDE THE CURVE	% SENSITIVITY	% SPECIFICITY
Less Than 13 Years	1.0	100	100
13 or More Years	.96	100	84.8

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Brian Fogel. Validity of Mild Cognitive Impairment Touch Screen Tests: The CANS-MCI Study. International Psychogeriatric Association 11th Congress, Chicago, August 2003.

According to Memória *et al* (2014), "the Brazilian version of the CANS-MCI battery demonstrated its robust capacity to discriminate MCI from normal controls (81% of sensitivity and 73% of specificity) and almost perfect accuracy to identify AD (100% of sensitivity and 97% of specificity) even in a sample comprising early AD cases."

Summary of ROC analyses with cut-off scores (Memória et al, 2014)

GROUPS	AUC	CUT-OFF (Z-SCORE)	SENSITIVITY (%)	SPECIFICITY (%)	IC
NC × MCI	0.80	1.31	81	73	0.70–0.90
NC × AD	0.98	−2.38	100	97	0.93–1.00

Cláudia M. Memória, Mônica S. Yassuda, Eduardo Y. Nakano and Orestes V. Forlenza Contributions of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) for the diagnosis of MCI in Brazil. International Psychogeriatrics, Volume 26 / Issue 09 / 1483-1491, 2014.

In a study at Oxford (Ahmed et al, 2012) comparing the utility and sensitivity of the CANS-MCI compared to traditional cognitive screening tools for MCI, the CANS-MCI and MoCA revealed highly significant differences between normal controls and MCI ($p<.0001$), while the MMSE discrimination between groups was much less significant ($p<.05$). Specificity and sensitivity of the tests was assessed using ROC curve analysis. The ACE-R and MoCA total scores showed similar and very high sensitivity (90%) but lower specificity (67%). The CANS-MCI revealed similarly high sensitivity (89%), and the highest specificity (73%) overall. The MMSE showed the lowest sensitivity (80%) and specificity (60%) in discrimination of the groups.

Ahmed, S., de Jager, C. and Wilcock, G. (2012). A comparison of screening tools for the assessment of mild cognitive impairment: preliminary findings. *Neurocase*, 18, 336–351.

Sensitivity for detecting change over time

To determine the ability of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) as an accurate screen for mild cognitive impairment (MCI), scores on the CANS-MCI were compared with the results of a full neuropsychological examinations that were blind to the CANS-MCI results. Logistic regression models were used to predict the dichotomous outcomes of MCI vs. normal cognitive functioning (as determined by the neuropsychological exam). The same analyses were performed using full independent neuropsychological

evaluation classifications on the 74 subjects who returned a year later. ROC curve analyses on the two educational levels revealed that cut-points lead to sensitivities/specificities of .93/.83 (<=12 yrs) and .84/.74 (13+ yrs). Areas under the curve were high: .917 for <= 12 yrs education and .888 for 13+ yrs. Criterion Standard: Full, Independent Neuropsychological Examination (2.5-3.5 hours) discrimination between normal and MCI.

CANS-MCI Logistic Regression Analyses (1-year follow-up) (Tornatore et al, 2005a)

EDUCATION	X^2	NAGELKERKE R^2	PREDICTED CLASSIFICATION % CORRECT
Less Than 13 Years	11.7	.63	85.0
13 or More Years	31.4	.59	79.6

CANS-MCI ROC Analyses

EDUCATION	AREA UNDER THE CURVE	% SENSITIVITY	% SPECIFICITY
Less Than 13 Years	.917	92.9	83.3
13 or More Years	.888	83.9	73.9

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Brian Fogel. One year Follow-Up Analyses of Scoring Algorithms for a Mild Cognitive Impairment Screen: The CANS-MCI Study, Alzheimer's Association International Conference on Prevention of Dementia: Early Diagnosis and Intervention, Washington, D.C., June, 2005a.

Construct and face validity

The specific cognitive domain factors, constructed because of their face validity with respect to dimensions predictive of MCI, had their construct/face validity verified independently in the US and Brazil. The robust consistency of the CANS-MCI factor analyses is particularly impressive, since the versions differ in language and in some of the images presented. All CANS-MCI versions are specific to one country and one language (e.g. English/USA; English/Canada; Spanish/USA; Spanish, Canada; French/Canada; Portuguese/Brazil).

Factor Analysis (Tornatore et al, 2005) – USA

Score	Memory	Language/Spatial Fluency	Executive Function/Mental Control
General Reaction Time (Latency)			0.45
Design Matching			-0.80
Word-to-Picture Matching (Latency)			0.65
Stroop (Discordant Latency)			0.61
WAIS Digit Symbol			-0.82
Clock Hand Placement		0.70	
Picture Naming		0.73	
Picture Naming (Latency)		-0.63	
DRS Initiation		0.61	
Free Recognition I	0.73		
Guided Recognition I Errors	-0.61		
Free Recognition II	0.64		
WMS-R LMS-I	0.70		
WMS-R LMS-II	0.78		
DRS Memory	0.64		

Results for Factor Analysis (Memória et al, 2014) – Brazil

SCORE	MEMORY	LANGUAGE/SPATIAL FLUENCY	EXECUTIVE FUNCTION MENTAL CONTROL
General reaction time (latency)			0.60
Design matching			0.61
Word-to-picture matching (latency)			0.76
Stroop (discordant latency)			0.63
Clock hand placement		0.82	
Picture naming		0.76	
Picture naming (latency)			0.81
Free recognition I	0.87		
Guided recognition I errors	−0.86		
Free recognition II	0.90		

Test-Retest Reliability

TEST-RETEST RELIABILITIES AND T-TESTS OF CANS-MCI AT BASELINE, 1-AND 6-MONTHS (TORNATORE ET AL, 2005)

CANS-MCI Test	Time 1 Baseline Mean (SD)	Time 2 1 Month Mean (SD)	Time 3 6-Month Mean (SD)	Coefficient Alpha 1-2	Time 1-2 t	Coefficient Alpha 2-3	Time 2-3 t
General Reaction Time	0.77 (0.21)	0.73 (0.17)	0.74 (0.16)	0.702	3.6‡	0.620	-0.92
Word-to-Picture Matching (Latency)	2.0 (0.55)	1.9 (0.50)	1.9 (0.54)	0.825	6.1‡	0.704	-1.6
Design Matching	39.4 (9.7)	41.4 (8.9)	41.7 (8.6)	0.820	-6.5‡	0.839	-0.52
Stroop (Discordant Latency)	1.67 (0.49)	1.61 (0.52)	1.62 (0.51)	0.795	4.0‡	0.801	-0.06
Clock Hand Placement	30.7 (9.7)	32.9 (8.9)	33.4 (9.3)	0.792	-5.5‡	0.759	-1.0
Free Recognition I	17.7 (2.1)	18.1 (1.9)	18.1 (2.0)	0.681	-3.7‡	0.760	-0.79
Guided Recognition I (Errors)	2.9 (5.5)	2.0 (4.6)	2.3 (4.9)	0.766	3.1†	0.895	0.16
Free Recognition I & II	35.4 (4.0)	35.9 (3.9)	35.9 (4.0)	0.738	-3.7‡	0.826	-0.32
Picture Naming	31.7 (4.8)	32.0 (4.9)	32.3 (4.8)	0.788	-3.1†	0.806	-0.83
Picture Naming (Latency)	4.4 (1.1)	4.1 (1.1)	4.1 (1.1)	0.822	7.3‡	0.834	0.16

†p_0.01 ‡p_0.001

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Mary E. McGann. Self-Administered Screening for Mild Cognitive Impairment: Validation of a Computerized Test Battery. Journal of Neuropsychiatry and Clinical Neurosciences, Volume 17, No. 1, 98-105, 2005.

Internal consistency

INTERNAL CONSISTENCY (ALPHA COEFFICIENT RELIABILITY) OF CANS-MCI TESTS (TORNATORE ET AL, 2005)

CANS-MCI TEST SCORES	NO. OF ITEMS	COEFFICIENT ALPHA
General Reaction Time	10	0.828
Word-to-Picture Matching (Latency)	14	0.865
Stroop (Discordant Latency)	48	0.963
Clock Hand Placement	30	0.902
Free Recognition I †(5 Trials of 20 Items)	5	0.939
Guided Recognition I Errors	5	0.927
Guidance Recognition I (Percent Correct)	5	0.588
Free Recognition II (1 Trial)	20	0.637
Free Recognition I & II Combined (6 Trials)	6	0.935
Picture Naming	42	0.766

INTERNAL CONSISTENCY OF THE CANS-MCI SUBTESTS (MEMÓRIA ET AL, 2014)

CANS-MCI SUBTESTS	NUMBER OF ITEMS	CORRELATION COEFFICIENT
General reaction time	10	0.787
Word-to-picture matching latency	14	0.841
Stroop (discordant latency)	24	0.980
Clock hand placement	20	0.724
Free recognition I (five trials of 20 items)	5	0.933
Guided recognition I errors	5	0.954
Guidance recognition I (percent correct)	5	0.852
Free recognition II (one trial)	20	0.768
Free recognition I & II combined (six trials)	6	0.939
Picture naming	42	0.924

Relevant publications

Jane B. Tornatore, Emory Hill, Jo A. Laboff and Mary E. McGann. Self-Administered Screening for Mild Cognitive Impairment: Validation of a Computerized Test Battery. Journal f Neuropsychiatry and Clinical Neurosciences, Volume 17, No. 1, 98-105, 2005.

Cláudia M. Memória, Mônica S. Yassuda, Eduardo Y. Nakano and Orestes V. Forlenza Contributions of the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI) for the diagnosis of MCI in Brazil. International Psychogeriatrics, Volume 26 / Issue 09 / 1483-1491, 2014.