Applicability of the Abbreviated Neuropsychologic Battery (NEUROPSI) in Alzheimer Disease Patients

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Abstract: NEUROPSI is a brief neuropsychologic battery developed to briefly assess a wide spectrum of cognitive functions. The aim of this study was to examine the applicability of a Portuguese version of this battery and verify the efficacy in detecting cognitive impairment in Alzheimer disease (AD) patients. NEUROPSI was applied to 75 elderly people, 25 patients with probable AD in mild stage (AD1), 25 patients in moderate stage (AD2), and 25 healthy elderly persons (control group), matched with the AD patients for age and schooling. Before testing all participants were applied the Mini-Mental State Examination. Results showed significant differences in total scores of the tests; NEUROPSI ($P < 0.001$) and Mini-Mental State Examination ($P < 0.001$), and the control group scored highest in both of the tests followed by groups AD1 and AD2. Differences were also found between the initial phase and the moderate phase. Results indicate that NEUROPSI is an efficient instrument for detecting AD patients in the initial stage of the disease.

Key Words: neuropsychologic assessment, screening test, dementia, Alzheimer disease

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A predictable increase in the prevalence of dementias throughout the aging populations in the world is foreseen, and the most frequent cause is Alzheimer disease (AD).

A number of scientifically sound and clinically relevant practical parameters for AD diagnosis have been developed and published in consensus form for use in different populations.[1–6] Since then, considerable progress has been made in the identification of elderly people who are in the initial stage of the disease.

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As cognitive decline, particularly memory impairment, is the most significant evidence for detecting AD patients,[7–9] neuropsychologic tests have been viewed as an essential part of initial diagnosis.

Although neuropsychologic testing is a useful approach, there are a number of problematic aspects when conducted in underdeveloped countries, for a number of reasons, particularly educational and cultural factors.[10–15] Most studies relate to white populations in the northern hemisphere, usually with about 12 years of formal education.[16] The few investigations of the subject seem to indicate that cultural and educational aspects should be approached separately; whereas some studies found differences for education, but not for ethnicity,[17,18] others showed differences even when the educational factor was controlled.[19] If these differences occur in groups that share common cultural antecedents and education models, it is quite likely that transposing the tests to other countries may introduce variables that are much more difficult to control. For some materials, a literal translation is sometimes not sufficient, and a high degree of freedom is required when adapting the tests to different cultural environments. For example, even asking for information about seasons of the year may be inappropriate in certain cultural contexts, as Ostrosky-Solís et al[20] pointed out. In this respect, a different kind of approach is required, using tests with materials that are familiar from the cultural point of view, and items in which the influence of education can be minimized.

For Latin America, the problem is a little more complicated. In addition to cultural bias related to existing tests, professionals trained in this type of testing are not available in many places. Overburdened health services and the consequent pressure on time mean that prolonged testing is not feasible. Ideally, for Latin America, in addition to adapting tests from the cultural point of view, they should neither be as long as conventional batteries (eg, Luria-Nebraska or Wechsler Adult Intelligence Scale) nor as short as screening tests [eg, Mini-Mental State Examination (MMSE)], the former requiring training and long application time whereas the latter is inappropriate for both well and less educated people and nonspecific in relation to dementia.[12,21]

Abbreviated neuropsychologic battery (NEUROPSI) was devised to solve these issues,[20] and was standardized for Spanish speaking Latin Americans in

Mexico. Application time is short (about 25 min), and the test is concise and reliable, providing initial or predictive diagnoses of cognitive alterations in populations with different levels of schooling, including illiterate persons.[11,21] The battery includes high-validity neuropsychologic tests, and in some cases other tests were adapted to assess elderly and psychiatric patients population.

One of the aims of this study is to verify the applicability of a Portuguese version of this battery for AD patients.

METHODS

Subjects

A sample of 78 individuals, including 53 patients and 25 healthy controls, was selected for this study from a survey comprising 140 subjects. The patients were selected by the Behavioral Neurology Outpatients Clinic at São Paulo Hospital, all diagnosed with "probable Alzheimer Disease" using the criteria of the National Institute of Neurological Disorders and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association[1] and the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition.[22] Patients were tested using clinical-neurologic examinations comprising laboratory tests and imaging (computerized tomography and magnetic resonance) and neuropsychologic tests.

Severity of clinical state was assessed on the clinical dementia rating (CDR) scale,[23] applied by the medical staff. A clinical examination and semistructured interview were carried out previously and confirmed by an informant (eg, a family member). At the end, patients who presented CDR = 1 were selected in mild-stage (AD1) and patients who presented CDR = 2 in moderate-stage (AD2). All patients were using acetylcholinesterase inhibitors and 7 of them (2 AD1 and 5 AD2) had been treated with antipsychotics (to control behavioral alterations) before the experiment; 3 of the moderate AD subjects were removed from the study because they continued to present behavioral alterations at the time of evaluation.

The control group comprised volunteers from the community of the City of Sao Paulo recruited with the help of communication media (news papers, radio, etc). Inclusion and exclusion criteria for this group were analyzed by researchers from the Psychobiology Department of University Federal of Sao Paulo, in a semistructured interview that included MMSE[24,25] and CDR to verify whether they were functionally independent. The subjects selected did not score on the CDR scale.

Exclusion criteria were reports of other neurologic diseases, abuse of psychotropic drugs or alcohol, and psychiatric disorders or depression. Volunteers with sensory or motor impairment or chronic diseases such as arterial hypertension, diabetes mellitus, or cardiopathy, were included if the latter were corrected.

At the end of this process, 78 people remained, from which 25 were selected to compose a convenience sample (paired by age and educational level) comparable to the AD sample. Table 1 shows the classification of the sample by sex, age, and education.

TABLE 1. Sex, Age, and Education in the Different Groups

	Controls	AD1	AD2
Sex	18 women 7 men	14 women 11 men	15 women 10 men
Age*	M = 72.2 SD = 5.3	M = 72.6 SD = 6.0	M = 73.6 SD = 6.1
Education*	M = 9.6 SD = 4.5	M = 10.5 SD = 4.8	M = 8.8 SD = 5.0

*No significant difference.
M indicates mean.

This study was authorized by the Ethics Committee of the University Federal of Sao Paulo, Brazil, and participants signed consent forms before research.

Procedure

After classification, all participants were tested using an extensive neuropsychologic battery with several cognitive tests. Memory was evaluated by subtests derived from the Wechsler Memory Scale (WMS) that included tasks to evaluate logical memory (narrative of stories, verbal content), visual reproduction (geometric drawings, visual memory), and associated pairs (verbal learning task), all tasks recalled immediately and after a delayed period. We also applied subtests for information, mental control (mental arithmetic task), and forward and backward digit span. This assessment was complemented with other quick application tests such as trail making (A and B) to evaluate attention and cognitive flexibility and the Colored Raven Progressive Matrices (test of intelligence through visual stimuli).

NEUROPSI was individually applied by trained testers in the first session. The examiner did not know the subject's diagnosis and scores from this battery as it was not used to generate the participants' CDR scales or AD diagnosis. Testing time for the control group was a minimum of 22 minutes and maximum of 34 minutes; for AD patients the minimum was 25 minutes and the maximum 42 minutes.

Characteristics of the Instrument

As NEUROPSI was developed for Spanish speaking Latin American populations, authorization to translate it into Portuguese was sought. To ensure the quality of the translation and its adaptation, 3 neuroscience specialists, 2 of them Portuguese speakers and 1 Spanish speaker, were asked to translate the battery and provide a back-translation to reach a consensual translation. The translated battery was subsequently applied to a small sample representative of the Brazilian population; on the basis of the results slight changes were made to the original battery's stimuli and terminology to adapt it to the Brazilian cultural context.[26]

NEUROPSI comprises a number of subtests described below; the original version of the battery may

be found in the manual developed by Ostrosky-Solís et al.[20,27]

Orientation

Questions evaluating the subject's temporal and spatial orientation (date and place) and personal data (age) were asked.

Attention and Concentration

Attention was tested by reverse repetition of digits and mental control tasks such as mentally calculating 20 to 3 (5 consecutive times); cancellation tasks are used to examine spatial hemi-inattention or visual negligence processes.

Memory

Information encoding, storage, and retrieval processes are tested. Verbal memory tasks include a series of 6 words read aloud (2 animals, 2 fruits, and 2 parts of the body), which subjects are asked to repeat; 3 trials are included: after 20 minutes (without previous warning) the 6 words are recalled (free recall), then a number of clues are provided to increase recall according to the semantic content of the word (cued recall), and finally a word recognition is required. For the visual test, the subject is asked to copy a drawing of a semicomplex figure (Rey's figure adapted for the battery); without previous warning, the drawing is recalled after 20 minutes.

Language

Evaluated through semantic fluency (naming all animals they know during 1 min) and phonologic fluency (recalling as many words as possible beginning with the letter *F*) tests. Comprehension subtest comprises a sheet with 4 figures (2 circles and 2 squares, large and small), on which the subject is asked to mark the figure following verbal instructions from the tester. Repetition subtest requires subjects to repeat certain words or sentences. In Naming subtest, subjects are shown 8 figures (1 at a time) of several objects and asked to name them.

Reading and Writing

The task consists of reading a story aloud and then answering 3 questions related to it. *Dictation*: A sentence is read aloud for the subjects to write. *Copying*: Subjects are asked to copy a sentence supplied in the test.

Executive Functions

Executive functions are divided into conceptual and motor subtests. Conceptual tasks include identifying similarities between pairs of stimuli (animals, fruits, parts of the body). Other tasks in this subtest include solving some mental arithmetic operations and continuing a sequence of circles and crosses. For the *executive motor functions* test, the subject is asked to reproduce 3 consecutive movements changing the position of the hands (initially with the right hand and then with the left), then perform alternate movements with both hands and finally respond to opposite stimuli (for instance, when a finger is shown, the subjects must respond with a fist and vice versa).

The maximum score possible for this battery is 130 points, corresponding to the sum of the subtests scores.

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS 11.5.1 for Windows).

Chi-square test (without Yates' correction) was used to compare nominal category data and Spearman's coefficient of correlation to evaluate relationship between continuous variables outside normal distribution.

Differences between means of continuous data for scores obtained in the NEUROPSI and MMSE tests were analyzed through parametric tests; 1-way analysis of variance test and statistically significant differences were analyzed using Bonferroni's a posteriori multiple comparison test.

Cutoff scores for each test were determined using receiver operating characteristic curves on the basis of the sensitivities and specificities of the scores obtained by each group.

All tests were 2-tailed and the probability of 0.05 or less was assumed to indicate statistical significance, except when a potential problem of multiple comparisons was identified, in which case Bonferroni's correction was used.

RESULTS

No statistically significant differences between groups were found for the variables; sex [$\chi^2(2) = 1.48$, $P = 0.477$], age [$F(2, 72) = 0.43$, $P = 0.65$], and education [$F(2, 72) = 0.81$, $P = 0.44$].

In the descriptive analysis of data (Table 2), we found statistically significant differences in total scores on NEUROPSI [$F(2, 72) = 286.6$, $P < 0.001$] and MMSE [$F(2, 72) = 108.9$, $P < 0.001$] and the control group scored highest on both instruments, followed by group AD1 and then group AD2 (Figs. 1, 2).

Correlation between both tests (n = 75, $r^2 = 0.89$, $P < 0.001$) was also observed. When cutoff score for each test was determined, we noted that NEUROPSI was more sensitive and specific than MMSE in differentiating AD1 patients and controls, and differences were found between

TABLE 2. Descriptive Analysis on Total Score NEUROPSI and MMSE in the Different Groups

	Mean	SD	Median	Minimum	Maximum
Controls					
MMSE	27.8*	1.8	28.0	23	30
NEUROPSI	102.6*	6.7	103.5	90	117.5
AD1					
MMSE	23.0*	2.8	23.0	18	27
NEUROPSI	73.6*	8.5	72.5	56	91
AD2					
MMSE	16.7*	3.2	17.0	10	21
NEUROPSI	49.4*	8.3	50.0	33	63

*Significant group difference, $P < 0.001$ = controls > AD1 and AD2, AD1 > AD2.

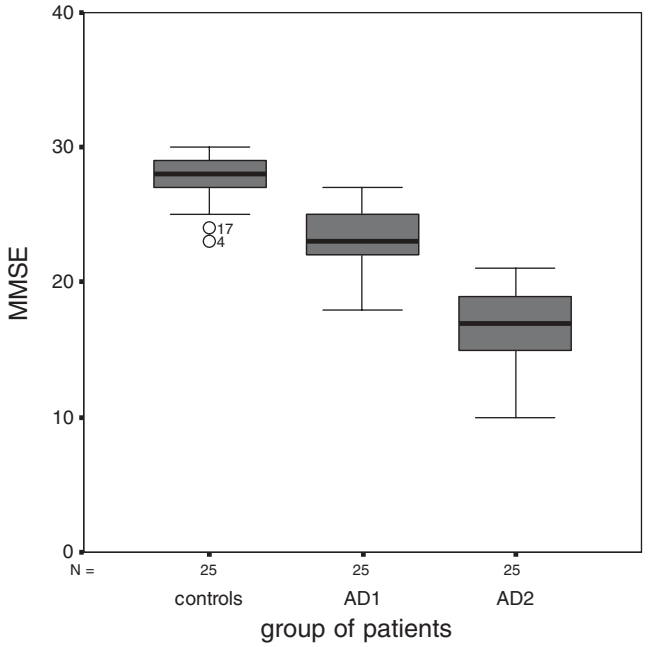

FIGURE 1. Differences between patients and controls in the MMSE total score.

mild-stage and moderate-stage. The respective sensitivity and specificity are shown in Table 3.

The scores on the different NEUROPSI subtests were analyzed in groups by the cognitive function being tested (descriptive data are shown in Table 4); significant differences in each of them were found: orientation [$F(2, 72) = 73.5$, $P < 0.001$], attention and concentration [$F(2, 72) = 67.4$, $P < 0.001$], memory [$F(2, 72) = 164.9$, $P < 0.001$], language [$F(2, 72) = 42.0$, $P < 0.001$], reading and writing [$F(2, 72) = 25.9$, $P < 0.001$], and executive functions [$F(2, 72) = 95.0$, $P < 0.001$]. Table 4 shows statistically significant differences across the 3 groups.

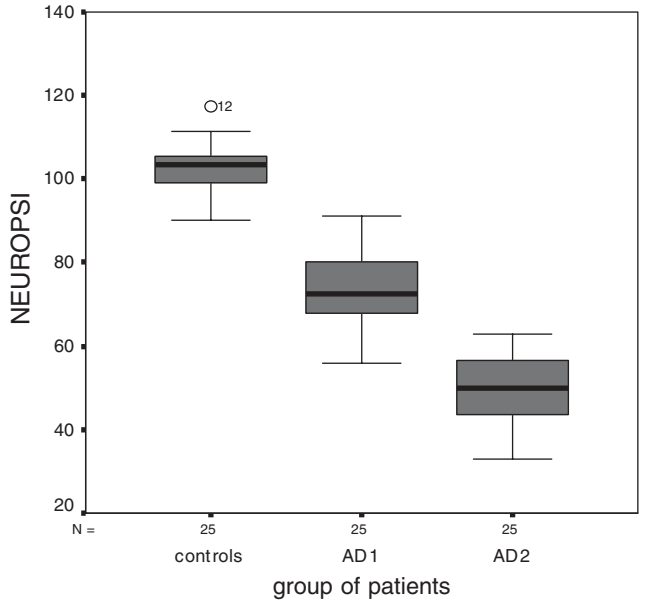

FIGURE 2. Differences between patients and controls in the NEUROPSI total score.

TABLE 3. Sensitivity and Specificity, CI for the MMSE and NEUROPSI Tests

Tests	Cutoff*	Sensitivity	Specificity	Area	95% CI
MMSE					
Controls × AD1	27	88	84	0.930	0.854-1.005
AD1 × AD2	22	100	80	0.940	0.878-1.002
NEUROPSI					
Controls × AD1	88.3	96	100	0.997	0.988-1.005
AD1 × AD2	63.5	100	92	0.986	0.958-1.013

*Subjects with score below the cutoff score are classed as AD patients.

Table 5 shows the cutoff scores for each subtest and under-the-curve areas, with their respective confidence levels.

DISCUSSION

NEUROPSI proved to be efficient in recognizing initial-stage AD patients as seen in the distribution of cutoff scores and high levels of sensitivity (96%) and specificity (100%) differentiating groups (control vs. AD1). Furthermore, it was sensitive enough (100%) to determine differences between mild and moderate stages of the disease, which are often overlooked by other cognitive testing instruments.

The results were expected, as this battery's original design included stimuli measuring various cognitive

TABLE 4. Descriptive Analysis on NEUROPSI Subtests in the Different Groups*

	Mean	SD	Median	Minimum	Maximum
Orientation					
Controls	6.0*	0.0	6.0	6.0	6.0
AD1	4.5*	1.1	5.0	2.0	6.0
AD2	2.9*	1.1	3.0	1.0	5.0
Attention					
Controls	20.3*	2.9	21.0	15.0	25.0
AD1	15.7*	4.2	15.0	9.0	24.0
AD2	8.9*	3.3	8.0	4.0	15.0
Memory					
Controls	36.0*	4.2	37.0	26.5	42.0
AD1	19.8*	4.5	20.0	12.0	27.5
AD2	14.6*	4.4	15.5	5.5	25.5
Language					
Controls	22.4*	2.8	22.0	19.0	33.0
AD1	19.1*	1.8	19.0	15.0	22.0
AD2	16.5*	2.1	17.0	10.0	21.0
Reading and writing					
Controls	4.4*	1.0	5.0	2.0	5.0
AD1	3.2*	1.2	3.0	1.0	5.0
AD2	2.0*	1.3	2.0	0.0	5.0
Executive functions					
Controls	13.9*	1.9	14.0	11.0	17.0
AD1	11.4*	2.9	12.0	4.0	16.0
AD2	4.8*	2.4	5.0	1.0	10.0

*Significant group difference, $P < 0.05$ = controls > AD1 and AD2, AD1 > AD2.

TABLE 5. Sensitivity and Specificity, CI on NEUROPSI Subtests in the Different Groups

Subtests	Cutoff*	Sensitivity (%)	Specificity (%)	Area	95% CI
Controls × AD1					
Orientation	6	84	100	0.920	0.832-1.008
Attention	17	64	88	0.801	0.678-0.924
Memory	28.3	100	96	0.994	0.979-1.008
Language	21	80	84	0.886	0.796-0.976
Reading and writing	5	88	64	0.784	0.655-0.913
Executive functions	14	84	52	0.752	0.619-0.885
AD1 × AD2					
Orientation	4	72	84	0.834	0.721-0.948
Attention	10	64	96	0.895	0.812-0.978
Memory	18.8	92	56	0.797	0.675-0.919
Language	19	92	68	0.834	0.720-0.949
Reading and writing	3	72	64	0.742	0.604-0.879
Executive functions	9	96	84	0.944	0.881-1.007

*Subjects with score below the cutoff score are classed as AD patients.

domains that extensive cognitive neuroscience research has found to be sensitive to brain damage. Similarly, although this battery was devised and standardized for populations aged 16 years and over, it did not exclude tasks involving age-sensitive and cognitive skills. Therefore, subtests were included to evaluate cognitive functions that depend on prior knowledge of the subjects, named collectively as "crystallized intelligence" skills (eg, reading, general knowledge, language), and other domains that require learning new situations, or "fluid intelligence" skills (eg, memory, attention, and overall speed), the latter being highly sensitive in seniors affected by dementia.[20]

Cognitive decline of both crystallized and fluid skills was observed even in initial stages of AD. However, more diagnostic accuracy was provided by memory tasks, followed by the orientation subtest, as shown in Table 5. Similar results were obtained in Brazil with other cognitive testing instruments (translated into Portuguese) for AD diagnosis.[28–30]

These data reaffirm the well-established conclusion that memory deficits, especially those related to the ability to learn and retain new information, characterize initial-stage AD.[7–9,31] On the other hand, although MMSE has been a popular instrument for diagnosing dementia because of its ease of application, in this study it provided less diagnostic accuracy than NEUROPSI in terms of discriminating initial-phase AD subjects.

It is also noteworthy that several studies using MMSE for AD patients have prompted controversies in relation to the test's predictive value, as some studies have shown its high specificity and low sensitivity in detecting mild-stage AD,[32,33] whereas others have found the opposite.[34] Therefore, although apparently quite useful for quickly screening dementia patients, this instrument seems to have limitations when testing a general population unless variables such as age and education are taken into account. Explanations of discrepancies related to predictive value might be associated with the original purpose of the test, which was developed for clinical testing of cognition in bedridden hospital patients whose health was already affected. Furthermore, being a short screening test, there are few scores and highly educated subjects may score well (ceiling effect), thus missing a chance to detect the early onset of the disease. On the other hand, this test when conducted in illiterate populations tends to show lower scores that may be mistaken for dementia syndromes, confirming what several researchers,[10,12,20,21,25,35,36] have emphasized in relation to the ceiling and floor effects of fast-application instruments, which may often endanger the sensibility of a study.

Being aware of these shortcomings, we believe that NEUROPSI has advantages when compared with the MMSE and other neuropsychologic instruments that have been translated into Portuguese, even though it takes longer to apply than MMSE. Its predictive value was found to be quite adequate for detecting mild-stage AD patients, and its cutoff score reached a better level of sensitivity (96%) and specificity (100%) than those obtained by Porto et al[29] in their study of the dementia rating scale[37] (sensitivity 91.7% and specificity 87.8%). Furthermore, the NEUROPSI subtests were efficient in distinguishing the different groups tested (controls vs. AD1 and AD1 vs. AD2) as shown in Figures 1 and 2.

Studies of normal and pathologic cognitive aging require instruments to be sufficiently attractive and challenging to keep individuals motivated to complete them to the best of their abilities. They must not appear very difficult for subjects with low educational level or whose cognitive skills are affected. They must be short, as many seniors tire easily, and long testing sessions are more expensive, but must not fail to provide information on residual cognitive functions, especially in the initial phases of the disease. The NEUROPSI meets several of these requirements, as its application does not take long and it includes relevant tasks that may also be analyzed qualitatively, such as retrieval of information using semantic clues, showing not only overall cognitive performance but also strategies still in use by patients in the moderate phase of dementia. This valuable data supplemented by functional scales may be of great help in

deciding clinical conduct, helping to design nonpharmacologic interventions, and providing guidance to family members on how to stimulate the patient.

Another point to bear in mind is its use in a number of standard international procedures for Spanish and Portuguese speaking immigrant populations living in America and/or Europe, thus facilitating comparative cross-cultural studies.[38,39]

However, a limitation of this instrument to be used in public health services (where time is a serious burden) is the time of execution (22 to 45 min), more than that required by MMSE.

Sampling for our study was devised to obtain a specific distribution of AD patients and controls, so the sample is not representative of the Brazilian seniors population. Therefore, further research is being undertaken in Brazil to facilitate more extensive application of these conclusions, with longitudinal testing and follow-up of a sample of healthy individuals, selected and classified on several variables (such as age, educational level, and cultural differences),[40,41] in the hope that the standardized version of this battery will improve comparisons across different studies, and verify its power to distinguish AD from dementia caused by other etiologies.

Preliminary findings for the use of this battery obtained by Abrisqueta-Gomez et al[42] suggest that NEUROPSI may provide important data for devising neuropsychologic rehabilitation plans, including mental illness prevention policies, and may facilitate the task of determining basal cognitive profiles before, during, and after treatments.

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REFERENCES

1. Mckhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspice of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34:939–944.
2. Morris J, Heyman A, Mohs R, et al. The consortium to establish a registry for Alzheimer's disease (CERAD). *Neurology*. 1989;39: 1159–1165.
3. Small GW, Rabins PV, Barry PP, et al. Diagnosis and treatment of Alzheimer disease and related disorders. Consensus statement of the American Association for Geriatric Psychiatry Society, the Alzheimer's Association, and the American Geriatrics Society. *JAMA*. 1997;278:1363–1371.
4. Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001;56:1143–1153.
5. Cummings JL, Frank JC, Cherry D, et al. Guidelines for managing Alzheimer's Disease: Part I. Assesment. *Am Fam Physician*. 2002;65:2263–2272.
6. Engelhardt E, Brucki SM, Cavalcanti JLS, et al. Tratamento da Doença de Alzheimer. Recomendações e sugestões do Departamento Científico de Neurologia Cognitiva e do Envelhecimento da Academia Brasileira de Neurologia. *Arq Neuropsiquiatr*. 2005;63: 1104–1112.
7. Morris RG, Kopelman MD. The Memory deficits in Alzheimer-type dementia: a review. *Q J Exp Psychol*. 1986;38A: 575–602.
8. Carlesimo GA, Oscar-Berman M. Memory deficits in Alzheimer's patients: a comprehensive review. *Neuropsychol Rev*. 1992;3: 119–169.
9. De Vreese LP, Neri M, Fioravanti M, et al. Memory rehabilitation in Alzheimer's disease: a review of progress. *Int J Geriatr Psychiatry*. 2001;16:794–809.
10. Ostrosky-Solis F, Canseco E, Quintanar L, et al. Sociocultural effects in neuropsychological assessment. *Int J Neurosci*. 1985;27: 53–65.
11. Ostrosky-Solís F, Ardila A, Rosselli M, et al. Neuropsychological test performance in illiterates. *Arch Clin Neuropsychol*. 1998;3: 645–660.
12. Ostrosky-Solís F, López G. Ardila a sensitivity and specificity of the mini-mental state examination in Spanish-speaking population. *Appl Neuropsychol*. 2000;1:25–31.
13. Cobb JL, Wolf PA, Au R, et al. The effect of education on the incidence of dementia and Alzheimer's disease in the Framingham study. *Neurology*. 1995;45:1707–1712.
14. Principe M, Casini AR, Ferretti C, et al. Prevalence of dementia in an elderly rural population: effects of age, sex, and education. *J Neurol Neurosurg Psychiatry*. 1996;60:628–633.
15. Hall KS, Gao S, Unverzagt FW, et al. Low education and childhood rural residence: risk for Alzheimer's disease in African Americans. *Neurology*. 2000;54:95–99.
16. Bachman DL, Wolf PA, Linn R, et al. Prevalence of dementia and probable senile dementia of the Alzheimer type in the Framingham study. *Neurology*. 1992;42:115–119.
17. Schmand B, Smit J, Lindeboom J, et al. Low education is genuine risk factor for accelerated memory decline and dementia. *J Clin Epidemiol*. 1997;50:1231–1238.
18. Ripich DN, Carpenter B, Ziol E. Comparison of African-American and Euro-American persons with Alzheimer's disease on language measures. *Neurology*. 1997;48:781–783.
19. Welsh KA, Fillenbaum G, Wilkinson W, et al. Neuropsychological test performance in African-American and Euro-American people with Alzheimer's disease. *Neurology*. 1995;45:2207–2211.
20. Ostrosky-Solís F, Ardila A, Rosselli M. NEUROPSI: a brief neuropsychological test battery in Spanish with norms by age and educational level. *JINS*. 1999;5:413–433.
21. Mejia S, Gutierrez L, Villa M, et al. Cognition functional status education and the diagnosis of dementia and mild cognitive impairment in Spanish Speaking Elderly. *Appl Neuropsychol*. 2004;4:196–203.
22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed. Washington, DC: American Psychiatric Association; 1987.
23. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412–2414.
24. Folstein MF, Folstein SE, McHugh PR. The Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189–198.
25. Bertolucci PHF, Brucki SMD, Campacci SR, et al. O Mini-Exame do Estado Mental em uma população geral: Impacto da escolaridade. *Arq Neuropsiquiatr*. 1994;52:1–7.
26. Abrisqueta-Gomez J. *Avaliação Neuropsicológica nas fases inicial e moderada da doença de Alzheimer*. *Doctoral Thesis*. Brazil: Universidade Federal de São Paulo (UNIFESP); 1999.
27. Ostrosky-Solís F, Ardila A, Rosselli M. *NEUROPSI Evaluación Neurospicológica Breve em Español. Manual instructivo y protocolo de aplicación (NEUROPSI: A brief neuropsychological evaluation in Spanish Manual Instructions and application protocol)*. Mexico, DF: Bayer; 1997.
28. Bertolucci PHF, Okamoto HI, Brucki SMD, et al. Applicability of the CERAD neuropsychological battery to Brazilian elderly. *Arq Neuroppsiquiatr*. 2001;59:532–536.
29. Porto CS, Fichman HC, Caramelli P, et al. Brazilian version of the Mattis Dementia Rating Scale. *Arq Neuropsiquiatr*. 2003;61: 339–345.

30. Schultz RR, Siviero MO, Bertolucci PHF. The cognitive subscale of the Alzheimer's Disease Assessment. *Braz J Med Biol Res*. 2001;34: 1295–1302.
31. Petersen RC, Stevens JC, Ganguli M, et al. Practice parameter: early detection of dementia; Mild Cognitive Impairment (an evidence-based review). *Neurology*. 2001;56:1133–1142.
32. Galasko D, Klauber MR, Hofstetter R, et al. The Mini-Mental State Examination in the early diagnosis of Alzheimer's Disease. *Arch Neurol*. 1990;47:49–52.
33. Sabe L, Jason L, Juejati M, et al. Sensitivity and specificity of the Mini-Mental State Exam in the diagnosis of dementia. *Behav Neurol*. 1993;6:207–210.
34. Fountoulakis KN, Tsolaki M, Mohs RC, et al. Epidemiological Dementia Index: a screening instrument for Alzheimer's disease and other types of dementia suitable for use in population with low education level. *Dement Geriatr Cogn Disord*. 1998;9:329–338.
35. Brayne C, Calloway P. The association of education and socio-economic status with the Mini Mental State Examination and the clinical diagnosis of dementia in elderly people. *Age Ageing*. 1990; 19:91–92.
36. Nelson A, Fogel B, Faust D. Bedside screening instruments: a critical assessment. *J Nerv Ment Dis*. 1986;174:73–83.
37. Mattis S. Mental status examination for organic mental syndrome in elderly patients. In: Bellak L, Karsu T, eds. *Geriatric Psychiatric*. New York: Grune & Stratton; 1976.
38. Ardila A, Rosselli M, Ostrosky-Solís F, et al. Syntactic comprehension, verbal memory and calculation abilities in Spanish-English bilinguals. *Appl Neuropsychol*. 2000;7:3–16.
39. Rosselli M, Ardila A, Araujo K, et al. Verbal fluency and repetition skills in healthy older Spanish-English bilinguals. *Appl Neuropsychol*. 2000;7:17–24.
40. Abrisqueta-Gomez J, Ostrosky-Solís F, Bertolucci PHF, et al. Preliminary results of Brief Neuropsychological Evaluation—NEUROPSI (in a Brazilian sample). *Arq Neuropsiquiatr*. 2001;59:51.
41. Abrisqueta-Gomez J, Bueno OFA, Bertolucci PHF. Brief Neuropsychological battery for the early diagnosis of Alzheimer's disease. *Neurobiol Aging*. 2000;21:427.
42. Abrisqueta-Gomez J, Canali F, Vieira VLD, et al. A longitudinal study of a neuropsychological rehabilitation program in Alzheimer's disease. *Arq Neuropsiquiatr*. 2004;62:778–783.