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Accuracy of the Brazilian version of the Prefrontal Symptoms Inventory (PSI-16) in the neuropsychological assessment of patients diagnosed with Alzheimer's disease

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Abstract: The aim of the present study was to ascertain the accuracy of the Prefrontal Symptoms Inventory (PSI-16) for patients with probable Alzheimer, as well as to compare it with the Mini Mental State Examination (MMSE) and the Frontal Assessment Battery (FAB). The study included 159 elderly people, aged over 60 years, 50 with a diagnosis of probable Alzheimer and 109 without the pathology. In the total sample, the cut-off point of the PSI-16 was > 19 points, with sensitivity and specificity moderate. Accuracy in the group with a ≥ 8 years of education was superior in all instruments. The AUCs of PSI-16 and MMSE remained similar, the SE of all instruments increased, and the SP obtained a decline, considering the elderly over 70 years old. PSI-16 is a self-report instrument suitable for tracking behavioral problems related to the prefrontal cortex, with little impact from age and education level.
Keywords: neuropsychological tests, Alzheimer, Accuracy, Prefrontal cortex.

Introduction

The prevalence rate of dementia increases as the global population ages. Worldwide, about 50 million people have this condition, with almost 60% living in low- and middle-income countries. Every year, there are almost 10 million new cases, with the estimated proportion of the general population aged 60 and over between 5-8%. The total number of people with dementia is expected to reach 82 million in 2030 and 152 million in 2050 (WHO, 2015).

Dementia is a syndrome of a chronic or progressive nature, in which there is deterioration of cognitive functioning, in addition to what can be expected from regular aging. It affects memory, executive functions (EF), thinking, guidance, understanding, calculation, learning ability, language skills and judgment. Impaired cognitive function is usually accompanied and sometimes preceded by deterioration of emotional control, social behavior, or motivation and of the ability to perform daily life activities (WHO, 2015).

Alzheimer's disease (AD) is by far the most common cause of dementia and accounts for up to 80% of all diagnoses (CROUS-BOU *et al.*, 2017). The main histopathological characteristics involve the presence of senile extracellular plaques composed of filamentous aggregates of β-amyloid protein (Aβ), intracellular neurofibrillary masses, formed mainly by the tau protein, as well as the loss of neurons and synapses in specific areas of the brain (NHO *et al.*, 2013).

Low literacy and education levels are important risk factors for dementia, while higher education can be a protective factor, contributing to the cognitive reserve (FARFEL *et al.*, 2013). The annual incidence rate of AD increases significantly with advancing age. In the age groups of 65 to 74; 75 to 84; and over 84 years of age, it is approximately 53; 170; and 231 new cases per year in 1,000 individuals, respectively (NITZSCHE; MORAES; JÚNIOR, 2015).

Definitive diagnosis of AD requires post-mortem assessment of brain tissue, although biomarkers such as cerebrospinal fluid (CSF) and positron emission tomography (PET) combined with various clinical indicators can help in the diagnosis of living patients (MANTZAVINOS; ALEXIOU, 2017). The most characteristic symptom is the loss of recent memory and, as the disease progresses, more severe symptoms are noticed, such as memory loss from older facts, language problems, difficulty in orienting in time and space, difficulty in finding ways that were crossed frequently and easily, difficulty expressing feelings and ideas and changes in EF.

For the diagnosis, clinical judgment is associated with tests of cognitive functions and differential diagnosis with other conditions. In the cognitive evaluation, the Mini Mental State Examination (MMSE) and tests for specific cognitive functions (memory and EF) are frequently used, when indicated (JOE; RINGMAN, 2019). It is necessary to consider, in the evaluation process, the fact that the educational level affects the performance in several neuropsychological tests, particularly when test items access domains which are sensitive to certain knowledge and skills acquired at school.

The MMSE has been translated into several languages and it is widely applied clinically (gold standard). Estimates of the degree to which the MMSE can be used to accurately identify cognitive impairment vary according to the population assessed and the cut-off point established. When considering a commonly used cut-off score of 25, the sensitivity of the test was reported to be of 82%, with a specificity of 80% among elderly people in the community. With a cut-off score less than 21 points, researchers found a sensitivity of 80% and a specificity of 98% for the detection of cognitive deficits in elderly people in the community (MACKIN *et al.*, 2010).

To assess dementia, the cut-off point of the MMSE is between 24 and 26 points, with sensitivity from 89% to 95% and specificity from 87% to 98%. However, the judgment can be affected by age, education, language and cultural background, and it can easily result in a ceiling effect (TSAI *et al.*, 2016).

Araújo *et al.* (2018) when looking for validity evidence for the Rowland Universal Dementia Assessment Scale (RUDAS-BR) in the Brazilian population with AD, compared the ROC curves of that instrument with the MMSE. The areas under the curve were similar for RUDAS-BR (0,87 [CI95% 0,82-0,93]) and for MMSE (0,84 [CI 95% 0,7-0,90]). The score 23 in RUDAS-BR indicated dementia, with a sensitivity of 81.5% and specificity of 76.1%. In the MMSE, the cut-off point 24 indicated dementia, with a sensitivity of 72.3% and specificity of 78.9%, being influenced by the years of education.

Executive function changes are common in AD and they are usually associated with a marked deterioration of episodic memory. In this regard, screening instruments to understand executive functioning and prefrontal symptoms have also been used in clinical evaluation to assist in diagnosis. The Frontal Assessment Battery (FAB) it is a short-term screening instrument, comprising six domains, which explore the functions related to the frontal lobe in a practical way. Researches used FAB to differentiate AD from frontotemporal dementia, from subcortical vascular dementia (SVaD) and dementia with Lewy Bodies (NAKAAKI *et al.*, 2007; OGURO *et al.*, 2006).

Chong *et al.* (2010) sought to validate FAB in the Chinese population with mild cognitive impairment (MCI) and mild dementia. The ideal cut-off point was considered in the 12/13 range (sensitivity 92%, specificity 78.7%), after adjusting age and education, a similar score was found. It is important to note that the ideal cut-off point for individuals with more than six years of education was 13/14 (sensitivity 91.8%, specificity 70.3%).

Studies with a Brazilian sample carried out by De Paula *et al.* (2013) used FAB to track the executive functioning of 391 healthy older adults and 93 patients diagnosed with AD. The results showed good internal consistency, significant correlations with other tests and moderate accuracy (64%) for the diagnosis of AD. The cut-off point used was 9/10 with a sensitivity of 71% and specificity of 61%.

In recent years, it is recommended that, along with the measurement of cognitive performance through neuropsychological tests and objective screening instruments, the use of a questionnaire or inventory of symptoms to investigate functioning in daily life should be performed. The use of these self-report tools comprises quantitative and qualitative aspects, enabling the assessment of emotional/motivational behaviors, going beyond inferences about cognitive domains. In this point of view, there is the Prefrontal Symptoms Inventory (PSI) developed by de León *et al.* (2013), which allows a systematic collection of information, with a list of questions directed to typical everyday situations.

For the Spanish population, the PSI has demonstrated adequate psychometric properties in patients with addictive behavior and with acquired brain damage and degenerative dementia (DE LEÓN, *et al.*, 2015). In the Brazilian elderly population with and without a diagnosis of probable AD, the inventory has shown satisfactory adjustment indexes and adequate reliability (Ω of 0.83 and α = 0.80) for the uni-factorial model, containing 16 items (FERREIRA; BARBOSA; ALCHIERI, 2020). However, its sensitivity and specificity for diagnostic accuracy has not been investigated.

Therefore, the present study aimed to ascertain the sensitivity and specificity of the PSI-16 for patients with the diagnosis of probable AD, since it is an inventory that measures behavioral symptoms, through everyday situations. As well as to compare with the diagnostic impressions provided by the most direct measurement screening instruments, such as the MMSE and FAB. The influence of education and age on the scores of the instruments mentioned above was also verified, in order to understand whether these variables cause changes in accuracy.

Materials and Methods

Participants

In the group diagnosed with probable mild/moderate AD, 50 elderly participated, of both sexes, aged over 60 years and having at least one year of formal education, recruited from the cities of João Pessoa (PB) and Recife (PE). For screening of the level of probable AD, a wide clinical interview was carried out with the caregivers, as well as the application of the Clinical Dementia Rating (CDR), considering the criteria of the DSM V (AMERICAN PSYCHIATRIC ASSOCIATION, 2013) and from NINCDS-ADRDA (TIERNEY *et al.*, 1988). Participants with probable AD who had a severe level (CDR 3) were excluded; the ones who reported vascular injuries, diagnosis of psychiatric disorders, dependence on psychoactive substances, severe visual and/or hearing impairment - which could impair the assessed performance - and those who refused to complete any cognitive testing were also excluded.

The second group was composed of 109 active elderly people from the community, of both sexes over the age of 60 and with at least one year of formal schooling, recruited from social centers and recreational spaces in the greater João Pessoa (PB). Participants were excluded if they had a diagnosis of psychiatric problems, severe motor and cognitive disorders, abuse of psychoactive substances and who gave up at some stage of the research.

Instruments

PSI

It is an instrument of Spanish origin (DE LEÓN, *et al.*, 2013), composed of 46 items ($\alpha > 0.94$), with psychometric properties also suitable for the abbreviated version, containing 20 items ($\alpha > 0.89$), answered on a Likert-type scale (0 to 4 points). Composed in its original version by three subscales, theoretically independent, the first one evaluates *behavioral problems*, including motivational problems, executive control problems and attention problems (composed of 12 items); the second involves *problems in social behavior* (composed of four items) and the third involves *problems in emotional control* (composed of four items)

In the Brazilian Portuguese version, however, the evidence of validity showed satisfactory indexes for a single factor model (Ω of 0.83 and $\alpha = 0.80$), containing 16 items (version used in the present research), that is, it did not present division between subscales (FERREIRA *et al.*, 2020). The purpose of the instrument is to explore behaviors of daily life that relate to changes in the prefrontal cortex, in the behavioral, cognitive and emotional sphere in a qualitative way.

Frontal Assessment Battery (FAB)

The FAB instrument was validated for Brazil by Beato *et al.* (2012), consisting of six neuropsychological tasks that assess the abstract reasoning, mental flexibility, cognitive programming for motor action, sensitivity to interference, inhibitory control, and autonomy in the internal control of environmental stimuli. Each test corresponds to an activity controlled by the frontal lobe, adapting FAB to the detection of executive dysfunction, which refers to the deficit in brain functions essential for directed, flexible and adaptive behavior, especially in new situations. Each test can be scored between 0 and 3, the total corresponds to the sum of the scores of each activity (total result/variation = 0-18 points/best performance).

Mini Mental State Examination (MMSE)

The MMSE was developed in the United States by Folstein, Folstein and McHug (1975) in five dimensions (orientation, attention, concentration, memory, calculation, language, and praxis) based on theoretical analysis and clinical practice. It is the most widely used test to assess cognitive function because it is fast to be taken (around 10 minutes), easy to apply, and does not require specific material. It should be used as a screening instrument, not substituting a more detailed evaluation, because, despite evaluating several domains, it does not serve as a diagnostic test, but rather to indicate functions that need to be investigated. In the present research, the adaptation developed by Brucki *et al.* (2003) was used, with a maximum score of 30 points.

Procedures

This study was approved by the research ethics committee of the Hospital Universitário Onofre Lopes from the Federal University of Rio Grande do Norte (CAEE 50929115.7.0000.5292) and all participants have provided written informed consent before any procedure. Each volunteer was assisted in a session of approximately 25 to 30 minutes, in which a structured interview was conducted to collect demographic, physical and mental data, as well as a brief assessment through PSI-16, MMSE and FAB. In order to minimize anosognosia (GERSTENECKER *et al.*, 2018) participants with probable AD were interviewed together with their respective caregiver.

Statistical analysis

The individual data were grouped in a specific spreadsheet of the IBM SPSS Statistics software (version 22.0), analyzed in a descriptive, comparative and associative way, according to the research objectives. Normality tests of the distribution of results were performed (Kolmogorov-Smirnov test), identifying that the variables have met the criteria.

When comparing groups in sociodemographic and clinical variables (PSI-16, MMSE and FAB), Student's t test was used for mean values at a significance level of 5%. Cohen's d was calculated to obtain the effect size of the differences identified in the comparative analyzes, considering: d close to 0.20 = small or weak effect, d close to 0.50 = medium or moderate effect, d greater than 0.80 = large effect. In both groups, Pearson's r correlation test was used to verify the association between PSI-16, MMSE and FAB.

The ROC curve analysis was used to compare the accuracy of PSI-16, MMSE and FAB for the diagnosis of AD. Sensitivity, specificity, positive likelihood ratio (LR) and negative LR were calculated using MedCaul 19. Based on Swets (1988) the guidelines for interpreting the power effects of the ROC curve were classified as weak (0.50-0.69), moderate (0.70-0.89) and large (0.90-1.00). The ideal cut-off point was determined for the instruments, balancing sensitivity, and specificity (≥80% was defined as high, 79% - 60% as moderate and <60% as low) according to Youden's index.

The positive likelihood ratio was calculated as the ratio between the proportion of true positives and the proportion of false positives. The negative LR was obtained by dividing the proportion of false negatives by the proportion of true negatives. Values greater than one are desirable for the positive likelihood ratio and values less than zero are appropriate for the negative likelihood ratio. The Positive Predictive Value (PPV) was the percentage of people who tested positive for the disease (true positive or true positive + false positive), and the Negative Predictive Value (NPV) estimated the percentage of people who tested negative for the disease (true negative or true negative + false negative). To assess the impact of education and age, these analyzes were repeated in groups with <8 years of education and ≥ 8 years of education and then in the group divided into ≤ 70 years and > 70 years.

Results and discussion

Table 1 presents sociodemographic and clinical characteristics of 159 participants divided into a control group (*n* = 109) and a study group (*n* = 50). Participants with probable AD exhibited an average age of 74.5 years (*max* = 93; *min* = 60; *SD* = 9.72), the majority being female (70%), with a high educational level (52%), married (60%), using medication (100%) and without frequent physical activity (52%). Whereas, the average age of the control group was 71.3 years (*max.* = 94; *min* = 60; *SD* = 7.82), most of whom were women (78%), with a high level of education (65,1%), married (42.1%), with few subjective complaints of cognitive deficits (56.9%) and with frequent practice of physical activity (86.2%).

In the statistical comparison between the groups, there were statistically significant differences between the age of the participants (*t (157) = -2.19; [95% CI -6.03 - -0.32]; p <0.01, d = 0.36*), PSI-16 performance, (*t (157) = -5.70; [95% CI -12.88 - -6.25]; p <0.01; d = 0.93)*, in the MMSE *(t (157) = 6.29; 95% CI 3.45 - 6.61; p <0.01; d = 1.03)* and in the FAB *(t (157) = 4.60; [95% CI 1.63 - 4.09]; p <0.01; d = 0.78)*. The group with probable AD had the highest average age, highest score in PSI-16 and worst performance in MMSE and FAB.

A correlation analysis was performed with both groups and there were statistically significant weak negative correlations between PSI-16 and MMSE *(SG r = -0.23, p <0.01; CG r = -0.24 , p <0.01*) and FAB (*SG r = -0.31, p <0.01; CG r = -0.29, p <0.01*). Moderate positive correlations were also found between MMSE and FAB (*SG r = 0.47, p <0.01; CG r = 0.65, p <0.01*).

Table 2 and Figure 1 represent the area under the curve (AUC), the sensitivity (*SE*) and the specificity (*SP*), of the PSI-16, MMSE and FAB instruments for the total sample. AUC for PSI-16 was 0.745 (p <0.001), in the analysis of the ROC curve, the cut-off point considered ideal for diagnostic inferences was > 19 points, with SE, SP, PPV and NPV of 72%, 68 %, 50.7% and 84.1%, respectively. Therefore, AUC, SE and SP were considered moderate.

The accuracy of FAB was similar to that of PSI-16, and the MMSE showed a higher *AUC* (0.812), as well as better *SE* and *SP* (80% and 72%, respectively), at the cut-off point of < 24. However, in the statistical comparison of the areas of the ROC curve, there were only statistically significant differences between MMSE and FAB *(z = 2.61, [95% CI 0.0251- 0.174], p <0.001).*

The sample was divided considering the levels of education <8 years (1 to 7) and ≥ 8 years and the diagnostic accuracy of PSI-16, MMSE and FAB was measured (Table 3). It can be seen that *AUC, SE* and *SP* in ≥ 8 years level of education were superior for all instruments. In PSI-16 the cut-off point increased from > 18 (*AUC = 0.686; SE = 71% and SP = 61%*); to > 19 (*AUC = 0.781, SE = 73% and SP = 76%*). In the MMSE, the cut-off point also increased from < 20 (*AUC = 0.731, SE = 67%* and *SP = 71%*) to < 25 (*AUC = 0.910, SE = 88%* and *SP = 79%*). FAB had the worst accuracy in ≥ 8 years level of education, as well as moderate SE (75%) and low SP (39.4%), the cut-off point went from < 10 to < 12 points in ≥ 8 years education (*AUC = 0.762; SE = 69% SP = 79%*).

Table 1: Sociodemographic and clinical data of the elderly population with and without dementia.

		CG (N = 109)	SG (N = 50)
Age (Mean, SD)		71.3 (7.82)	74.5 (9.72)*
Sex	Female	85 (78%)	35 (70%)
	Male	24 (22 %)	15 (30%)
Education	Low (up to 4 years)	25 (22.9%)	14 (28%)
	Average (4 to 8 years)	13 (11.9%)	10 (20%)
	High (8 years)	71 (65.1%)	26 (52%)
Civil status	Single	13 (11.9%)	3 (6%)
	Married	47 (42.1%)	30 (60%)
	Divorced	14 (12.8%)	2 (4%)
	Widow	35 (32.1%)	15 (30%)
Medication	Yes	101 (92.7%)	50 (100%)
	No	8 (7.3%)	0
Subjective complaints in cognition	Yes	47 (42.1%)	50 (100%)
	No	62 (56.9%)	0
Physical Activity	Yes	94 (86.2)	24 (48%)
	No	15 (13.8%)	26 (52%)
PSI-16		16.21 (8.98)	25.78 (11.43)*
MMSE		25.38 (4.37)	20.34 (5.30)*
FAB		12.74 (3.66)	9.88 (3.60)*

Note: CG – Control Group; SG – Study Group; SD = Standard Deviation *$p < 0.01$.

Table 2: Measures based on the analysis of the ROC curve (receiver operating characteristic).

Variables	PSI-16 (159)	MMSE (159)	FAB (159)
Cut-off point	>19	≤ 24	≤ 12
Accuracy CI 95%	0.745 (0.669 – 0.810)*	0.812 (0.742 -0.869)*	0.712(0.635 – 0.781)*
Sensitivity %	72	80	78
Specificity%	68	72	61
Standard Deviation	0.041	0.034	0.043
Youden's Index	0.395	0.516	0.394
PPV %	50.7	56.7	47.8
NPV %	84.1	88.6	85.8
LT+	2.39	2.81	2.02
LT -	0.45	0.28	0.36

Note: CI 95%: Confidence Interval 95%; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LT^+: positive likelihood ratio; LT-: negative likelihood ratio. * $p < 0.001$.

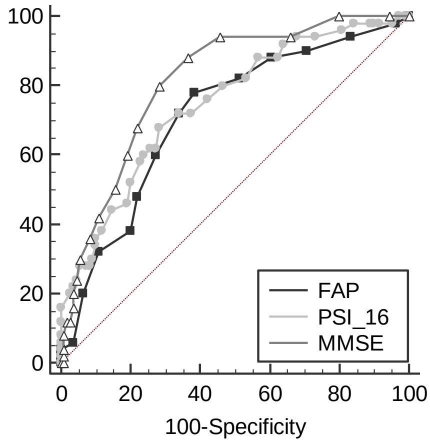

Figure 1: ROC curves for PSI-16, MMSE and FAB.

Table 3: Measures based on the analysis of the ROC curve (receiver operating characteristic), according to the level of education of the participants (<8 years and ≥ 8 years) .

Variables	PSI-16 < 8 years (n= 62)	PSI-16 ≥ 8 years (n = 97)	MMSE < 8 years (n = 62)	MMSE ≥ 8 years (n = 97)	FAB < 8 years (n = 62)	FAB ≥ 8 years (n = 97)
Cut-off point	>18	>19	≤ 20	≤ 25	≤ 10	≤ 12
Accuracy	0.686*	0.781*	0.731*	0.910*	0.605	0.762*
CI 95%	(0.555; 0.798)	(0.685; 0.859)	(0.604; 0.836)	(0.835; 0.959)	(0.473; 0.727)	(0.665; 0.843)
Sensitivity %	71	73	67	88	75	69
Specificity%	61	76	71	79	39.4	79
Standard Deviation	0.070	0.051	0.069	0.028	0.073	0.058
PPV %	59.3	52.6	59.3	60.5	43.8	54.6
NPV %	76.9	88.4	77.3	94.7	71.3	87.4
LT+	1.79	3.05	2.30	4.19	1.24	3.28
LT -	0.48	0.35	0.47	0.15	0.32	0.39

Note: CI 95%: Confidence Interval 95%; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LT+: positive likelihood ratio; LT-: negative likelihood ratio. * p < 0.001.

When comparing the ROC curves (Figure 2A and B), there were no statistically significant differences between the instruments with level of education < 8 years. Whereas, in ≥ 8 years level of education, statistically significant differences were found between MMSE and PSI-16 (*z = 2.28; [95% CI 0.0184 - 0.241]; p <0.001*) and between MMSE and FAB *(z = 2.61; [95% CI 0.0364 - 0.260]; p <0.001*).

Table 4 represents the investigation of the diagnostic accuracy of PSI-16, MMSE and FAB considering the division of the sample according to the age of the participants (≤ 70 years and> 70 years). It can be seen that the AUCs of PSI-16 and MMSE remained similar between the two groups, while the SE of all instruments increased and SP suffered a decline, when considering the elderly over 70 years. When comparing the ROC curves (Figure 2C and 2D), statistically significant differences were found in the ≤ 70 years group between MMSE and FAB *(z = 2.77 [95% CI 0.055 - 0.321], p <0.001*), demonstrating that FAB represented the test with the worst accuracy in that population.

The present study aimed to analyze the accuracy of PSI-16 in the assessment of elderly people with dementia, as well as to compare it with other screening tools such as MMSE and FAB. The performance of the instruments was also investigated, considering the education and age of the participants. It was a pioneer research in a Brazilian sample of great relevance, considering that the purpose of the instrument was to investigate qualitatively and quantitatively the behavioral symptoms related to the prefrontal cortex.

It can be seen from the clinical data that the group with the diagnosis of probable AD has a lower performance than the control group in all instruments used (PSI-16, MMSE and FAB). Emphasizing the cognitive and behavioral difficulties observed in the diagnosis of AD, sensibly captured by the screening tools used - which are associated with each other - according to what was observed in the correlation analyzes. Studies point to the importance of neuropsychometric assessments in the differential diagnosis of dementia syndromes, especially regarding aspects of learning, memory and EF (DONG *et al.*, 2012).

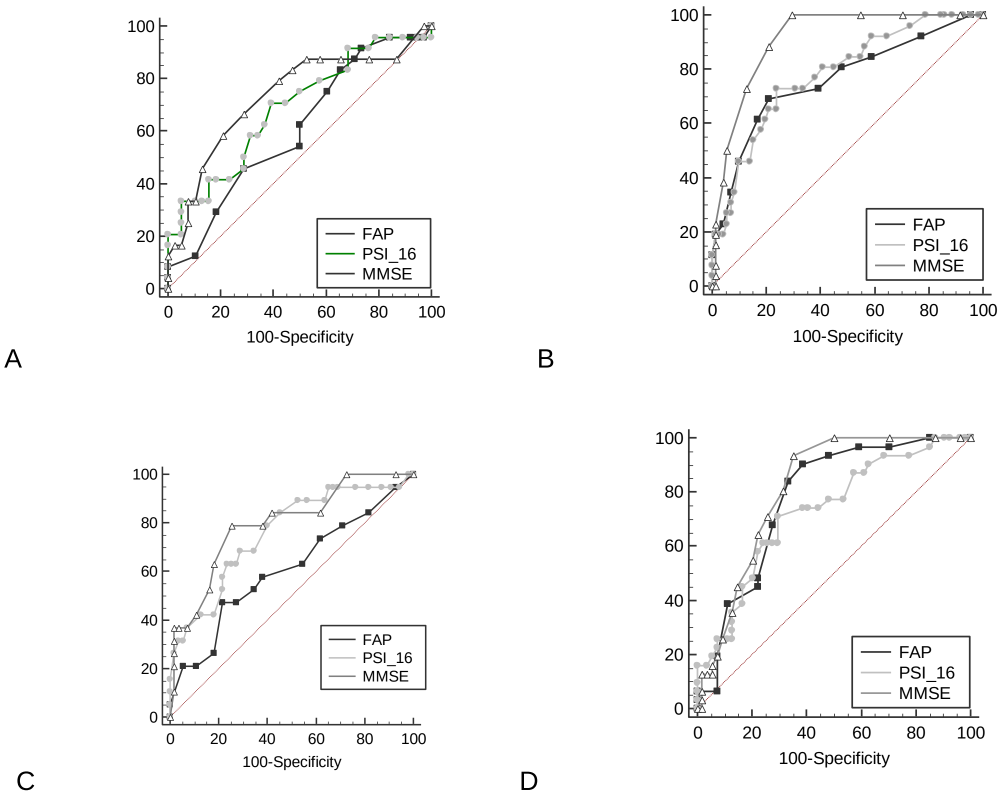

Figure 2: ROC curves for PSI-16, MMSE and FAB for the elderly with < 8 years and ≥ 8 years level of education (A and B, respectively) and aged ≤ 70 and > 70 years (C and D, respectively).

Table 4: Measures based on the analysis of the ROC curve (receiver operating characteristic), according to the age of the participants.

Variables	PSI-16 ≤ 70 years (n= 74)	PSI-16 > 70 years (n = 85)	MMSE ≤ 70 years (n = 74)	MMSE > 70 years (n = 85)	FAB ≤ 70 years (n = 74)	FAB > 70 years (n = 85)
Cut-off point	>21	>19	≤ 24	≤ 25	≤ 9	≤ 12
Accuracy CI 95%	0.757* (0.644;0.850)	0.728* (0.621; 0.819)	0.795* (0.685; 0.880)	0.813* (0.713;0.889)	0.607 (0.487; 0.719)	0.777* (0.674; 0.860)
Sensitivity %	63.1	70.9	78.9	93.5	47.3	90.3
Specificity%	76.3	70.3	74.5	64.8	78.1	61.1
Standard Deviation	0.065	0.056	0.060	0.045	0.079	0.050
PPV %	47.8	57.7	51.5	60.3	42.6	57
NPV %	85.7	80.8	91.1	94.5	81.1	91.6
LT+	2.67	2.40	3.10	2.66	2.17	2.32
LT -	0.48	0.41	0.28	0.10	0.67	0.16

Note: CI 95%: Confidence interval 95%; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LT+: positive likelihood ratio; LT-: negative likelihood ratio. * $p < 0.001$.

In the search for the diagnostic precision of the PSI-16, it was noticed that the accuracy was considered adequate, with the area under the curve significantly moving away from the “chance line”. The ability to detect cases of elderly people with dementia was moderate (sensitivity), as well as the ability to identify healthy individuals (specificity). If the test value is positive, the probability of the disease being present is of 50.7% (PPV) and if it is negative, the probability of the disease not being present is of 84.1% (NPV). As presented in the results section, all PSI-16 measurements were similar to those found in other screening tools already established in the literature, such as MMSE and FAB.

Therefore, despite the problems related to the use of self-report measures to assess subjective cognitive decline in elderly people with and without an associated pathology, the PSI-16 can represent an objective instrument that can be easily applied, which helps clinical practice in identifying behavioral symptoms, derived from prefrontal problems (PEDRERO-PÉREZ *et al.*, 2016). A possible alternative to improve sensitivity and specificity would be an item-by-item analysis to see if there are one or more items capable of contributing to the prediction of the diagnosis or if there were one or more items that acted as confounding factors in the diagnosis.

A good screening tool assists in the identification of possible cases and in the differential diagnosis, which is more relevant than reaching a defined diagnosis. The diagnosis can be obtained in subsequent steps, after further evaluation (APRAHAMIAN *et al.*, 2011). This scenario may be important in developing countries, such as Brazil, where dementia is still a hidden problem, as there is a lack of information to help people in the community to detect signs and differentiate dementia from normal aging (PATEL; PRINCE, 2001).

In the present study, the cut-off point for PSI-16 was 18, for those with low education, and 19 for those with a ≥ 8 years level of education. This contrasts with the different cut-off points suggested by the MMSE, 20 points for those with a < 8 years level of education and 25 points for those with a ≥ 8 years level of education. The influence of education on the MMSE had already been observed in other Brazilian studies (LAKS *et al.*, 2003; YOKOMIZO *et al.*, 2018).

It is also noticed that the sensitivity of the PSI-16 had less variability in the comparison between the levels of education, whereas in the FAB the specificity in the low level of education was considered weak (39.4%). In the ≥ 8 years level of education, the ROC curve of the MMSE was significantly better than that of PSI-16 and FAB, representing the superiority of this measure in the cognitive screening process for dementia. Currently, the MMSE is the most widely used cognitive screening test for elderly people in the world, considering literate people. There are translated and authorized versions for over 35 countries, being considered an elementary test for psychiatrists, neurologists, geriatricians, and psychologists of aging (MELO; BARBOSA, 2015).

The effects of formal education on cognition appear to be complex. A Mexican study (PERTL *et al.*, 2017) evaluated the performance of 806 subjects (between 16 and 85 years old, educational level from 0 to 10 years) using a neuropsychological battery. Individuals with less education had significantly worse performance in almost all tests. Even if they make use of instruments with valid evidence, developing countries face challenges to detect cognitive impairments, especially when there are items in the instruments that require formal education, since a significant portion of their population is illiterate or has little schooling (APRAHAMIAN *et al.*, 2011).

It was also observed that, regarding the division of the sample by age group, the PSI-16 exhibited greater accuracy in the group under 70 years of age, unlike the other instruments, which showed superiority in the group over 70 years of age. The FAB was characterized as the tool that most changed with the adjustment for age, demonstrating a low sensitivity for ages below 70 years and a high sensitivity for the upper ones.

The cut-off point of the PSI-16, on the other hand, went from 21 to 19, with moderate sensitivity and specificity indexes, that is, even though it is an exam with qualitative questions, it demonstrated the ability to differentiate the groups, considering the aspects of age. It can be concluded that the cognitive screening in elderly people with advanced age is more evident in the screening measures, since there are more declines and more cognitive impairment (PERTL *et al.*, 2017), making the instruments more sensitive to capturing them (SALTHOUSE *et al.*, 2012).

Considering 60 years as a criterion to be perceived as an elderly person may generate bias in the results of cognitive assessments, since certain participants, who are analyzed as elderly, may not be so if their living conditions are currently similar to those of developed countries. It is added that the adoption of this criterion for developing countries compromises, for example, the comparison between national and international studies, since they analyze samples of different ages (MELO; BARBOSA, 2015).

Conclusion

In general, from the instruments that evaluated the frontal lobe functions, in the present study, there is a superiority of the PSI-16 in the accuracy values in both levels of education, as well as a lower variability in the other measures (sensitivity, specificity, PPV and NPV) and in the adjustment for age. Studies with a Brazilian sample, such as the one by De Paula *et al.* (2013), found that the total FAB score was significantly affected by age and formal education, but not by gender. In this same research, the authors found that specific subtests of the instrument (verbal fluency, motor sequence and conflicting instructions) contributed significantly to the differential diagnosis between healthy and pathological aging. FAB is generally associated with general measures of cognitive functioning, such as the Dementia Rating Scale (DUBOIS *et al.*, 2000) and MMSE.

Cognitive impairment in mild AD is generally not very pronounced and it is more expressive in episodic memory deficits, which may explain the moderate accuracy of both FAB and PSI-16 alone in the diagnosis. Since these are tests for screening, their accuracy for detecting executive impairment in patients with AD may be limited, and this assessment should be complemented with neuropsychological tests designed for examining more specific components (PEREIRA *et al.*, 2010).

The choice of cut-off point can generate insecurities and concerns among those who intend to use screening instruments, since they may incur in the error of including false positives or false negatives for cognitive deficits. Studies approaching the adjustment for other variables such as socioeconomic level, socio-cultural aspects and more specific samples of the elderly population are needed.

This study has some limitations that must be recognized. The current sample included only participants in mild or moderate stages of dementia and the results do not apply to the assessment of individuals with severe dementia. One can also cite the number of participants with low education as one of the factors that may have prevented the understanding of the PSI-16 items, also the age disparity between the groups, as well as the difficulties - both healthy and pathological - imposed by the aging process.

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