Philadelphia Brief Assessment of Cognition in healthy and clinical Brazilian sample

Avaliação Cognitiva Breve da Filadélfia numa amostra brasileira clínica e saudável

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ABSTRACT

The Philadelphia Brief Assessment of Cognition (PBAC) is a neuropsychological screening instrument that assesses five cognitive domains: working memory, visuospatial functioning, language, episodic memory and comportment. The aim is to verify if PBAC can properly be used in the Brazilian sample. Participated in this study: (a) 200 healthy volunteers - 100 young [21.6(2.5) years old] and 100 older adults [70.1(7.3) years old]; >12 years of education; (b) 30 Alzheimer's patients (AD) [73.7(5.7) years old], 4-11 years in education. The PBAC scores: (a) 95.8(2.6), 90.0(4.4) and (b) 65.0(10.8) were correlated with the Mini-Mental State Examination (MMSE) for young 29.1(0.9), older adults 28.3(1.4) and AD 18.4(3.0) groups. A positive correlation between MMSE and PBAC ($r=0.9$, $p<0.001$) was found. Negative correlations were observed between PBAC domains [memory (-0.63), visuospatial abilities (-0.44) and working memory (-0.3) tasks]. MANOVA showed a better male performance in visuospatial functioning ($F=8.5$, $p=0.004$). The Brazilian version of PBAC proved to be a promising screening instrument for clinical purposes.

Key words: Philadelphia Brief Assessment of Cognition, Alzheimer´s disease, cognition, dementia.

RESUMO

O instrumento de rastreio neuropsicológico *Philadelphia Brief Assessment of Cognition* (PBAC) avalia cinco domínios cognitivos: memória de trabalho, habilidade visuoespacial, linguagem, memória episódica e comportamento. O objetivo é verificar a viabilidade do PBAC em amostra brasileira. Participaram: (a) 200 voluntários - 100 jovens com 21,6(2,5) anos e 100 idosos com 70,1(7,3) anos, ambos com média de escolaridade maior que 12 anos; (b) 30 pacientes com Alzheimer, com 73,7(5,7) anos e escolaridade entre 4 e 11 anos. Os escores do PBAC para os respectivos grupos (a) 95,8(2,6), 90(4,4) e (b) 65(10,8) foram correlacionados com o Mini Exame do Estado Mental (MEEM). Houve correlação positiva ($r=0,9$; $p<0,001$) entre MEEM e PBAC, e negativas entre os domínios do PBAC [memória (-0,63), habilidades visuoespaciais (-0,44) e memória de trabalho (-0,3)]. Foi demonstrado pela MANOVA melhor desempenho no funcionamento visuoespacial em homens ($F=8,5$, $p=0,004$). A versão brasileira do PBAC provou ser promissora como um instrumento de rastreio para propósitos clínicos.

Palavras-Chave: *Philadelphia Brief Assessment of Cognition*, doença de Alzheimer, cognição, demência.

Dementia assessment implies measuring cognitive functions and some instruments have been used in Brazil for this purpose. One of the most frequently used is the Mini-Mental State Examination (MMSE)[1], a short screening assessment of cognitive impairment. This success is due to the fact that it requires only 5-10 minutes to be administered and has good reliability[2].

However, MMSE presents some limitations[3]. For example, it emphasizes function rather than verbal skills and non-dominant hemisphere executive functions. This indicates that MMSE may be of little screening use for frontal executive dysfunction and visuospatial deficits[4]. This is a major flaw if one considers the important role of executive functions in early clinical stages of dementia[3]. Another limitation is that the MMSE has a low sensitivity for patients with mild memory deficits[5], since only three words are required to be remembered in the recall task. Finally, MMSE does not analyze behavioral changes, which are important in Alzheimer's disease (AD) and frontotemporal dementia (FTD) diagnosis[6,7]. Therefore, MMSE may not be sufficient to assess the severity of clinical course of other types of dementia[8].

Considering these MMSE limitations, Dr. David Libon created in 2007 the Philadelphia Brief Assessment of Cognition (PBAC), a neuropsychological screening instrument sensitive to neuropsychological deficits associated with AD and patients with FTD dementia[7]. It is easy to apply and can be

administered quickly, lasting about 15 to 20 minutes. In comparison with other brief batteries, the PBAC presents some advantages: it provides more detailed information about those cognitive functions that are impaired or preserved, as well as having greater sensitivity to a broad spectrum of dementias. The 23 tasks are grouped into 5 functioning domains, each one evaluating different cognitive areas. These are: working memory/mental search, visuospatial functioning, language, verbal/visual episodic memory and social comportment/behavior. The total PBAC (3th brief version, 2010) score ranges between 0 and 100. Its first version (2007) ranged between 0 and 126. Recently, the PBAC has been used to determine patterns of neuropsychological impairment in FTD[6].

The aim of this work is to test the PBAC (3th version) into a Brazilian sample looking for aging effects by comparing young and old adults. The sensitivity of PBAC to determine severity of Alzheimer's disease was assessed by correlating the total PBAC score with the MMSE.

METHODS

Subjects

Comparison sample was formed by 200 healthy volunteers: 100 younger adults (mean age: 21.6±2.5; 56 men and 44 women) and 100 older adults (mean age: 70.1±7.3; 27 men and 73 women) with >12 years of education (with no memory disorders and they were self-sufficient in terms of daily activities).

Clinical sample was used to obtain PBAC sensitivity and specificity analysis. This group was formed by 30 AD patients (mean age: 73.7±5.7), 7 men and 23 women with 4 to 11 years of education. Seventeen patients were recruited from a public hospital in Brasilia (HUB - Brasilia University Hospital) and thirteen from the IBNeuro - Brazilian Institute of Neuropsychology and Cognitive Sciences based on the criteria of the National Institute of Neurological Disease and Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA). They had received a diagnosis of probable AD in their most current evaluation by a Medical and Neuropsychological Committee (ranging from 1 to 2 in Clinical Dementia Rating).

All subjects were screened for dementia using the MMSE[1] and the average scores were 29.1(0.9) to the young group, 28.3(1.4) to the older group and 18.4(3.0) to AD patients. Written informed consent in accordance with the ethical guidelines for research with human subjects (196/96 CNS/MS Resolution) was obtained from all participants and their caregivers (when appropriate). The study was approved by the Human Subjects Ethical Committee from the University of Brasilia.

Education profile was analyzed in younger adults, older adults and AD patients. They were divided into four

Table 1. Distribution according to gender and education level for young, old and Alzheimer's disease (AD) groups.

		Young	Old	AD	Total
Gender	Male	56	27	15	98
	Female	44	72	16	132
Education	<4 years	0	5	12	17
	5-8 years	0	6	11	17
	9-11 years	6	22	6	34
	>12 years	94	66	2	162

educational level groups: 1 to 4 years, 5 to 8 years, 9 to 11 years, and more than 12 years of schooling (Table 1).

Instrument

The PBAC (3th brief version, 2010) was generously given by Professor Dr. David Libon[7] (Department of Neurology, Drexel University College of Medicine, Philadelphia, Pennsylvania). It was translated (and back-translated) to a Brazilian version by neuropsychologists fluent in English and Portuguese. Twenty-four young and six old adults were used as a pilot study group in order to test the comprehension of the Brazilian translation.

This Brazilian version of the PBAC was individually applied to all subjects in a single session and in a fixed order. The number of points credited for the correct response varied in accordance with the task. SPSS/PASW (18.0 version) software was used to statistical and data analysis.

The total PBAC (3th version) score ranges between 0 and 100. The first version (2007) ranged between 0 and 126[7]. The principal component analysis yielded a five-factor solution related to executive control, processing speed, lexical access, semantic memory and episodic memory.

The PBAC working memory/mental search scale contains Letter Fluency Test [60 s to generate words with a specified letter (letter "F")] and an Oral Version of the Trial Making Test, part B (linking numbers and letters; i.e., 1-A, 2-B, etc). Language scale contains five tests: naming, sentence writing, conversational speech and word reading. Visuospatial/visuoconstructional skills were assessed by three tests: copying a modified version of the Rey Complex Figure Test, line orientation and matching lines to a target in the non-line array. Episodic memory (verbal memory and learning) were scored with a four dependent variables – number of words reproduced on the third learning trial of the word list, delayed free recall for a word list, delayed recognition test, delayed visual episodic memory (using a modified Rey Complex Figure Test). Social comportment/behavior scale was assessed by clinical observation of six behavioral domains: apathy/poor initiation, disinhibition, social comportment, agitation/irritability, ritual/obsessive compulsive behavior and lack of empathy.

RESULTS

Psychometrical analysis was performed to determine PBAC's reliability and validity. Because unequal variances, a non-parallel estimate of reliability was performed (Cronbach's alpha, $\alpha=0.804$). Two components were extracted using principal component analysis method to determine factorial validity. Only one PBAC task (Lecture) was obtained in a second order factor in the factor intercorrelation matrix (0.772). Internal consistency was also obtained by Pearson correlation ('item-item' and 'test-item') and all values were significant at $p<0.01$.

The PBAC raw scores of all 230 participants were divided into three groups: younger 95.8(2.6), older adults 90.0(4.4) and AD patients 65(10.8). As noted here, there is little overlap between healthy old adults and AD patients.

An item analysis for each PBAC subtest within each of the five subscales (working memory/mental search, visuospatial functioning, language, verbal/visual episodic memory and social comportment/behavior) was conducted. A *post-hoc* one-way ANOVA Dunnett test showed significant differences ($p<0.001$) in memory, executive functions and visuospatial tasks, but not in language [comparing younger and older adults ($p=0.147$), younger and AD patients ($p=0.93$), older adults and AD patients ($p=1.85$)] and in behavior [younger and AD patients ($p=0.159$)].

To evaluate the difference in each task, *t*-test was used showing that there were differences in these same PBAC tasks between younger and older adults. However, there was no statistical difference between social behavior and language ($t=1.959$, $p=0.052$) scores.

Differences were observed between older adults and AD patients in all domains (Table 2), except behavior ($t=1.976$, $p=0.057$) and language ($t=1.896$, $p=0.067$) tasks. It is worth noting, however, that the values were close to the $p<0.05$ criterion. Note that variances in MMSE and PBAC scores were higher in AD group (s.d=3.0 and 10.8, respectively) than the others groups. Average mean and standard error analysis of each PBAC subtest showed that slope was great in memory, followed by visuospatial abilities and executive functions.

Regarding gender, a multivariate analysis of variance (MANOVA) was performed using only younger and older adults data, and results revealed no significant differences among the groups in memory ($F=2.27$, $p=0.133$), executive functions ($F=0.57$, $p=0.451$), language ($F=0.168$, $p=0.683$) and behavior tasks. However, males performed better than females in visuospatial abilities tasks ($F=8.56$, $p=0.004$).

Possible correlations among the PBAC tasks were performed using Pearson correlation. Age had a stronger negative correlation ($r=-0.63$) with memory and a weak negative correlation with language tasks ($r=-0.193$). The PBAC raw scores were negatively correlated to age in the old group ($r=-0.452$, $p<0.01$), but not for AD group. The PBAC and MMSE were strongly correlated: $r=0.897$ ($p<0.001$, $n=230$). Regression R^2 value was 0.82. Correlations were calculated between PBAC and MMSE raw scores with young ($r=0.115$, $p=0.253$), old ($r=0.38$, $p<0.001$) and AD groups ($r=0.697$, $p<0.001$).

Excluding young group of the sample, the total area under ROC curve (sensitivity versus 1-specificity) showed cut-off point in PBAC (0.991, s.e.=0.05) scores.

DISCUSSION

In the present research, we described a relatively brief screening instrument that could be used within the context of clinical practice. The sensitivity of the PBAC to assess AD is supported by its robust correlation with the MMSE as found in this study and in a previous research[7]. However, education disparity is a problem in our study: higher education level in healthy volunteers (mean above 12 years) compared to the low level (4-11 years) in AD patients. Two domains in the PBAC were not very sensitive: language and social comportment/behavior, and they should be excluded of raw score.

Some questions can properly be answered in this study. A major challenge for neuropsychological evaluation is distinguishing changes in some cognitive domains that occur during the so-called "normal" aging and certain diseases, such as Alzheimer's disease[9-11]. This is important because they

Table 2. Mean, standard deviation and median of age, education, MMSE score and PBAC tasks.

	Young (n=100)	Old (n=100)	AD (n=30)	*t*-test
Age (years)	21.6(2.5) 18-29	70.1(7.3) 60-89	73.7(5.7) 61-91	Y<O<AD*
Education	≥12	≥5−12	>4<11	Y=O=>AD*
MMSE raw score	29.1(0.9) 29.3	28.3(1.4) 28.5	18.4(3.0) 17.9	Y > O > AD*
PBAC raw score	95.8(2.6) 96.3	90.0(4.4) 90.5	65.0(10.8) 62.5	Y > O > AD*
Memory	24.9(1.8) 25	21.1(3.0) 22	7.87(3.1) 7	Y > O > AD*
Executive function	10.2(1.7) 10	9.1(2.0) 9	7.9(3.1) 7	Y > O > AD*
Visuospatial ability	17.8(0.7) 18	16.9(1.2) 17	10.9(4.7) 11	Y > O > AD*
Language	18.9(0.3) 19	18.8(0.5) 19	18.1(1.9) 19	Y = O = AD
Behavior	24(0) 24	24(0) 24	23.8(0.4) 24	Y = O = AD

Y = young; O = old; AD = Alzheimer's disease; PBAC: Philadelphia Brief Assessment of Cognition; MMSE: Mini-Mental State Examination.
* ($p<0.001$)

may vary widely between individuals[12]. Results from Seattle Longitudinal Study[13,14] showed that there is a large degree of overlap in younger, older and very older adults over several cognitive dimensions. In orientation, spatial vocabulary, inductive reasoning, numerical abilities, immediate memory and daily activities tests a 90% overlap in scores was found between young and older adults up to 67 years-old. Inductive reasoning scores showed signs of cognitive decline after this point, in which the overlap was stable until age of 74 years-old.

In neuropsychological evaluations, we seek to compare patients' level of cognitive performance with the expected level of standard comparison. Significant discrepancies occur in one or more test scores enabling the cognitive functioning assessment of psychiatric, educational or cultural impairment as is done in the patient's experiences, considering their historical circumstances[11,15,16] and emotional memories[17-19]. Several studies also suggest the effect of education level on the performance of cognitive tasks[20].

The Brazilian version of the PBAC is quick and easy to apply and, in the sample studied, presented good screening evaluation instrument, differentiating patients with AD from the control group. Regarding gender, differential performance was observed only in visuospatial abilities, but the PBAC raw score had no gender influence.

Age differences had negative impacts on PBAC cognitive tasks, which were higher in memory than in language (Table 2). It is consistent with studies conducted by Salthouse[13,14] based on 33 of their own studies with a total sample of almost 7,000 subjects ranging from 18 to 95 years old. He concluded that age has a correlation of 0.63 with performed tasks to assess vocabulary, -0.31 with processing speed tasks, -0.15 and -0.48 with memory tasks and the intelligence g factor. In turn, the g factor has a correlation of 0.97 with reasoning, 0.91 with spatial abilities, 0.66 with memory, 0.60 and 0.73 with through and vocabulary[13]. Other studies used neuropsychological measures of attention, memory and visuospatial abilities in which individuals aged from 60 to 80 years had their performance compared with individuals between 16 and 60 years of age[12]. Different tests have shown different rates of change between groups, being the memory test the first to show a significant decline[11]. In other tests, there was no evidence of significant change with increasing age[21-23]. These studies are important because they show that not all assessment tests are equally sensitive to the decline and that not all individuals experience a decline with the same intensity.

A test which compares strings of letters and symbols does not show any significant change in scores for all ages[24]. It was only by the age of 75 years means that the results of the tests in almost all areas were significantly lower than the average score of the control subjects. This great variability among the elderly people poses problems when one tries to assess the significance of test results for each patient[24]. The most consistent finding in both transverse and longitudinal studies is that the delayed recall scores of attention are more vulnerable to the impact of aging[13]. Since these functions are also central to Alzheimer's disease symptoms, identifying the very early onset of this disease is complicated. Petersen and colleagues[25] demonstrated in their classical research that recognition memory is relatively little affected by normal aging, but is especially sensitive in dementia.

Learning scores (i.e., acquisition) steadily declined with increasing age and had no relation to scholarship level. Delayed recall (i.e., the rate of forgetting) remained relatively stable with age, when adjusted for the amount of early learned material[25]. These results suggest a strategy for deciding whether a patient's memory is impaired (learning, delayed recall or recognition memory scores drop below average levels). Screening tests such as the MMSE do not have many items to assess these cognitive domains[7]. PBAC screening test, in turn, evaluates them using a modified Rey Auditory Verbal Learning Test through these mnemonics domains.

In large cohort studies, declines in measures of delayed recall or accelerated forgetting were the best discriminators between patients with mild and non-dementia[8,20,25,26]. With increasing severity of illness, patients also have a constriction of immediate recall. Yet, these studies showed that patients may have impaired naming of objects, both in social interaction or through formal tests, even that they did not show any language disturb[10,15,27]. Since early studies, there are some discussion as to whether or not a loss of appointment reflects semantic system dissolution in general or whether it is a true aphasic deficit[16,28]. Very early, researches have shown that the degree of anomia has been associated with rapid progression of Alzheimer's disease[29].

Tests results of line orientation (as used in PBAC test) can often be preserved and be useful to detect progressive visuospatial dysfunction as Balint's syndrome, visual agnosia or simultagnosia (unusual distribution of plaques and tangles in the visual cortex of association[30]).

On the other hand, a negative point is PBAC behavior task which makes a subjective evaluation about the participant's behavioral changes. The main difficulty in this task is that researchers often do not have enough time or clinical training and this task should be performed by professionals with some diagnostic or assessment expertise. Perhaps for this reason ceiling effect was observed in this task. By contrast, this behavior task can be very useful in assessing psychiatric disorders which are quite common in dementia patients[20].

In continuing PBAC studies to obtain clinical normative data, it is necessary to grade the participant's dementia into groups based on clinical dementia rating (CDR) classifications and using different groups of dementia, such as frontotemporal dementia or mild cognitive impairment. Still, it is necessary to study a broader sample to obtain normative T-scores.

Taking into account the above mentioned aspects, the present work indicates that PBAC is a promising screening instrument for research and clinical purposes in Brazilian sample. However, in order to validate this instrument with reliability and validity for the Brazilian population, is necessary to do a large sample test including representatives from different Brazilian regions and different education level groups.

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