

Screening for cognitive impairment in late onset depression in a Brazilian sample using the BBRC-EDU

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ABSTRACT: Depression and dementia are the most prevalent neuropsychiatric disorders in the elderly population. Alzheimer's disease is the leading cause of dementia in most countries, being responsible for more than half of all dementia cases. Late-onset depression is a frequent cause of cognitive decline in the elderly. Differentiating between cognitive impairment secondary to depression and incipient dementia poses a challenge in the clinical setting. **Objective:** To evaluate the performance of elderly depressed patients using the BBRC-Edu. **Methods:** We studied 25 patients with late onset depression (mean age: 73.6 y (6.6); schooling: 9.1 y (5.7)) and 30 patients with mild AD (mean age 76.6 y (5.4); schooling: 7.5 y (7.1)), who were compared to a control group of 30 healthy elderly (mean age 73.8 y (5.8); schooling: 9.1 y (5.4)) using the CERAD and BBRC-Edu batteries. **Results:** For the CERAD battery, depressed patients performed better than AD patients on all tasks ($p < 0.0001$) except for Constructional Praxis ($p > 0.05$), and performed poorer than controls on verbal fluency (animals) and Word List Recall tasks ($p < 0.0001$). For the BBRC-Edu, depressed patients performed better than AD patients on all tasks ($p < 0.0001$) except for Digit Span (direct order) ($p = 0.076$) and Incidental Memory ($p > 0.05$), and performed worse than controls on Learning (second presentation) and verbal fluency (fruits) tasks ($p < 0.0001$). **Conclusion:** Overall performance on the BBRC-Edu allowed differentiation of controls and depressed patients from AD patients.

Key words: Alzheimer's disease, CERAD, BBRC-Edu, depression, screening test, cognition, elderly.

RASTREIO DE COMPROMETIMENTO COGNITIVO NA DEPRESSÃO DE INÍCIO TARDIO EM UMA AMOSTRA BRASILEIRA USANDO O BBRC-EDU

RESUMO: Depressão e demência são os transtornos neuropsiquiátricos de maior prevalência na população idosa. A doença de Alzheimer é a principal causa de demência na maioria dos países, sendo a responsável por mais da metade dos casos de demência. Depressão de início tardio é uma causa frequente de declínio cognitivo no idoso. A diferenciação entre transtorno cognitivo secundário à depressão e demência em fase inicial é um desafio na prática clínica. **Objetivo:** Avaliar o desempenho de pacientes idosos deprimidos usando a Bateria Breve de Rastreo Cognitivo (BBRC-Edu). **Métodos:** Estudamos 25 pacientes com depressão de início tardio, (idade média 73,6 (6,6); escolaridade: 9,1 (5,7)) e 30 pacientes com DA leve (CDR=1), (idade média 76,6 (5,4); escolaridade: 7,5 (7,1)). O desempenho de ambos os grupos foi comparado a um grupo controle de 30 idosos saudáveis (idade média 73,8 (5,8); escolaridade: 9,1 (5,4)). **Resultados:** Na Bateria CERAD pacientes deprimidos tiveram desempenho melhor que pacientes com DA em todos os testes ($p < 0,0001$) exceto para Praxia Construcional ($p > 0,05$), e desempenho pior que os controles na fluência verbal (animais) e Recordação da Lista de Palavras ($p < 0,0001$). Na BBRC-Edu, pacientes deprimidos tiveram melhor desempenho comparados aos pacientes com DA em todos os testes ($p < 0,0001$) exceto para Spam de Dígitos (ordem direta) ($p = 0,076$) e Memória Incidental ($p > 0,05$), e tiveram desempenho pior que os controles na Aprendizagem (segunda apresentação) e na fluência verbal (frutas) ($p < 0,0001$). **Conclusão:** A Bateria Breve de Rastreo Cognitivo permite a diferenciação de controles e pacientes com transtorno depressivo, de pacientes com doença de Alzheimer.

Palavras-chave: doença de Alzheimer, CERAD, BBRC-Edu, depressão, testes de rastreo, cognição, idosos.

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INTRODUCTION

Depression and dementia are two of the most prevalent neuropsychiatric diseases in the elderly, yet this population is far from homogeneous in terms of cognitive decline and depressive symptoms. Major depressive disorder is common in the general population having an estimated lifetime prevalence of 15-17%.¹ Clinically significant depressive symptoms are present in 11-39% of older adults²⁻⁴ while cognitive impairment is estimated to affect 17-36% of adults aged over 65 years.⁴⁻⁶ Elderly demented patients have shown an even higher prevalence of depression (24%) in epidemiological studies.⁷

Age-related cognitive decline is usually characterized by mild impairment in a number of cognitive domains,⁸ typically manifested as changes in episodic memory or reduced ability to access information stored in long-term memory^{9,10} resulting from decreased speed of the central processing required to encode and retrieve information.¹¹ In this population, working memory becomes affected^{12,13} while retention usually remains preserved^{8,12} as does implicit memory.¹⁴ Other changes associated with normal aging include mild deficits in language functioning (naming, verbal fluency), visuospatial abilities, perceptual speed and executive functioning.¹⁵⁻¹⁷ Amongst patients who suffer from late-life depression, 20-50% display deficits across a wide range of cognitive domains including processing speed,¹⁸ attention and executive functions^{19,20} as well as episodic and working memory.²¹

Furthermore, the level of generalized cognitive impairment associated with depression can be so marked in the elderly that depression is often misdiagnosed as dementia. Indeed, 9-43% of elderly persons who have depression subsequently develop some kind of dementia.²² This cognitive impairment can persist despite improvement in depressive symptoms.^{2,23} However, the true pattern of cognitive impairment in late-onset depression remains a matter of controversy because most studies available are modest or small in size, and cognitive deficits tend to differ in both nature and severity, between and within studies.²⁴

In view of the above-mentioned interrelationship between depression and AD, diagnosing dementia in depressed patients, regardless of depression, poses a challenge.²⁵ The aim of this study was to evaluate the performance of elderly depressed patients, healthy elderly, and patients with early stage AD using the BBRC-Edu, a screening battery fully developed by Brazilian researchers.²⁶ To the best of our knowledge, this is the first study

to employ the BBRC-Edu in the assessment of depressed elderly.

METHODS

Thirty patients with mild AD, 25 with depression and 30 control subjects were studied. All participants were native speakers of Brazilian Portuguese, aged over 60 years, and had at least 2 years of formal education. Subjects with a past history or neurological evidence of stroke, neurodegenerative disorders, head injury, serious non-compensated medical illness, drug abuse, hearing, visual or motor impairment that could have affected their cognitive performance were not included. The control group was defined as subjects living in the community, who fulfilled the MOANS criteria²⁷ and achieved normal scores on the cognitive evaluation (corrected for age and schooling). The diagnosis of depression was determined according to the DSM-IV criteria,²⁸ while the diagnosis of Probable AD was based on the NINCDS-ADRA criteria.²⁹ Only mild AD patients (CDR 1) were included.³⁰

The cognitive evaluation entailed application of the Brazilian version of the Consortium to Establish a Registry for Alzheimer's Disease Battery (CERAD).^{31,32} Depressive symptoms were evaluated using the Geriatric Depression Scale (GDS),³³ the Hamilton Depression Scale (HAM-D),³⁴ and the Montgomery & Asberg Depression Rating Scale (MADRS).^{35,36} Functional abilities were assessed using the Pfeffer Functional Activities Questionnaire (PFAQ).³⁷ Depressed patients were evaluated within one week of introducing antidepressant medication.

After the initial evaluation, subjects were classified into controls, depression or mild AD. Participants were then assessed using the Brief Cognitive Battery-Edu (BBRC-Edu), which was developed in Brazil and has proven suitable for screening cognitive impairment in the Brazilian population, being less impacted by educational level.²⁶

The performance of the three groups on each task was compared using one-way ANOVA with Tukey's post-hoc test. All statistical analyses were performed using the SPSS for Windows® 10.0.1 software, and a significance level of 0.05 was adopted.

This study was approved by the local Research Ethics Committee (Hospital das Clínicas – University of São Paulo School of Medicine) and all participants or their legal representatives signed an informed consent prior to enrolling on the study.

RESULTS

The demographic and clinical characteristics of the

sample are shown in Table 1. The mean values for age and schooling level were similar across the three groups. Women predominated in the depression and AD groups. AD patients had lower scores on the PFAQ, as expected. Controls and Depression patients did not differ for PFAQ scores. All groups differed in GDS, HAM-D and MADRS scores, with patients from the Depression group exhibiting the highest scores while patients from

the AD group had scores between those of the Control and Depression groups.

Table 2 shows performance of the three groups on the CERAD battery. Depressed patients performed better than AD patients on all tasks except for Constructional Praxis, but performed poorer than controls on verbal fluency (animals) and Word List Recall tasks.

On the BBRC-Edu, depressed patients performed

Table 1. Demographic and clinical characteristics of the sample.

Variable	CG			DG			AD			p (two-tailed)		
	Mean	(SD)	range	Mean	(SD)	range	Mean	(SD)	range	Multiple comparison		
Age	73.8	(5.8)	60-87	73.6	(6.6)	65-93	77.6	(5.4)	60-85	0.055*		
Schooling	9.1	(5.4)	2-23	9.1	(5.7)	2-20	7.5	(7.1)	2-33	0.519*		
Gender	M		16			20			23	0.0005**		
	F		14			5			7	CG × DG p=0.005 CG × AD p=0.006		
PFAQ		0	(0)		1.2	(2)		19.9	(5.2)	<0.0001*		
		0-0		0-5		5-28				CG & DG × AD (p < 0.0001)		
GDS		2.2	(2.6)		24.6	(4.6)		10.3	(4.5)	<0.0001*		
		0-9		16-30		3-17				all groups differ		
HAM-D		2.4	(3.9)		32.8	(5.4)		14.6	(8.3)	<0.0001*		
		0-20		27-46		1-26				all groups differ		
MADRS		2.4	(5)		36.3	(7.2)		16.5	(8.4)	<0.0001*		
		0-24		30-51		2-28				all groups differ		

CG: control group; DG: depression group; F: female; M: male; NA: not applicable; *ANOVA with Tukey's post hoc test; **Chi-square test.

Table 2. Performance of the three groups on the CERAD battery.

Variable	CG			DG			AD			p (two-tailed)*		
	Mean	(SD)	range	Mean	(SD)	range	Mean	(SD)	range	Multiple comparison		
Verbal fluency (Animals)	18.1	(4)		15.1	(2.3)		9.7	(2.8)		<0.0001		
	14-30			12-20		0-14				all differ		
Naming 15 items	13.2	(1.7)		12.9	(1.7)		10.6	(2.1)		<0.0001		
	10-15			10-15		5-14				CG & DG × AD (p<0.0001)		
MMSE	27.2	(1.4)		26	(2.3)		20.7	(3.2)		<0.0001		
	23-30			21-30		13-26				CG & DG × AD (p<0.0001)		
Word List Memory	15.8	(3)		15.3	(3.1)		7.9	(3.8)		<0.0001		
	12-24			18-24		2-16				CG & DG × AD (p<0.0001)		
Constructional Praxis	9.7	(1.7)		9.2	(1.9)		8.1	(2.9)		0.022		
	7-11			7-13		4-13				CG × AD (p<0.018)		
Word List Recall	4.7	(1.6)		3.4	(1.2)		0.7	(0.9)		<0.0001		
	3-10			1-7		0-3				all differ		
Word List Recognition	8.9	(0.8)		8.3	(1.5)		4.3	(2.8)		<0.0001		
	7-10			5-10		0-10				CG & DG × AD (p<0.0001)		
Praxis Recall	7.6	(3.1)		6.3	(2.9)		1.5	(2.4)		<0.0001		
	2-11			2-11		0-10				CG & DG × AD (p<0.0001)		

CG: control group; DG: depression group; F: female; M: male; NA: not applicable; *ANOVA with Tukey's post hoc test.

Table 3. Performance of the three groups on the BBRC-Edu battery.

Variable		CG	DG	AD	p (two-tailed)*
		Mean (SD) range	Mean (SD) range	Mean (SD) range	Multiple comparison
Digit Span	Direct order	8.8 (1.7) 6-12	8.9 (1.4) 6-12	7.9 (1.9) 5-11	0.076
	Reverse order	4.5 (1.5) 2-8	4.1 (1.5) 2-8	2.8 (1.6) 1-8	0.0001 CG × AD (p<0.0001) DG × AD (p=0.004)
Learning and memory	Perception/Naming	10 (0) 10-10	10 (0) 10-10	9.8 (0.3) 9-10	0.020 CG & DG × AD (p=0.037)
	Incidental memory	4.7 (1.4) 3-9	4.1 (1.5) 2-7	3.5 (1.7) 0-7	0.011 CG × AD (p=0.008)
	Learning 1	7 (1.4) 5-10	6.7 (2) 3-10	4.6 (1.7) 1-8	<0.0001 CG & DG × AD (p<0.0001)
	Learning 2	8.9 (0.9) 7-10	7.4 (1.9) 3-10	5.2 (1.3) 2-8	<0.0001 all differ
	Delayed recall	7.5 (1.7) 4-10	6.3 (2.3) 2-10	2.4 (2.2) 0-7	<0.0001 CG × AD (p<0.001) DG × AD (p<0.0001)
	Picture recognition	9.7 (0.5) 8-10	9.5 (0.8) 7-10	6.9 (2.8) 0-10	<0.0001 CG & DG × AD (p<0.0001)
	Verbal fluency (Fruits)	15.6 (2.4) 13-23	13 (2) 7-16	9 (2.7) 4-16	<0.0001 all differ
	Clock drawing	9.3 (1.6) 2-10	8.4 (2) 3-10	4.9 (2.5) 2-10	<0.0001 CG & DG × AD (p<0.0001)

CG: control group; DG: depression group; F: female; M: male; NA: not applicable; *ANOVA with Tukey's post hoc test.

better compared with AD patients on all tasks except for Digit Span (direct order) and Incidental Memory, yet performed worse than controls on Learning (second presentation), and verbal fluency (fruits) tasks. For the two latter tasks, depressed patients showed an intermediate performance compared to controls and AD patients (Table 3).

DISCUSSION

The choice of psychometric tests for use in Portuguese-speaking people classified into well-defined groups is limited.³² It is difficult to discriminate early dementia from depression based on clinical and neuropsychological evidence³⁷ because similar cognitive and affective problems can occur in both mild AD and “depressive pseudo-dementia”.³⁹ The hallmark of AD is marked impairment in episodic memory, which may exist years before a clinical diagnosis of dementia is established.^{40,41} However, semantic impairments also occur in approximately 50% of patients with mild AD where semantic memory may be the most important cognitive domain for performing everyday skills.^{10,42}

Depression is particularly associated with deficits in

executive control processes.^{43,44} Patients with late-onset depression have demonstrated impairments in executive functioning, processing speed, as well as episodic and semantic memory.⁴⁵ Notwithstanding, few studies in the literature on late-onset depression have investigated semantic memory. However, semantic memory tasks often require preserved executive function. Category fluency for example, although generally regarded as a valid measure of semantic memory, relies heavily on initiation, which may be impaired in depression.⁴⁵ In addition, the individual under test is required to perform this task within a set time limit, which makes processing speed an important factor for good performance.⁴⁶ In the present study, depressed patients consistently displayed impairment in verbal fluency, both for animal and fruits categories.

The presence of depression-related deficits in geriatric depression has been noted in episodic memory.^{23,47-49} Sheline et al. 2006⁴⁹ and Delaloye et al. 2008⁵⁰ have suggested that while slowed processing speed appears to be the core cognitive deficit in late-onset depression, it was closely followed by executive dysfunction. However, these authors hold that episodic memory impair-

ment cannot be explained solely by processing resource decreases in late-onset depression patients. Recent data suggest that the reduction in processing resources is a primary cognitive decrement in late-onset depression, which subsequently induces higher-level cognitive deficits.^{18-21,49} For instance, besides memory, impaired language abilities in old age have been associated with a reduction in processing resources, such as processing speed, working memory span and inhibition capacity. Processing speed, which denotes the pace at which elementary cognitive operations are carried out, is reduced in late-onset depression.²¹ Depression-related variance on higher-order cognitive tests is also thought to be mediated by reduced working memory span, which is able to maintain or suppress the activation of long-term memory units and allocation of intentional resources. Finally, inefficient inhibitory processes permit the entry and maintenance of irrelevant information in the working memory, affecting subsequent cognitive performance.⁵⁰ In this study, depressed patients did not differ

from controls in cued recall memory tasks (recognition) for verbal and non-verbal stimuli, thus suggesting an impairment of self-generated retrieval strategies, which may be secondary to lower processing speed associated to executive dysfunction.

In the clinical setting, it may be difficult to differentiate depression from incipient AD in patients with cognitive impairment. Brief cognitive tests may be helpful in assessing patients with suspected dementia in primary care facilities provided these instruments are sufficiently accurate. By comparing the performance of controls, depressed patients and mild AD patients using a well-accepted battery (CERAD) plus a battery developed in Brazil (BBRC-Edu), we found that the latter was suitable for detecting mild cognitive impairment in depressed patients and also proved able to discriminate this group from AD patients. Further studies are warranted in order to establish the degree of agreement between the BBRC-Edu and other broadly used screening tests, such as the MMSE and CERAD.

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