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ARTICLE

Verbal learning on depressive pseudodementia: accentuate impairment of free recall, moderate on learning processes, and spared short-term and recognition memory

Aprendizagem verbal na pseudodemência depressiva: comprometimento acentuado da evocação livre, moderado nos processos de aprendizagem e preservação da memória de curto prazo e reconhecimento

Jonas Jardim de Paula[1,2], Débora Marques Miranda[2], Rodrigo Nicolato[3], Edgar Nunes de Moraes[4], Maria Aparecida Camargos Bicalho[4], Leandro Fernandes Malloy-Diniz[1,2,3]

ABSTRACT

Objective: Depressive pseudodementia (DPD) is a clinical condition characterized by depressive symptoms followed by cognitive and functional impairment characteristics of dementia. Memory complaints are one of the most related cognitive symptoms in DPD. The present study aims to assess the verbal learning profile of elderly patients with DPD. **Methods:** Ninety-six older adults (34 DPD and 62 controls) were assessed by neuropsychological tests including the Rey auditory-verbal learning test (RAVLT). A multivariate general linear model was used to assess group differences and controlled for demographic factors. **Results:** Moderate or large effects were found on all RAVLT components, except for short-term and recognition memory. **Conclusion:** DPD impairs verbal memory, with large effect size on free recall and moderate effect size on the learning. Short-term storage and recognition memory are useful in clinical contexts when the differential diagnosis is required.

Key words: dementia, Alzheimer's disease, mood disorders, unipolar, memory.

RESUMO

Objetivo: A pseudodemência depressiva (PDD) é uma condição clínica onde sintomas depressivos são acompanhados por comprometimento cognitivo e funcional característicos da demência. Queixas de memória são um dos sintomas mais comumente relatados na PDD. O presente estudo almeja investigar a aprendizagem verbal de pacientes idosos com PDD. **Método:** 96 idosos (34 PDD e 62 controles) realizaram testes neuropsicológicos incluindo o Teste de Aprendizagem Auditivo-Verbal de Rey (RAVLT). Adotou-se um modelo linear geral multivariado para comparação dos grupos controlando variáveis sociodemográficas. **Resultados:** Pacientes com PDD apresentaram déficits em todo o RAVLT, com exceção no armazenamento de curto-prazo e reconhecimento, com tamanhos de efeito moderados ou altos. **Conclusão:** A PDD compromete a memória verbal mais intensamente na evocação livre e de forma moderada na aprendizagem. A memória de curto-prazo e de reconhecimento são úteis em contextos onde o diagnóstico diferencial é necessário.

Palavras-Chave: demência, doença de Alzheimer, transtornos de humor, unipolar, memória.

Depression is one of the most frequent causes of emotional disturbances and cognitive impairment and course with an important loss of quality of life[1]. Depressive symptoms are usually more frequent in elderly subjects than in younger adults but also more difficult to detect[1]. Depressive symptoms are associated with cognitive deficits, especially in

Instituto Nacional de Ciência e Tecnologia de Medicina Molecular, Medical School, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte MG, Brazil.
[1]Laboratory of Neuropsychological Investigations (LIN), UFMG, Belo Horizonte MG, Brazil;
[2]Instituto Nacional de Ciência e Tecnologia de Medicina Molecular, Medical School, UFMG, Belo Horizonte MG, Brazil;
[3]Mental Health Department, Medical School, UFMG, Belo Horizonte MG, Brazil;
[4]Internal Medicine Department, Medical School, UFMG, Belo Horizonte MG, Brazil.
Correspondence: Jonas Jardim de Paula; Avenida Alfredo Balena 190; 30130-100 Belo Horizonte MG - Brasil; E-mail: jonasjardim@gmail.com
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late-onset depression[2], usually associated with slow processing speed, memory impairment, and executive dysfunction[1-3]. The mechanism by which depression mediates the cognitive impairment is still controversial, but certainly is multidimensional and involves brain structural changes, monoaminergic neurotransmission, and chronic inflammatory processes resulting in an abnormal behavior[3]. In some cases, the magnitude of the cognitive impairment secondary to depression may simulate the pattern expected in demented patients; a condition referred to as depressive pseudodementia (DPD)[4].

The diagnostic criteria of pseudodementia[4] consist in the presence of intellectual (cognitive) impairment without a primary neurological or other psychiatric disorder other than depression that could explain the presentation and presence of reversible or partially reversible deficits. The pseudodementia diagnosis is still adopted in mental health services, although some criticism has been elicited[5], especially on the reversibility of the cognitive impairment[6]. Cognitive deficits in major depressive disorder may persist after treatment, particularly those related to episodic memory and executive functions but may become less intense[3].

Memory complaints are one of the most related cognitive symptoms in clinical assessment and are necessary for the diagnosis of dementia according to DSM-IV criteria. One of the most widely used paradigms for episodic memory assessment is the auditory-verbal learning after successive presentations of a list of a certain number of substantives. This procedure is very sensitive for the detection of memory impairments in dementia, mild cognitive impairment, and other neuropsychiatric disorders[7]. The present study investigates the pattern of memory impairment in pseudodementia using a verbal-learning test.

METHODS

Participants

For this study, 96 elderly were evaluated in a Reference Center for older adults in Belo Horizonte, Brazil. The Instituto Jenny e Andrade Faria de Atenção ao Idoso is a secondary/tertiary public health unity of this city specialized in health the aged population. Assessment procedures are performed by a multidisciplinary staff. Diagnosis was consensual by at least one geriatrician and one clinical neuropsychologist. The DPD group (n=34, 23 women) was composed of patients refereed to neuropsychology for evaluation of cognitive performance, since they have a diagnosis of major depressive disorder. These referred patients have specific impairment on cognitive screening tests but spared global cognitive functioning and presented subjective cognitive and functional complaints. After neuropsychological assessment, results were discussed for exclusion of other causes of cognitive impairment (such as mild cognitive impairment due to neurodegenerative conditions, vascular cognitive impairment, and dementia). The diagnosis of DPD was performed when all protocols were filled. A control group was composed of 62 (66% women) healthy older adults also assessed. A brief neuropsychological protocol validated for Brazilian elders[8], with the exception of the Corsi Blocks Test, was used in all sample assessments, which includes tests of executive functions language, constructive praxis, and working memory. The project was approved by the Local Ethical Board (COEP-334/06), and all participants gave written consent for participation.

Verbal learning assessment

The Rey auditory-verbal learning test (RAVLT)[9] was used for the memory assessment, adapted and validated version and with appropriated normative data for Brazilian elders. The test has five learning trials of a 15-word list (A1–A5), followed by a distractor list (B1), an immediate recall (IR), a delayed recall (DR), and a recognition trial (Rec), representing different aspects of verbal learning. A recent study of validity for the Brazilian elderly population[10] suggests that in normal elderly two main cognitive processes are assessed by the RAVLT, one related to information encoding and storage (comprising the first four learning trials) and the other related to information search and retrieving (comprising the free recalls and recognition), with the A5 component as an intermediate process. We used the version proposed by Malloy-Diniz et al.[9], where the words used in the learning and recognition trials were chosen based on their frequency in Brazilian Portuguese.

Statistical analysis

The sociodemographic variables were compared by independent sample *t* tests and χ^2 tests. These results indicate differences in age (t=2.30, p=0.024, d=0.49) and education (t=2.10, p=0.033, d=0.45), but not gender (χ^2=0.02, p=0.880). The groups, as expected, also differed on the Short Version of the Geriatric Depression Scale (GDS-15) score (t=17.05, p<0.001, d=3.4). Since differences were found on demographic data, a multivariate general linear model was adopted for group comparisons. The cognitive tests were entered as dependent variables, gender and group as factors, and age and education as covariates. Significance levels were established at 0.05.

RESULTS

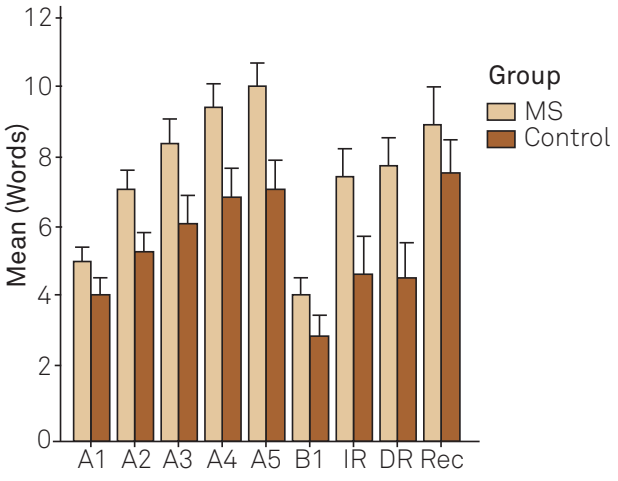
Main effects for group were found on almost all the RAVLT components, except for A1 and Rec (p>0.05) (Table and Figure). The effect sizes were moderate for the learning components of the RAVLT (A2–A4, RAVLT-Total) and

Table. Participants description, cognitive assessment and verbal-learning analysis.

Sociodemographic and cognitive measures	Participant description							
	Controls		DPD		Group		Corrected model	
	M	SD	M	SD	F	η^2	F	η^2
Age	73.94	7.84	70.21	7.12	–	–	–	–
Education	5.89	4.38	4.00	3.89	–	–	–	–
GDS-15	1.81	1.30	8.94	2.80	–	–	–	–
MMSE	27.34	2.96	22.85	3.62	19.98**	0.19	14.95**	0.46
CDT	4.10	1.18	2.47	2.18	18.17**	0.17	10.91**	0.39
DS	38.74	19.22	25.47	11.75	9.73*	0.10	5.54**	0.24
CFT	13.15	3.78	9.79	3.27	9.81*	0.10	9.93**	0.37
TT	31.63	3.22	29.47	3.36	3.45	–	4.76**	0.22
RAVLT-A1	4.92	1.83	4.00	1.44	2.69	–	6.40**	0.27
RAVLT-A2	7.06	2.19	5.21	1.72	8.90*	0.09	8.70**	0.34
RAVLT-A3	8.44	2.45	6.09	2.19	8.34*	0.09	5.53**	0.24
RAVLT-A4	9.42	2.60	6.82	2.38	10.06*	0.10	7.90**	0.31
RAVLT-A5	9.98	2.80	7.03	2.44	10.67*	0.11	8.74**	0.34
RAVLT-B1	4.06	1.64	2.82	1.64	5.04*	0.06	8.88**	0.34
RAVLT-IR	8.26	2.57	4.65	2.90	22.98**	0.21	9.48**	0.36
RAVLT-DR	8.24	2.82	4.47	2.96	27.17**	0.24	9.91**	0.37
RAVLT-Rec	8.90	4.30	7.13	3.13	1.38	–	6.85**	0.28
RAVLT–Total	38.32	11.89	29.15	9.18	7.05*	0.08	7.32**	0.30

*Significant at 0.05, **significant at 0.001.

SD: standard deviation; MED: median; DPD: depressive pseudodementia; GDS-15: short version geriatric depression scale; MMSE: mini-mental state exam; CDT: clock drawing test; DS: digit span; CFT: category fluency test; RAVLT: Rey auditory-verbal learning test; IR: immediate recall; DR: delayed recall, Rec: recognition.



RAVLT: Rey auditory-verbal learning test; DPD: depressive pseudodementia; NC: normal controls; IR: immediate recall; DR: delayed recall; NS: nonsignificant. Effect sizes of significant ($p<0.05$) comparisons are reported. Error bars indicate the standard deviation.

Fig 1. Comparison of the verbal learning profile on the Rey auditory-verbal learning test of normal controls and depressive pseudodementia patients.

large for the recall components of the test (RAVLT-IR and -DR), according to the two-factors solution proposed on a construct validity study of this memory task[10]. The DPD group also performed below the control group on the other cognitive measures with moderate or large effect sizes, except for the token test.

DISCUSSION

Memory impairment is a common symptom related to depressed older adults and is usually associated with depression severity[1,3]. The pattern of verbal memory impairment found in this study indicates deficits on learning (moderate) and recall (severe), with spared recognition. This pattern was also reported by other studies using list-learning tests[2,11,12]. This memory profile is expected due to the neurobiology of depression. According to a recent review[3], depression impairs most prominently the prefrontal cortex and the mesial temporal lobe regions (particularly the amygdala and the hippocampus). Verbal learning is particularly associated with an intricate circuitry involving the amygdala and its connections with frontal and temporal structures, such as the bilateral anterior cingulate cortex, bilateral medial temporal gyrus, and the left prefrontal cortex; regions also related to depressive symptoms[13].

Posterior cortical regions are usually preserved in depression. Studies of functional neuroimage suggest that in verbal learning tasks, such as the RAVLT, learning and recall process are more dependent of the mesial temporal lobe and prefrontal cortex connections than the recognition memory[14]. Aligned with this neurobiological base, the cognitive component of familiarity from the recognition memory, usually spared in depression, is a possible cognitive mediator for the spared performance on the recognition trial of verbal learning observed on the DPD group[15].

The current work has important limitations. First, although the diagnosis of DPD was performed by multidisciplinary consensus, the participants of this study were not followed-up systematically. This limits the analysis of cognitive symptom remission (or at least they attenuation) after depression treatment. A second limitation is the small sample size and the heterogeneity of the participants of the DPD group, which may limit the generalization of the current results. However, to our knowledge, this is the first Brazilian work with pseudodementia patients aiming specific memory process analysis in a verbal learning paradigm. The comparison of DPD patients with dementia and mild cognitive impairment in longitudinal studies with larger samples is important for a better comprehension of the relationship of DPD and memory processes.

Our results suggest that DPD presents a moderate impairment in verbal learning, a marked impairment in memory recall but spared recognition memory. This memory profile might be useful for clinical purposes, in contexts where the distinction between DPD, mild dementia, mild cognitive impairment, and normal aging is necessary.

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