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Executive function in patients with late onset depression

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Background. Depression is the most frequent psychiatric disorder in the elderly. Some authors consider late onset depression as a partially different phenomenological entity from that of the adult depression. The reason is its frequent association to dysexecutive cognitive impairment and cardiovascular risk factors.

Objective. This study aimed to analyze cognitive performance in neuropsychological screening tests in a group of late onset depression patients and non-depressed older adults.

Methods. Data was analyzed from 20 adults ≥ 60 years old with late-life depression in partial or total remission and 10 individuals with the same characteristics but without previous affective disorders. Data was gathered on age, gender, education level, medical and psychiatric history and pharmacological history. Overall cognitive functions, executive performances, depressive symptoms, vascular risk factors and comorbid medical illness were measured using standardized test such as the Mini-mental State Examination (MMSE), Executive Interview (EXIT-S), Geriatric Depression Scale (GDS), Cumulative Illness Rating Scale (CIRS). The differences between groups were analyzed with Analysis of Variance (ANOVA).

Results. Patients with late-onset depression had statistically significant greater executive difficulties regarding the control group on the EXIT-S scale.

Conclusions. Executive dysfunction can be considered a biological marker of late-life depression, although studies in larger samples of patients are needed.

Key words:
Vascular depression, Executive functions, Elderly depression, Major depression, Cognitive functions, Affective disorder.

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Disfunción ejecutiva en pacientes con depresión de inicio tardío

Introducción. La depresión es la enfermedad psiquiátrica más frecuente en ancianos. La depresión de inicio tardío (DIT) se considera una entidad fenomenológica parcialmente diferente de la depresión del adulto, debido a su frecuente asociación a disfunción cognitiva de características disejecutivas y a factores de riesgo cerebrovasculares.

Objetivos. Analizar el rendimiento cognitivo en pruebas neuropsicológicas de cribado de un grupo de pacientes con DIT respecto de un grupo de ancianos no deprimidos.

Métodos. Se evaluaron 20 individuos ≥ 60 años con antecedentes personales de DIT, GDS < 7, y 10 individuos de las mismas características sin antecedentes de trastorno afectivo. Se recogieron datos como edad, sexo, nivel educativo, historial médico, psiquiátrico y farmacológico. El funcionamiento cognitivo global, las funciones ejecutivas, los síntomas depresivos, los factores de riesgo vascular y las enfermedades médicas comórbidas fueron medidos utilizando: el Mini-Examen Cognoscitivo (MEC), el Executive Interview Scales (EXIT-S), la Cumulative Illness Rating Scale (CIRS) y la Escala de depresión geriátrica (GDS). Las diferencias entre los grupos fueron analizadas mediante ANOVA.

Resultados. Los pacientes con DIT presentaron mayores dificultades ejecutivas medidas a través de la escala EXIT-S respecto del grupo control.

Conclusiones. La alteración en pruebas de cribado de funciones ejecutivas podría ser un marcador biológico de los pacientes con DIT, si bien son necesarios estudios con muestras más amplias de pacientes.

Palabras clave:
Depresión vascular, Funciones ejecutivas, Depresión geriátrica, Depresión mayor, Función cognitiva, Trastorno afectivo.

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INTRODUCTION

Depression is the most frequent psychiatric condition in the elderly population.[1] Onset age of the first depressive episode has been used by many authors to differentiate geriatric depressions from early or late onset ones.[2] Compared with patients with recurrent early- onset depression (RED) in the adult state, patients with Late-Onset Depression (LOD) have fewer family history of affective disorder, less frequency of personality disorders and drug consumption, greater prevalence of comorbid medical conditions, greater impairment on the neuropsychological tests, greater subsequent incidence of dementia,[3] greater growth of lateral ventricles and more frequent findings of white matter hyperintensities.[4] Response to antidepressive treatment is generally poorer, late and unstable.[5]

Many of these abnormalities may be found by chance or non-specifically contribute to the appearance of the depressive symptoms while others may play a central role in the pathogenesis of these episodes. The richness of these findings has made it possible to create new diagnostic categories[6] with the frequent symptoms found in these elderly subjects such as the «depression–dysexecutive syndrome» (DES),[4] «Depression with Reversible Dementia» (DRD),[7] or «Vascular Depression» (VD).[8] All of these include cognitive impairment. Thus, the cognitive impairment of the elderly with depression could be considered as a *continuum* whose onset includes patients in whom the cognitive impairment is only the result of the depressive symptoms and the age, at the end of which the intellectual deterioration is due to a subclinical dementia condition with a major or minor contribution of the affective symptoms. Several grades of interaction between depression and brain disease (progressive or non-progressive) would exist between the two extremes.

This study aims to analyze the cognitive performance in neuropsychological screening tests in a group of patients with LOD and a group of non-depressed elderly subjects. We expect to find that the group of patients with LOD will present higher scores of executive dysfunction screening tests such as the Executive Interview Scale (EXIT-S), but not in other global deterioration evaluations such as the Mini-Mental State Examination (MMSE).

MATERIAL AND METHODS

Participants

Late-Onset Depression (LOD) was conceptualized as a first episode of Major Depression in accordance with the DSM-IV criteria after 60 years of age with or without the presence of subsequent relapses and absence of affective disorder prior to that age. The following patients were excluded: those with 1) active major depressive episode; 2) severe or acute medical diseases; 3) neurogical diseases such as Parkinson, Multiple Sclerosis, delirium, Brain Damage, Epilepsy, Dementia, Huntington's Chorea; 4) Schizophrenia, Bipolar Disorder and other psychiatric conditions, except personality disorder; 5) personal history of chronic substance abuse (including alcoholism); 6) visual, auditory or motor deterioration that infers in the neuropsychological tests; 7) institutionalized patients. The cases (n = 20) were selected consecutively for three months in two outpatient psychiatric clinics of the Mental Health Centers of both the Madrid and Castilla y Leon Communities. The controls (n = 10) were selected through volunteers from primary care out-patient clinics in the same health care areas. All gave their written informed consent.

Evaluation

The following data were included in the evaluation: age, gender, marital status, education, personal psychiatric (PD) and family (FD) history. The following psychometric scales were also used: Yesavage Geriatric Depression Scale (GDS)[9,10] and the cardiorespiratory subscale of the Cumulative Illness Rating Scale (CIRS).[11,12] The cognitive evaluation was made with the Mini-Mental State Examination (MMSE)[13] and the Executive Interview (EXIT-S).[14]

The Yesavage Geriatric Depression Scale (GDS) is a depression scale specifically made for the elderly. It is a test of detection of possible presence of depression. The 15-point brief version is used in this study, with a cut off of 7 for the positive cases. The Cumulative Illness Rating Scale (CIRS) is an instrument that has been validated in Spanish for the measurement of organic disease, organized into six groups of organs —cardiorespiratory, gastrointestinal, genitourinary, musculoskeletal, neuropsychiatric and general systems. Each system was scored with a severity of 0-4. The MEC (abbreviation of Spanish version of MMSE) is a translation and adaptation to Spanish of the MMSE[15] that evaluates time and space orientation, mnesic registry, attention and calculation, recall, speech and constructive praxis. The Executive Interview Scale (EXIT-S) is a tool that includes different tests such as frontal release, motor or cognitive perservation signs, verbal intrusions, disinhibition, loss of spontaneity, imitation and utilization behaviors, impairment verbal fluency tests, go/no go tests, word/color interference tests, design fluency test. The range of possible scores is 0-50, with higher scores indicating greater impairment of the executive functions. Scores above 15 correlate with significant cognitive impairment and behavioral changes.

Statistical analysis

The differences between both groups were evaluated using the analysis of variance (ANOVA) model. Because of the possible influence of the depressive symptoms on the scores of the neuropsychological tests used, an analysis of the covariance (ANCOVA) was also made with the GDS scale used as covariable. A $p < 0.05$ was considered statistically significant.

RESULTS

Sociodemographic characteristics of the sample

Eleven out of the 20 patients from the case group were men and 9 women with a mean age of 73.90 years. In the control group, 5 men and 5 women with a mean age of 69.90 years were evaluated. Both groups were similar regarding the sociodemographic characteristics, personal and family history but not in regards to antidepressant treatment (table 1).

Psychometrics

No differences were found between both groups in age, educational level, GDS, MMSE and cardiorespiratory CIRS using the ANOVA method. Statistically significant differences were only found on the EXIT-S scale with a $p < 0.03$. Due to the possible influence of depressive symptoms, an ANCOVA was performed again with the GDS scale as covariable, the difference found on the EXIT-S remaining between both populations ($p < 0.014$). In the analysis of the correlations, only an inverse correlation was found between the MMSE and EXIT-S scales, that was expected and already described by the authors of the EXIT-S.[14]

Table 1 Medical and sociodemographic information

CASES (n = 20)	CONTROLS (n = 10)
Gender: • Man: 11 • Woman: 9	**Gender:** • Man: 5 • Woman: 5
Marital Status: • Married: 16 • Widow(er): 4	**Marital Status:** • Married: 7 • Widow(er): 3
Education: • Illiterate: 1 • No studies: 6 • Primary education: 9 • Secondary -1st Cycle: 2 • Secondary -2nd Cycle: 1 • Upper education: 1	**Education:** • Illiterate: 1 • No studies: 3 • Primary education: 4 • Secondary -1st Cycle: 0 • Secondary -2nd Cycle: 2
Personal Psychiatric History: • None: 16 • Anxiety type disorder: 1	**Personal Psychiatric History:** • None: 9 • Anxiety type disorder: 1
Family PH: • None: 9 • Affective type: 6 • Substance disorder type: 1 • Infant, childhood or adolescent onset disorder type: 1 • Personality disorder: 0 • Psychotic disorder: 0 • Exists but unknown: 0	**Family PH:** • None:6 • Affective type: 0 • Substance disorder type: 0 • Infant, childhood or adolescent onset disorder type: 0 • Personality disorder: 1 • Psychotic disorder: 1 • Exists but unknown: 2
Family medical PH: • Dementias: 3 • Cardiovascular disease: 7 • Both: 4	**Family medical PH:** • Dementias: 2 • Cardiovascular disease: 6 • Both: 1
Psychopharmaceutical Treatment: • SSRI: 7 • SSRI + NaSSa: 3 • SSRI + Trazodone: 2 • SSNRI: 5 • SSNRI + NaSSa: 3 • Benzodiazepines: 9	**Psychopharmaceutical Treatment:** • Trazodone: 2 • Benzodiazepines: 3

SSRI: Selective Serotonin Reuptake Inhibitors; NaSSa: Noradrenergic and specific serotonergic antidepressants (mirtazapine); SSNRI: Selective-Serotonin Norepinephrine Reuptake Inhibitor (venlafaxine).

Table 2 Psychometric evaluation

	Cases	Controls	P
Age	73.90 (9.22)	69.6 (10.25)	0.25
Education (years)	5.33 (2.25)	6 (3.63)	0.59
GDS	4.70 (2.99)	2.80 (1.93)	0.08
Mini Mental	29.85 (4.31)	32.30 (1.42)	0.93
EXIT-S	15.60 (5.52)	8.70 (5.44)	0.03
Cardiorespiratory CIRS	1.10 (1.21)	1.70 (1.64)	0.26

(Standard Deviation between brackets)

DISCUSSION

The main finding of this study is the presence of higher scores on the executive function screening task in patients with personal history of late onset depression (LOD) and GDS < 7 compared to controls with no personal history of affective disorders. This executive functions could be a typical trait of these patients, independently of whether there is or not an active depressive episode, produced by subclinical dysfunctions of the cortico-subcortical structures. These results are also in accordance with other authors, who have already described the possibility of executive dysfunction as a risk factor or risk trait of these patients.

This study has many limitations. In the first place, all the subjects were under psychotropic treatment during the psychometric evaluation. This could have a possible effect on the cognitive processings (although an elevated number of patients under hypnotic treatment were also found in the control group). In the second place, the evaluation was based on a series of neuropsychological screening tests of executive function and cognitive deterioration (EXIT-S and MMSE, respectively) that measure some cognitive domains, but that are insufficient for the focal diagnosis of the brain lesions or an objective analysis of the findings. The reduced sample size also makes it necessary to accept these results cautiously.

This study is of interest because its design reproduces the usual context of an outpatient psychiatric clinic where cognitive deterioration screening tests are generally used. In this study, they have been effective in detecting differences, which increases the capacity of extrapolating their results.

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