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EXECUTIVE DYSFUNCTION IN DEPRESSION: A STUDY OF PREFRONTAL DYSFUNCTION

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Background

Depression is a serious and common psychiatric disorder that affects millions of people around the world. A growing body of scientific literature has correlated depression with dysfunction in the region of the frontal lobes and consequently, executive dysfunction. The aim of this study was to examine performance of executive functioning in patients with depression. We predicted impaired performance in executive function for depressed patients in comparison to healthy controls.

Material/ Methods:

50 depressed patients (mean age = 43.46, *SD* = 10.71) and 35 from the control group (mean age = 40.91, *SD* = 10.46), of both genders were assessed with the Behavioural Assessment of Dysexecutive Syndrome (BADS), the Wisconsin Card Sorting Test (WCST), the Stroop Color and Word Test (Stroop Test), and the Trail Making Test (TMT).

Results:

Our results revealed that patients with depression have significant deficits in executive functioning when compared with healthy controls, which was confirmed in all the neuropsychological tests we used.

Conclusions:

Our results point up the need to implement programs of neuropsychological rehabilitation in patients with depressive disorder, since neuropsychological impairments predict an unfavorable outcome of antidepressant therapy and cognitive behavior therapy. It can also be assumed that an improvement in cognitive abilities will have a positive effect on therapeutic outcome.

Key words: mood disorder, executive functions, frontal lobes

SUMMARY

INTRODUCTION

Depression is a serious and common psychiatric disorder that affects millions of people around the world (Andrews, Poulton & Skoog, 2005; Murray & Lopez, 1996; Ustun, Ayuso-Mateos, Chatterji, Mathers & Murray, 2004), and one of the most serious public health problems confronting industrialized countries (Gusmão, Xavier, Heitor, Bento & Almeida, 2005). Depression is included among mood disorders, because it is a change in mood or affect. It is simultaneously defined as a mood disorder, characterized by a set of signs, symptoms, behaviors and physiological manifestations presented by individuals, described in different ways by different theories (Del Porto, 1999, Montgomery, 1995).

A growing body of scientific literature has correlated depression with dysfunction in the areas of the frontal lobes. Studies of regional cerebral blood flow involving patients with major depressive disorder suggest a hyperactivity of the ventromedial prefrontal cortex and the orbital lateral prefrontal cortex (Baker, Frith & Dolan, 1997; Drevets, 1998), and a hypoactivity of the dorsolateral prefrontal cortex, especially in the left cerebral hemisphere, compared with controls (Bench, Friston, Brown, Frackowiak & Dolan, 1993; Drevets, 1998; Mayberg, Lewis, Regenold & Wagner, 1994). Given the functions of these regions, this pattern of abnormal activity seems to be responsible for the appearance of the symptoms associated with depressive disorder: hyperactivity in the ventromedial prefrontal cortex is associated with an increased sensitivity to pain, anxiety, depressive thoughts, and tension, while hypoactivity of the dorsolateral prefrontal cortex, in addition to producing psychomotor retardation and apathy, likewise produces attentional deficits, working memory deficits and, consequently, executive dysfunction (Drevets, Gadde & Krishnan, 2004). Another frontal area in which decreased blood flow and metabolism has repeatedly been reported in depressed patients is the anterior cingulate cortex, and hypoactivity in the dorsal regions of the anterior cingulate cortex also appears to be associated with deficient modulation of executive functions and attention (Davidson, Pizzagalli, Nitschke & Putnam, 2002).

Thus, although depression may affect processing speed (Mondal, Sharma, Das, Goswami & Gandhi, 2007), learning ability, and memory (Elliott, Sahakian, Herrod, Robbins & Paykel, 1996; Fossati, Coyette, Ergis & Allilaire, 2002; Goodwin, 1997), as well as the attentional capacity of individuals (Porter, Gallagher, Thompson & Young, 2003), hypofrontality is the most common finding when the range of functional deficits in depressive disorder is analyzed (Drevets, 1998), which leads to executive dysfunction (Austin, Mitchell & Goodwin, 2001). The term "executive functions" refers to the mental capacities that enable individuals to participate successfully in independent, intentional, and self-oriented behavior. These include the ability to initiate actions, plan and provide means to solve problems, anticipate consequences, and modify strategies flexibly (Funahashi, 2001; Lezak, 1995).

The aim of our study was to examine performance in executive functioning among a group of patients with depression. We predicted impaired performance in executive function for depressed patients in comparison to healthy controls.

MATERIAL AND METHODS

Participants

The study included 85 individuals of both sexes allocated in two groups, an experimental group and a control group.

The experimental group consisted of 50 participants diagnosed with depression, ranging in age between 20 and 55 years ($M = 43.46$, $SD = 10.71$). Of these 50 participants, 46 (92%) were female and 4 (8%) were male, the average of completed years of schooling was 6.88 ($SD = 2.88$, ranging between 3 and 16 years of schooling). Included in this group were all those who presented a diagnosis of depression of any kind at any stage of disturbance and were attending psychology and psychiatry screening at the Centro Hospitalar Alto Ave, EPE, Guimarães. We excluded those who presented psychiatric co-morbidities, as well as bipolar disorder, a history of neurological disease, physical disability or sensory impairment, a history of drug use, and mental retardation. The control conditions were measured by performing a semi-structured interview with the participant, and the Mini-Mental State Examination (MMSE) was also used as a control. The information given by the participants was checked against information provided by clinical procedures.

The control group consisted of 35 participants, ranging in age between 20 and 55 years ($M = 40.91$, $SD = 10.46$). Of the 35 participants, 30 (85.7%) were female and 5 (14.3%) were male, the average of completed years of schooling was 7.20 ($SD = 3.89$, range between 3 and 16 years of schooling). We excluded from this group those who had a history of severe depression or other psychiatric disorders, a history of neurological disease, physical disability or sensory impairment, a history of drug use, or mental retardation.

All participants were informed of the nature and objectives of the study, and assured that their participation was voluntary.

MATERIALS

Tests

All participants were submitted to an assessment of executive functioning using the following tests:

- The *Behavioural Assessment of Dysexecutive Syndrome* (BADS; Wilson, Alderman, Burgess, Emslie & Evans, 1996) is a neuropsychological battery consisting essentially manipulative tests and has high ecological validity. The BADS is divided into six subtests with tasks that emulate real-life activities, conceived in order to diagnose the existence of a deficit in general executive

functioning, or in specific types of executive functioning. It is especially sensitive to the capacities affected by problem-solving skills, as well as planning and intentional organization of behavior over prolonged periods of time. More specifically, the subtests in the battery allowed us to assess the subject's ability to plan effective strategies and allow the monitoring of problem-solving behavior, correct responses to a rule of conduct, adaptation as a function of changing environmental contingencies, anticipation of consequences, and the organization of actions across time and space to achieve specific goals (Spreen & Strauss, 1998).

- The *Wisconsin Card Sorting Test* (WCST; Heaton, Chelune, Talley, Kay & Curtiss, 1993) is the pairing of 128 response-cards with four stimulus cards. In performing the task, the participants seek to place the response-cards according to a criterion that is not revealed to them, but rather must be inferred through the feedback provided by the evaluator, with matching possible according to six categories (color, shape, number, color, shape, number) that are arbitrarily changed in the course of the testing.
- The *Stroop Color and Word Test* (Golden, 1994); in this study we used only the scores from the basic color-word Stroop Test, where the task consists in naming the color of the letters in words whose color names that conflict with their actual coloration. This task allows us to evaluate selective attention using a process of inhibition of responses.
- In the *Trail Making Test Part B* (TMT Part B; Reitan & Wolfson, 1985), the subject must connect numbers and letters inside circles in alternating sequences, in ascending order, thus adding a dimension of cognitive flexibility that is not required in Part A.
- *Mini-Mental State Examination* (MMSE; Folstein, Folstein, & McHugh, 1975) was applied to avoid potential cognitive deficits.

Procedure

The study was commenced after the ethics committee of the Centro Hospitalar Alto Ave, EPE, Guimarães, issued a favorable opinion. Subsequently, first contact was established with each participant, and then, after obtaining informed consent, we conducted semi-structured interviews with the participants, always one to one. Each subject was then given MMSE to control for as the presence of global cognitive deficits. Next, we applied the neuropsychological tests listed above, in order to obtain results for the assessment of executive functioning. The instruments were administered in sequence, with a mean duration of two hours distributed over one or two sessions, depending on individual performance, and taking care to avoid the possible effects of fatigue. Identical procedures were used for the assessment of the control group. All participants completed the assessment. Sample collection was completed with the application of assessment tools, and the data were analyzed using statistical software.

Statistical Analysis

For the statistical analysis of the data we used the SPSS statistical software, version 19.0. For socio-demographic characterization of the sample we used descriptive analysis procedures, including measures of central tendency and dispersion (mean and standard deviation) and frequency distribution. The results from the neuropsychological test results from the experimental and control groups, with $n > 30$, were compared using the Student *t*-test for single-variable statistics. Significance was determined at the level of $p \leq .05$.

RESULTS

The results obtained by the two groups are presented in Figure 1 and Table 1. Figure 1 presents the mean values and standard deviations of the total score obtained by the two groups in the BADS.

The BADS results demonstrated that the group of patients with depression was less successful in achieving a high overall BADS score ($M = 10.00$, $SD = 3.75$); the differences were statistically significant - $t(83) = -14.84$, $p < .001$, 95% CI [-11.66, -8.91] - as compared to the control group ($M = 20.29$, $SD = 1.98$). The mean values and standard deviations were again calculated for the results obtained by the two groups in each of the subscales of the BADS.

As can be seen in Table 1, the group of patients with depression was less successful than the control group in all subscales of the BADS, without exception. The performance differences proved to be statistically significant ($p < .001$). Also, in the other neuropsychological tests, we found that the experimental group showed lower results than the control group on the WCST, the Stroop Test, and the TMT-B, to an extent that was highly significant ($p < .001$).

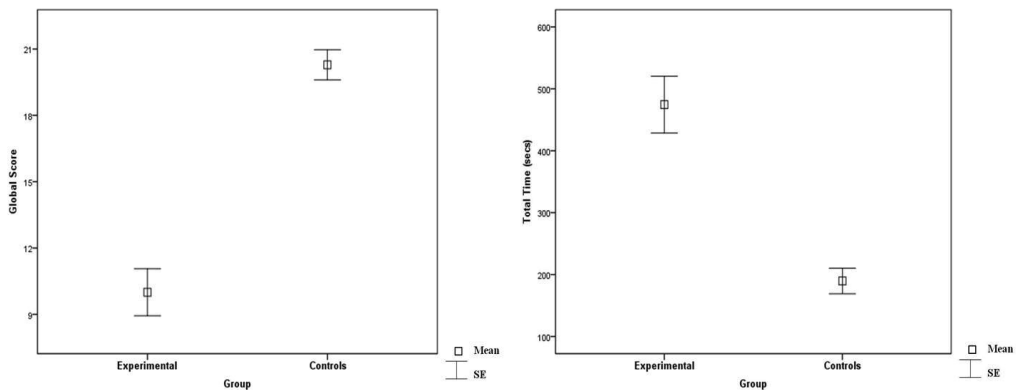


Fig. 1. Means and standard deviations of the results from the control and experimental groups' on the BADS global score

Table 1. Means, standard deviations, t values, significance levels and confidence intervals for the performance of the experimental and control groups on the neuropsychological tests

	Experimental Group		Control Group		95% CI		UL	LL
	M	SD	M	SD	t	p		
BADS								
Rule Shift	1.72	1.19	3.43	0.74	-7.50	<.001	-2.16	-1.26
Action Program	1.76	1.64	3.49	0.62	-5.95	<.001	-2.30	-1.15
Key Search	1.44	1.23	3.14	1.06	-6.63	<.001	-2.21	-1.19
Temporal Judgement	1.40	0.83	2.69	0.72	-7.40	<.001	-1.63	-0.94
Zoo Map	1.66	0.96	3.74	0.44	-11.95	<.001	-2.43	-1.74
Modified Six Elements	2.02	1.00	3.80	0.41	-9.96	<.001	-2.14	-1.43
WCST								
Total Errors	65.60	16.66	23.34	12.10	12.82	<.001	35.70	48.81
Perseverative Errors	34.04	16.42	12.66	6.92	7.26	<.001	15.52	27.24
Non-perseverative Errors	31.56	21.26	10.69	8.02	5.53	<.001	13.37	28.38
Perseverative Responses	44.86	22.58	13.80	7.25	7.85	<.001	23.19	38.93
Categories Completed	2.18	1.84	5.69	0.53	-10.96	<.001	-4.14	-2.87
Stroop Test	25.04	11.88	46.54	9.63	-8.86	<.001	-26.33	-16.67
TMT – B	148.80	85.61	57.97	28.95	6.03	<.001	60.87	120.79

DISCUSSION

The results of this study indicate that patients with depression have significant deficits in executive functioning when compared with healthy controls, which was confirmed in all neuropsychological tests we used.

Overall, the results obtained from the BADS revealed that the group of patients with depression had an executive functioning deficit: the depressed patients had lower performance in both overall BADS and all the subscales. This poor performance in BADS shows a reduced capacity for mental flexibility in depressed patients, planning strategies that are efficient and allow for performance monitoring to resolve a problem, judgment capacity and abstract thinking, as well as organizing and monitoring behavior (Spreeen & Strauss, 1998). However, comparison of these results with previous empirical evidence is a particularly difficult task, mainly because studies involving the assessment of executive dysfunction in depression through the BADS are scarce, with only two studies using the BADS, and even in these cases executive functioning was only measured in patients with

remission of depressive symptoms (Baba et al., 2010; Paelecke-Habermann, Pohl & Lepow, 2005) and elderly patients with depressive disorder (Baba et al., 2010). In any case, both studies, although they had different objectives, found in the same way that the executive functioning deficit remains even after the remission of symptoms of depression (Baba et al., 2010; Paelecke-Habermann et al., 2005).

Similarly, the results obtained from the WCST show that the group of patients with depression have an executive functioning deficit compared with controls. This performance deficit was confirmed in all dimensions studied, in that the experimental subjects had a higher number of perseverative errors, a greater number of total errors, non-perseverative, and perseverative errors, as well as a smaller number of categories completed, compared to the control group. These results are consistent with some previous studies in which the WCST was used as a measure of executive functioning (Channon, 1996; Franke et al., 1993; Grant, Thase & Sweeney, 2001; Merriam, Thase, Haas, Keshaven & Sweeney, 1999; Tandon, Singh, Sinha & Trivedi, 2002). Remarkably, Tandon et al. (2002), when evaluating a group of patients with depression and a group of healthy subjects using the WCST, found that the first group had a worse performance in executive functioning, with depressed patients presenting a greater number of perseverative errors and fewer categories completed compared to the control group. Merriam et al. (1999) likewise found that depressive patients show significant deficits in WCST, presenting a greater number of perseverative errors and nonperseverative errors, as well as a smaller number of categories completed, when compared with controls. However, it should be mentioned that, although our results show a general consistency with previous empirical evidence, some individual differences arise between studies. For example, Austin et al. (1999) reported a significant impairment only for errors and only for the melancholic patients, and there were no differences for the non-melancholic patients or performance in the other dimensions of the WCST.

Also, the results we obtained in the TMT and Stroop Color and Word Test are consistent with previous studies. Mondal, Sharma, Das, Goswami, and Gandhi (2007) evaluated a group of patients with major depression using TMT, and verified the existence in these patients of a significant impairment not only of visual-spatial attentional capacity and processing speed, but also executive functioning, including strategic planning and attentional set shifting (through TMT-B). Similarly, Trichard et al. (1995), using the Stroop Colour and Word Test to measure 23 severely depressed patients, found unsatisfactory results suggesting a deficit of executive attention, and this deficit could persist in patients with clinical improvement.

This severe impairment in executive functioning in depression, as seen in our investigation, appears consistent with the neuroanatomical findings in depressive disorder (Drevets, 1998; Soares & Mann, 1997). The executive performance deficit in these patients appears to result from an interruption in connectivity between the limbic/paralimbic areas and rostral integrative prefrontal cortex, in that the feedback regulation of limbic activity is impaired, and, consequently, the network cognitive executive is hypoactivated (Maletic et al., 2007), resulting in hypoactivation of the prefrontal cortex, particularly the dorsolateral prefrontal cortex,

but also cingulate cortex, as seen in studies of cerebral blood flow (Davidson et al., 2002; Drevets, 1998; Mayberg et al., 1994). Neuroimaging studies have implicated dorsolateral prefrontal cortex and the orbito-fronto-ventral region as major sites of functional and structural abnormalities in major depression, with a marked decrease in neuronal and glial density in these regions (Rajkowska et al., 1999; Sheline, Wang, Gado, Csernansky & Vannier, 1996). There is significant evidence suggesting the existence of distinct, parallel functional networks (Cummings, 1993) or loops linking pre-frontal and subcortical regions, and disruption of these functional networks is implicated in the pathogenesis of a number of psychiatric disorders, including major depression (Austin & Mitchell, 1995), with its effect on affective, vegetative and autonomic domains (Cummings, 1993).

CONCLUSIONS

We conclude that there is a significant impairment in executive functioning in patients diagnosed with depression, based on the results of a comprehensive battery of neuropsychological tests. The results of our study indicate the need to implement programs of neuropsychological rehabilitation in patients with depressive disorder. According to previous studies, neuropsychological impairments in major depression patients (statistically) predict an unfavorable outcome of antidepressant therapy (Kampf-Sherf et al., 2004) and cognitive behavior therapy (Crews & Harrison, 1995). Moreover, the deficit was most pronounced for attention (Cassens, Wolfe & Zola, 1990) and executive functions (Dunkin et al., 2000; Mohlman & Gorman, 2005). It can be assumed, then, that an improvement in cognitive abilities will have a positive effect on therapeutic outcome as well.

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