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Cognitive Performance in Non-Psychotic Non-Suicidal Unipolar Depressed Patients

Marco Moniz [1,2,3]

[1] Department of Psychiatry and Mental Health, Hospital and University Center of Algarve, Faro, Portugal.
[2] Research Centre for Spatial and Organizational Dynamics (CIEO), Faro, Portugal.
[3] Algarve Biomedical Center (ABC), Faro, Portugal

Corresponding author: Marco Moniz | emmoniz@gmail.com

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Abstract

Background: Cognitive impairment is central in depression and executive dysfunctions in patients with depression are frequent. However, little attention has been paid to the specificities of executive changes in patients with unipolar depression, though these modifications may have serious implications for psychosocial functions and treatment of these patients.
Goals: To compare neuropsychological performance, regarding executive functions, of two adult groups: non-psychotic non-suicide attempters with unipolar depression and healthy individuals.
Methods: This is a cross-sectional study with data collected in an outpatient clinic of mental health service of a general hospital. We compared a group of non-psychotic non-suicidal unipolar depressed patients to a group of individuals without depression. Depressed subjects were controlled for prior suicidal attempts, and their neuropsychological profile was assessed using a range of measures of attention, verbal fluency, memory, psychomotor speed, and executive functioning (planning, decision making, set shifting, response inhibition, and inhibitory control).
Results: The group with depression (n=23) was significantly outperformed by the group of healthy individuals (n=23) in all measures. Also, differences in the executive functions of planning, decision making, set shifting, and inhibitory control were confirmed. We were unable to identify differences between non-suicidal individuals with depression and individuals without depression in terms of response inhibition, as has been the case in previous studies with samples with suicidal unipolar depressive patients.
Discussion: These results reinforce the hypothesis that there are specific alterations in patients with depression and highlight the need to develop specific cognitive rehabilitation programs for this population.

Keywords: Unipolar depression, Executive dysfunction, Attention, Verbal fluency, Psychomotor speed.

Introduction

Cognitive impairment has several impacts on the psychosocial functions of depressed patients, with cognitive dysfunction being a primary mediator of functional impairment in major depression (Lam, Kennedy, McIntyre, & Khullar, 2014). Currently, we know the importance of cognitive dysfunction in depressed patients, the importance of their assessment for better rehabilitation, and the negative impact of antidepressant treatment on cognitive performance (Roca, Vives, Lopez-Navarro, Garcia-Campayo, & Gili, 2015). Although cognitive dysfunction is a subject of extreme importance for the understanding of depression, we find few references to this point in nosological systems, particularly in DSM-V (APA,

2013), which does not even refer to cognitive dysfunctions as criteria for major depression.
In a critical review, Roca et al. (2015) assessed the systematic reviews and meta-analysis studies published between 2004 and 2014, and identified a strong association between depression and cognitive impairment, particularly in psychomotor speed, attention, visual learning, memory, and executive functions. Although executive functioning is a central point in depression, particularly in unipolar depression (Rogers et al., 2004; Stordal et al., 2004; Wagner, Doering, Helmreich, Lieb, & Tadić, 2012), there is lack of knowledge about which type of executive functions are affected with depression. Previous studies indicate differences between unipolar depressed patients and healthy individuals in set shifting (assessed with the Wisconsin Card Sorting Test) (Degl'Innocenti, Agren, & Bäckman, 1998; Harvey et al., 2004; Moniz et al., 2016a; Moritz et al., 2002; Stordal et al., 2004), planning (assessed with the Tower of London) (Beats, Sahakian, & Levy, 1996; Elliott et al., 1996; Moniz et al., 2016b; Rogers et al., 2004; Wagner et al., 2012), decision making (assessed with the Iowa Gambling Task) (Cella, Dymond, & Cooper, 2010; Moniz, Neves de Jesus, Gonçalves, Pacheco, & Viseu, 2016c), and inhibitory control (assessed by Stroop tasks) (Gohier et al., 2009; Harvey et al., 2004; Moniz et al., 2016d; Stordal et al., 2004).

By considering the possibility of specific changes of executive functions among subjects with depression, the present study aims to compare neuropsychological performance, regarding executive functions, of two adult groups: non-psychotic non-suicide attempters with unipolar depression and healthy individuals. In light of previous studies, we hypothesize the following: (1) individuals with depression will perform more poorly than mentally healthy individuals on attention, verbal fluency, memory and psychomotor speed; (2) subjects with depression will generally exhibit more executive deficits than healthy individuals; and (3) subjects with depression and healthy individuals will not show differences regarding response inhibition.

Methods

This study followed a cross-sectional design, with data collected in an outpatient clinic of a mental health service of the Hospital and University Center of Algarve, according to a sequential sampling.

Participants

All subjects completed a battery of tests within one week (two different sessions). Each test was administered only once, and the order of presentation of cognitive tests was randomized for each of the subjects. All participants were Caucasian, right-handed, and Portuguese speakers. We circumscribe our clinical sample to non-psychotic non-suicide attempters with unipolar depression because the cognitive functions of bipolar subjects are believed to be influenced in a distinctive way (Stordal et al., 2004) and because suicide attempters with unipolar depression tend to reveal distinct cognitive functioning in response inhibition and planning (Moniz et al. 2017). Likewise, psychotic patients tend to exhibit more serious deficits (Stordal et al., 2004).

The exclusion criteria were: current or prior suicide attempts, bipolar disorder, schizophrenia, major psychosis, substance abuse, personality disorder, dementia, other neurological disease (including head injury involving a loss of consciousness), and suspected malingering.

Instruments

We conducted a detailed neuropsychological assessment, with computerized and standard paper-and-pencil instruments that included: tests of attention, verbal fluency, memory, psychomotor speed, and executive functioning (planning, decision making, set shifting, response inhibition, and inhibitory control). To assess education, we calculated the number of years of formal education for each participant. We employed the following computer-administered instruments from the Psychology Experiment Building Language (PEBL) Test Battery (Mueller & Piper, 2014):

Go/No-Go Task (GNG)
The GNG, in which a motor response must be either executed or inhibited, is one of the most useful

measures for assessing response inhibition (Bezdjian, Baker, Lozano, & Raine, 2009). We applied the "simple" paradigm in which the no-go stimulus was always the same. We used the Portuguese version (Moniz et al., 2016e) of the computerized GNG from the PEBL (Mueller & Piper, 2014), developed and validated previously by Bezdjian, Baker, Lozano, and Raine (2009). The GNG demonstrates reasonable test–retest reliability (Kindlon, Mezzacappa, & Earls, 1995).

Victoria Stroop Test (VST)
Inhibitory control is an important cognitive function associated with executive functioning and is assessed with tasks such as Stroop (Miyake et al, 2000). Our study employed the Portuguese version (Moniz et al., 2016d) of the computerized VST from the PEBL (Mueller & Piper, 2014), a version that is briefer and slightly different from the traditional VST. The original version of the VST (Troyer, Leach, & Strauss, 2006) demonstrated adequate psychometric data, namely regarding reliability and validity (Strauss, Sherman, & Spreen, 2006).

Tower of London Task (TOL)
Inspired by the Tower of Hanoi, a classic problem-solving puzzle (Kaller, Unterrainer, Rahm, & Halsband, 2004; McKinlay & McLellan, 2011; Newman, Greco, & Lee, 2009), the TOL is a visuospatial planning task (Kaller et al., 2004; McKinlay & McLellan, 2011; Newman et al., 2009). We used the Portuguese version (Moniz et al., 2016b) of the computerized TOL from the PEBL (Mueller & Piper, 2014), which does not differ from the manual versions in terms of the level of difficulty (McKinlay & McLellan, 2011). Its reliability and validity were demonstrated by Piper et al. (2015), with a test-retest correlation coefficient of $r = .36$.

Iowa Gambling Task (IGT)
The IGT aims to simulate real-life judgment alterations, allowing the assessment of the subject's emotions associated with decision making (Bechara, Damasio, Damasio, & Anderson, 1994). The participants were instructed to perform a series of 100 selections from a group of four decks of cards (A, B, C and D). We used the Portuguese version (Moniz, Neves de Jesus, Gonçalves, Pacheco, & Viseu, 2016c) of the computerized IGT from the PEBL (Mueller & Piper, 2014). Its reliability and validity were demonstrated by Piper et al. (2015), with a test-retest correlation coefficient of $r = .41$.

Wisconsin Card Sorting Test (WCST)
The WCST is one of the most frequently used neuropsychological measures for assessing executive functioning, and is commonly utilized to assess set maintenance and set shifting (Carrillo-de-la-Peña & García-Larrea, 2007). The participants are expected to place cards in one of four piles according to the characteristics of the stimuli. We utilized a total number of 128 cards (i.e., two packs of 64 cards) and the principles were color, form or number, which changed every ten trials. After each trial, feedback ("*correct*" or "*incorrect*") was displayed for 500 milliseconds. The results obtained for each trial were provided by the software. We applied the Portuguese version (Moniz et al., 2016a) of the computerized WCST from the PEBL (Mueller & Piper, 2014). Its reliability and validity were demonstrated by Piper et al. (2015), with a test-retest correlation coefficient of $r = .45$.

Finger Tapping Task (FTT)
The FTT assesses fine motor speed and motor control (Christianson & Leathem, 2004). The Portuguese version (Moniz, De Jesus, Pacheco, Gonçalves, & Viseu, 2016f) of the computerized FTT from the PEBL (Mueller & Piper, 2014) was used, with the left and right index fingers: five consecutive trials for each hand, with a 10-second break following each trial and a 30-second break every five trials. The average number of taps over five trials was calculated for each hand. The reliability and validity of the computerized FTT were demonstrated by Hubel, Yund, Herron, and Woods (2013a, 2013b), with a test-retest correlation coefficient of $r = .88$.
For computerized tests, we used a computer that ran Microsoft Windows 8.1, equipped with a touch screen (IGT, TOL, WCST), a keyboard (VST), and an external keypad (for FTT and GNG).

The paper-and-pencil instruments that were used are:

Trail Making Test (TMT)
The TMT, which comprises two parts (trials A and B). Trial A of the TMT assesses attention, visual scanning, and information processing (Cavaco et al., 2008a,

2013a). Participants are given two sets of dots targeting numbers and are expected to connect them in sequential order (e.g., 1-2-3). Trial B assesses working memory and executive functions, such as the ability to switch between sets of stimuli (Cavaco et al., 2008a, 2013a). The B/A performance ratio provides an index of executive function (Arbuthnott & Frank, 2000). For trial B, participants are given two sets of 25 dots, one corresponding to numbers (1-13) and the other corresponding to letters (A-L) in sequential order. The sequence begins with the first number, followed by the first letter alphabetically, then the second number, and so on (e.g., 1-A-2-B-3). We used the Portuguese version (Cavaco et al., 2013a).

Verbal Fluency Test (VFT)

In addition to executive functions, the VFT measures non-motor processing speed and language production, which recruit the pre-frontal cortex and temporal lobes (Cavaco et al., 2013b). The VFT consists of two tasks, measuring semantic and phonemic fluency. Subjects are asked to name as many animals as possible in 60 seconds and to say as many words as possible beginning with M, R, and P, in 60 seconds (for each letter), as described in the norms of the Portuguese version (Cavaco et al., 2013b).

Verbal Fluency Test (VFT)

Considered a measure that is sensitive to verbal memory deficits and neurological impairment, the AVLT evaluates memory and verbal learning (Cavaco et al., 2008b) through five consecutive trials. After a 30-minute break, participants are expected to recall the words that included the original word from a longer list. We used the Portuguese version (Cavaco et al., 2008b).

Procedures

All participants were assessed by a psychologist who was specifically certified for this purpose. During the selection of the sample, depression diagnoses were confirmed using the MINI International Neuropsychiatric Interview (MINI) (Sheehan et al., 1997) and the Portuguese version of the Brief Symptom Inventory (BSI) (Canavarro, 2007). Symptomatology of depression was evaluated using the 17-item Hamilton Depression Rating Scale (HAM-D-17) (Sousa, Lopes, & Vieira, 1979). To screen for the presence of personality disorders, the PDQ-4 + Personality Diagnostic Questionnaire (Hyler, 1994) was applied**.**

Data analysis

All analyses were conducted using the Statistical Package for Social Sciences (SPSS), version 21.0. The level of significance was set at $p < .05$. The normality of the distribution for continuous variables was tested with the Shapiro-Wilk test. A chi-square test was used to compare the categorical variables, and a t-test was used to compare continuous variables.

Ethical issues

This study was approved by the Hospital and University Center of Algarve Ethics Committee and was conducted according to the principles of the Declaration of Helsinki. After being provided with all information about the study, participants signed an informed consent form. For ethical reasons, we could not assess the clinical sample without medication.

Results

Group characteristics

The group of patients with depression was composed of 15 women and 8 men, with a mean age of 47.30 years old (*SD* = 14.97) and a mean of 8.73 (*SD* = 2.70) years of education. The group of healthy individuals, with analogous characteristics, included 15 women and 8 men, with a mean age of 43.70 years (*SD* = 11.89) and a mean of 9.70 (*SD* = 1.85) years of education. The group of patients with depression and the healthy individuals did not differ significantly regarding age ($t = .905$, $df = 44$, $p = .370$, $d = .27$) or education ($t = -1.527$, $df = 39.01$, $p = .135$, $d = -.45$) (Table 1).

Table 1. *Sociodemographic characteristics, clinical profile, and cognitive measures of participants*

	Patients with depression [a]	Individuals without depression [b]	*p*-value
	M (SD)	*M (SD)*	
Social and Clinical Measures			
Age, Years	47.30 (14.97)	43.70 (11.89)	.370
Education	8.73 (2.70)	9.78 (1.85)	.135
BSI-D, Score	2.23 (.92)	(a)	(a)
HAM-D-17, Score	17.13 (6.97)	(a)	(a)
Cognitive Measures			
VFT-Semantic Fluency-Animals	14.60 (4.65)	(a)	(a)
VFT-Phonemic Fluency-(M, R, P)	22.13 (7.62)	(a)	(a)
AVLT-Immediate Recall	47.17 (9.67)	(a)	(a)
AVLT-Delayed Recall (30’)	9.91 (2.19)	(a)	(a)
AVLT-Memory Retention	85.24 (9.39)	(a)	(a)
TMT-Part A	54.15 (16.69)	35.12 (14.16)	.001
TMT-Part B	145.65 (55.85)	71.89 (30.51)	.001
TMT-B/A	2.74 (1.0)	2.10 (.53)	.027
FTT-Dominant Hand	52.86 (7.55)	62.43 (7.32)	.000
FTT-Non-Dominant Hand	46,04 (7.30)	53.21 (6.48)	.001
TOL-Extra Moves	24.90 (10.55)	15.34 (7.06)	.001
TOL-Time	443.30 (193.47)	268.14 (59.53)	.000
IGT-Net Score	5.94 (22.35)	30.38 (23.49)	.002
WCST-CAT (Moves to Complete 1st Category)	23.95 (22.25)	14.61 (4.89)	.067
WCST-PE (Preservative Errors)	18.77 (10.46)	8.14 (5.81)	.000
WCST-CLR (Conceptual-Level Responses)	60.45 (16.07)	78.00 (10.51)	.000
VST-Errors	3.25 (3.24)	1.18 (1.73)	.017
VST-C Time	111.86 (73.85)	63.77 (22.16)	.010
GNG-CE (Commission Errors)	6.60 (4.10)	6.39 (3.10)	.840
GNG-OE (Omission Errors)	1.26 (2.02)	.21 (.51)	.025
Reaction Time, ms (Go)	560.37 (93.65)	504.89 (80.94)	.037
Reaction Time, ms (No-Go)	588.56 (81.15)	537.57 (53.00)	.015

[a] *n* = 23, [b] n = 23; BSI-D: Depression scale from the Brief Symptom Inventory; HAM-D-17: Hamilton Depression Rating Scale, 17 items; VFT: Verbal Fluency Test; AVLT: Auditory Verbal Learning Test; TMT: Trail Making Test; FTT: Finger Tapping Task; TOL: Tower of London; IOWA: Bechara (Iowa) Gambling Task; WCST: Wisconsin (Berg) Card Sorting Test
(a) these data were not collected

Neuropsychological performance

The patients with depression were significantly outperformed by the healthy individuals in almost all measures, with differences between the two groups for the TMT [part A (t = 3.719, df = 37, p = .001, d = 1.23), part B (t = 4.796, df = 37, $p \leq .001$, d = 1.53), and B/A ratio (t = 2.310, df = 37, p = .027, d = .80)], for the FTT [dominant hand (t = -4.357, df = 44, $p \leq .001$, d = 1.28), and non-dominant hand (t = -3.522, df = 44, p = .001, d = 1.04)], for the TOL [extra moves (t = 3.588, df = 43, p = .001, d = 1.06), time (t = 4.066, df = 24.78, $p \leq .001$, d = 1.22)], for the IGT-Net Score (t = -3.361, df = 38, p = .002, d = -1.06), for the WCST [moves (t = 1.919, df = 23.11, p = .067, d = .58), for preservative errors (t = 4.141, df = 33, $p \leq .001$, d = 1.26), for the CLR (t = -4.213, df = 41, p = .000, d = -1.29)], and for the VST [errors (t = 2.541, df = 28.44, p = .017, d = .80), time (t = 2.800, df = 22.10, p = .010, d = .88)].

In the GNG task, we found differences between the two groups with regard to commission errors (t = .203, df = 44, p = .840, d = .06) and omission errors (t = 2.391, df = 24.86, p = .025, d = .71). However, the difference in commission errors was not significant (p = .840).

For the VFT and AVLT, we did not assess healthy individuals; instead, we used Cavaco et al. (2008b, 2013b) as a reference. Analyzing the *z* score in these two instruments, although inferior to the average of the Portuguese population, we obtained values below standard deviation -.2, particularly on the AVLT (Figure 1).

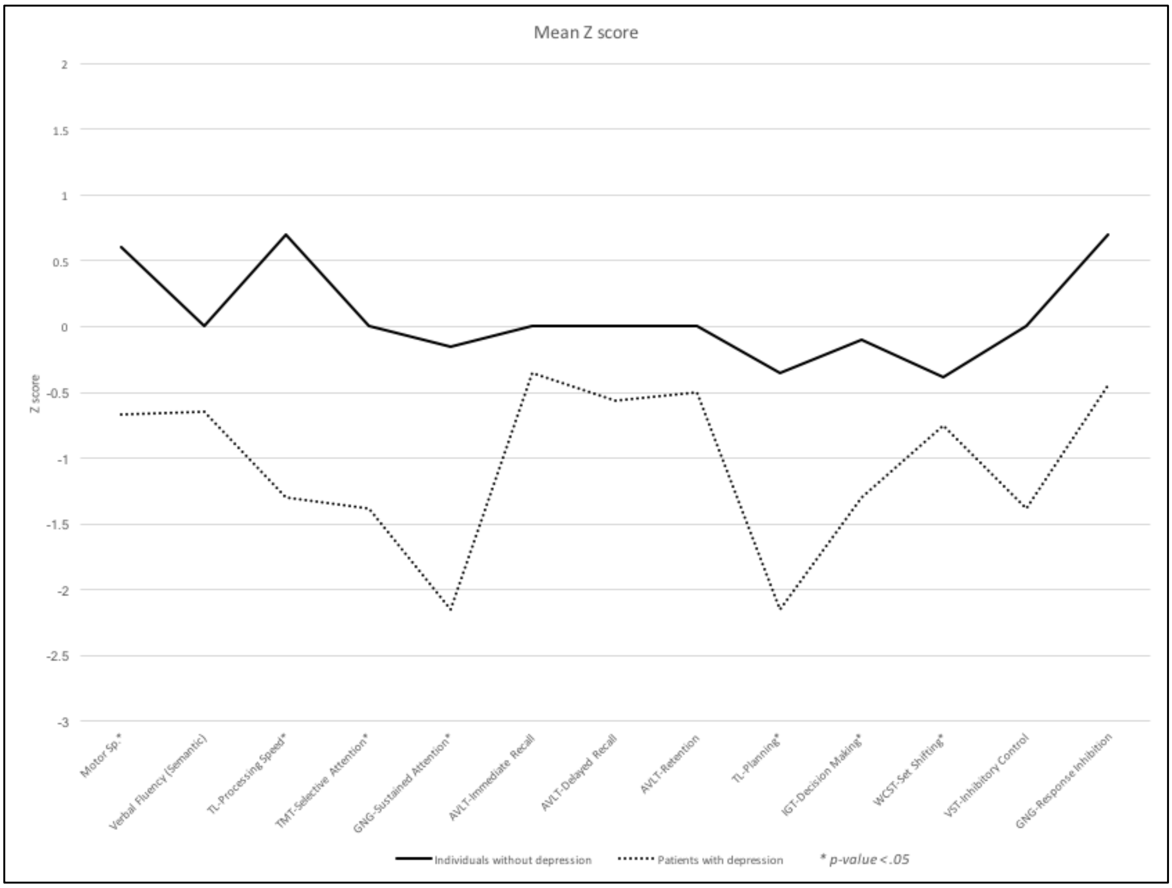

Figure 1. *Z-scores of the neuropsychological tests (cognitive domains) by sample*

Discussion

Our results are in line with studies that have revealed changes in attention, verbal fluency, memory and psychomotor speed (Bashir, Khade, Kosaraju, Kumar, & Rani, 2013; Hueng et al., 2011; Kertzman et al., 2010; Lampe, Sitskoorn, & Heeren, 2004; Moniz, De Jesus, Pacheco, Gonçalves, & Viseu, 2016; Roca et al., 2015; Rohling, Green, Allen, & Iverson, 2002), with the exception that in our study the differences in memory were not statistically significant. Therefore, our first hypothesis (i.e., that individuals with depression will perform more poorly than individuals without depression) was only partially confirmed.

Confirming our second hypothesis, the group of patients with depression were outperformed by the healthy individuals on most tests assessing executive functions, in line with studies that found changes in planning (Beats et al., 1996; Elliott et al., 1996; Moniz et al., 2016b; Rogers et al., 2004; Wagner et al., 2012), decision making (Cella et al., 2010; Moniz et al., 2016c), set shifting (Degl'Innocenti et al., 1998; Harvey et al., 2004; Moniz et al., 2016a; Moritz et al., 2002; Stordal et al., 2004), and inhibitory control (Gohier et al., 2009; Harvey et al., 2004; Moniz et al., 2016d; Stordal et al., 2004). Similar to what has been reported by Moniz et al. (2017), our group of patients with depression did not perform worse than healthy individuals in GNG commission errors. These finding confirms our third hypothesis (i.e., that individuals with depression and individuals without depression do not show differences regarding the performance of response inhibition).

Conclusion

The results of the present study confirm the association between executive functioning deficits and unipolar depression, particularly in the following executive functions: planning, decision making, set shifting, and inhibitory control. We also confirmed differences between patients with depression and healthy individuals in the performance of attention, verbal fluency and motor speed.

These results reinforce the need for clinicians and researchers to create a specific cognitive rehabilitation program for unipolar depression, taking into consideration cognitive changes inherent to this pathology. There are some existing cognitive rehabilitation programs for depression, but those programs target postinjury depression, which is considered a secondary and reactive clinical status, for example, of a stroke (e.g., Sohlberg & Mateer, 2001). Therefore, these programs are not very specific and do not really target the specific cognitive implications of depression. Since cognitive changes are transient in depressed patients, a rehabilitation program have the potential to allow faster improvement in cognitive performance, symptoms of depression, and psychosocial functions, thus promoting a faster return to working life and reduced costs associated with this disease.

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Declaration of Conflicting Interests

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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