

Assessment of Executive Functions in a Brazilian Sample of Bipolar Subjects

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Research has demonstrated impairments in executive functions in Bipolar Mood Disorder patients. Evidence shows that this impairment is present in both periods of active symptoms of the disorder, as well as euthymic stages, and is compounded by mood episodes, especially manic phases. The purpose of this study was to compare the executive performance of a sample of Brazilian bipolar patients in depressive episodes, (44 participants), euthymia (37 participants), and in controls (43 participants). The main instrument for evaluation was the *Wisconsin Card Sorting Test*. Significant differences were found in performance on the *Wisconsin Card Sorting Test* between Bipolar subjects (Type I) (both in depression and euthymia) and the controls. No significant correlations were found between the number of manic episodes and the performance on executive measurement variables. The findings suggest that the executive dysfunctions in Bipolar Disorder may be related to both transitory and permanent deficits.

Keywords: executive functions, *Wisconsin Card Sorting Test*, bipolar disorder, Brazil.

La investigación ha demostrado deterioros en las funciones ejecutivas de pacientes con desorden bipolar del estado de ánimo. Los resultados sugieren que el deterioro está presente en los periodos de los síntomas activos del trastorno, los estados de eutimia que pueden ser agravados por variaciones del ánimo, especialmente por fases maníacas. El objetivo de este estudio fue comparar el desempeño ejecutivo en una muestra de pacientes bipolares brasileños con diferentes diagnósticos. Participaron 44 depresivos, 37 eutímicos, y 43 controles. El principal instrumento de evaluación fue el test de clasificación de cartas de Wisconsin. Se observaron diferencias significativas en la ejecución de esta prueba entre participantes bipolares-depresivos y eutímicos (Tipo I)- y controles. No se observaron correlaciones significativas entre el número de episodios maníacos y el desempeño en la ejecución de medidas variables. Los resultados sugieren que las disfunciones ejecutivas en el desorden bipolar pueden estar relacionadas tanto con déficits transitorios como permanentes.

Palabras clave: funciones ejecutivas, *Test de clasificación de cartas de Wisconsin*, trastorno bipolar, Brasil.

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Currently, various studies highlight damages to cognitive (Toulopoulou, Quraishi, McDonald, & Murray, 2006) and executive functions (Goldberg & Chengappa, 2009) in patients with Bipolar Disorder (BD), a disorder affecting approximately 1% of the population for Type I, and 1.1% for Type II (Merikangas et al., 2007). Damages to the executive function in bipolar subjects are revealed through compromised performance on cognitive tasks that evaluate executive functioning (Borkowska, Leszczynska-Rodziewicz, Kapelski, Hauser, & Janusz, 2005; Clark, Kempton, Scarna, Grasby, & Goodwin, 2005; Deckersbach et al., 2006; Frangou, Dakhil, Landau, & Kumari, 2006; Goldberg & Chengappa, 2009; Morice, 1990; Smith, Muir, & Blackwood, 2006; Tabares-Seisdedos et al., 2003; Totic-Poznanovic, Marinkovic, Pavlovic, & Paunovic, 2005; Toulopoulou, Quraishi, McDonald, & Murray, 2006). In this context, in general, executive functioning is understood as planning abilities, reorienting thought and behavior through mental models and internal representations focused on future goals independent from the immediate context (Joseph, McGrath, & Tager-Flusberg, 2005). In bipolar subjects, alterations in this mental process occur more frequently in acute phases of the disorder (Maalouf et al., 2010; Martínez-Arán, Goodwin, & Vieta, 2001).

For Meyer and Deckersbach (2005), the relation between deficits in executive functions and BD may be associated with repetition of the occurrence of mood episodes, considered an aggravating factor for already existent cognitive impairments. In this sense, according to Rocca and Lafer (2006), manic phases would have a great importance, since they are the mood episodes that most affect cognition. For Lebowitz et al. (2001) this cognitive deterioration is not related exclusively with mood episodes, but is also explained by the increase in medication and hospitalization characteristic of this state. Even more specific evidence demonstrates that such cognitive impairments are present in euthymic bipolar subjects (Deckersbach et al., 2006), even though, for Martínez-Arán et al. (2001) the executive dysfunction in this period is classified as mild. Thus, bipolar subjects, whether euthymic, manic, or depressed, present executive dysfunctions compared to controls (Borkowska et al., 2005; Frangou et al., 2006; Goldberg & Chengappa, 2009; Smith et al., 2006; Totic-Poznanovic et al., 2005; Toulopoulou et al., 2006). Once the presence of executive impairments is confirmed, both in symptomatic and asymptomatic phases of BD, these impairments are related to both transient and permanent deficits that prevent complete remission of the symptomatology and cause significant functional impairment (Martínez-Arán et al., 2001).

Considering the importance of evaluating executive functions in bipolar subjects, depending on the actual course of the disorder, appropriate instruments are needed to identify any deficits. Among others, the *Wisconsin Card Sorting Test* (WCST) has been shown appropriate for measurement of performance related to executive functions (Forlenza,

2000; Heaton et al., 2005; Lezak, 2004), is the gold standard in this regard (Rzezak et al., 2009) and reveals differences between clinical and control groups (Heaton et al., 2005).

The measurements of the WCST most used to evaluate executive functions are perseverative errors and number of categories completed, followed by non-perseverative errors, conceptual level responses, trials to complete the first category, perseverative responses and failure to maintain context (Heaton et al., 2005). Since the WCST is considered as a measure for prefrontal functioning, people with damage in this region are able to begin the tasks of the Test, but have difficulties in adapting behavior during execution thereof. That is, they have difficulty adjusting to changes in environment, which may be demonstrated through performance with stereotyped deficiencies (Forlana, 2000; Miller & Cohen, 2001). As such, both, the relationship between deficits in executive functions and BD, as well as the importance of the prefrontal cortex in the ability to coordinate thought and behavior with internal goals were demonstrated by Miller and Cohen (2001).

The purpose of this study was to compare executive performance in bipolar subjects in depressive episodes, in euthymia, and in controls. More specifically, to investigate whether the executive functions from the sample of bipolar subjects were impaired compared with the executive functions in the control groups, and, if the executive performance in bipolar subjects in depressive episodes was impaired compared to those in euthymia. Additionally, the study intended to determine if the number of manic episodes interferes in performance on the WCST.

Method

Participants

A hundred and twenty four persons participated in this study, 81 of whom were diagnosed with bipolar disorder (Type I) through the criteria of the Diagnostic and Statistical Manual of Mental Disorders IV-TR (American Psychiatric Association, 2000), and 43 without the disorder (control group). Of the 81 bipolar subjects, 37 were in euthymia, and 44 were depressed. The participants diagnosed with BD were compared with the participants in the control group according to average age.

The participants diagnosed with BD came from the *Programa de Atendimento do Transtorno do Humor Bipolar do Hospital de Clínicas de Porto Alegre - HCPA* (Care Program for Bipolar Mood Disorder, Hospital de Clínicas of Porto Alegre - HCPA), and exhibited no psychotic symptoms during the data collection period. In turn, the control group participants were selected from persons visiting the Hospital de Clínicas campus in Porto Alegre, who were willing to participate in research and were accepted after completion of a Structured Clinical Interview for DSM-IV (SCID).

Hearing and/or visual impairments that would interfere in completion of the instruments were considered as an exclusion criterion. Additionally, other exclusion criteria established due to the possibility of confusing interpretation of data from the instruments included: abuse or dependence on psychoactive substances in the past year, significant physical or neurological illness, history of brain damage or degenerative disease, mental retardation, and electroconvulsive therapy during the past year.

Instruments

For evaluation of the participants, instruments were chosen that are able to assess the specific necessary and/or complimentary functions for the study of executive functions in bipolar subjects. Initially, all participants completed an Informed Consent form. Then they filled out a socio-demographics data sheet and the following instruments: Hamilton Anxiety Scale (HAM-A), Hamilton Depression Scale (HAM-D) Young Mania Scale (YMRS), WCST and the Wechsler Adult Scale (WAIS-III). Adaptation and standardization of the WCST for Brazil was finalized in 2008 for ages 60 to 89 years and in 2009 for 18 to 59 years.

In addition to the above mentioned instruments, the control group also responded to the Structured Clinical Interview for the DSM-IV (SCID) in order to rule out Axis I psychiatric diagnoses. It is important to note that the participants diagnosed with Bipolar Mood Disorder had been previously assessed with the SCID, used to identify the presence of psychiatric diagnoses (Kessler et al., 2006).

The following is a brief description of the instruments used:

- *Sociodemographic Data Sheet*: enabled evaluation of personal data, such as name, age, gender, date of birth, address, and information related to professional occupation. The bipolar participants were also asked for data on medication, hospitalization, and treatment duration, among other matters.
- *Structured Clinical Interview for the DSM-IV (SCID)*: a semi-structured interview (Spitzer, Williams, Gibbon, & First, 1992), adapted for Brazil in coordination with Tavares (2000). Enables differential diagnosis through evaluation of 44 psychopathologies considered common. The SCID is a current and comprehensive instrument for diagnosis of mental disorders. There are 7 specific disorders that can be diagnosed with the SCID, being: mood, adjustment, eating, and anxiety disorders, psychotic illnesses, and those related to use of psychoactive and somatoform substances (Spitzer et al., 1992; Tavares, 2000).
- *Hamilton Anxiety Scale (HAM-A)*: a rating scale developed to quantify the severity of anxiety symptoms. It contains fourteen items, each one defined by a series of symptoms. Each of these items is assessed on a *Likert* 5 point scale, varying from 0 (absence of symptoms) to 4 (severe symptoms) (Kobak et al., 2001).
- *Hamilton Depression Scale (HAM-D)*: provides an indication of the status of depressive symptoms, cognitive and vegetative symptoms of depression, as well as comorbidity of anxiety symptoms. If applied in a regular and systematic manner, it may serve as a means of monitoring therapeutic progress. This scale is composed of seventeen items, scored from zero to four: absence (0), mild (1), moderate (2), severe (3) and disabling (4). The higher the total overall score, the more severe the depression. However, if the classification of symptoms was difficult to obtain, we use the following convention: absence (0), doubtful or trivial (1) and present (2) (Kobak et al., 2001). The cutoff used was 10.
- *Young Mania Scale (YMRS)*: used since 1978 to evaluate status and severity of manic symptoms, especially appropriate for Type I bipolar subjects. However, it does not evaluate depressive symptoms. It is composed of 11 items (Young, Biggs, Ziegler, & Meyer, 1978). The cutoff used was 12.
- *Wisconsin Card Sorting Test (WCST)*: assesses abstract reasoning and capacity to change cognitive strategies in response to environmental modifications. It is a useful instrument for neuropsychological assessment of executive functions. This test has become popular, because it is sensitive to cerebral disorders that impair frontal and pre-frontal functioning. Its assessment includes abstract reasoning, adaptation, modulation of impulsivity, organization, planning, problem solving strategies, and goal-oriented behaviors, among other factors. Such characteristics are necessary for social responses and appropriateness of adult behavior in various contexts. It consists of various measures, such as perseverative errors, attempts to complete first category, Number of Categories Completed, Number of Tests Administered, Total Number Correct, Total number of errors, conceptual level responses and perseverative responses (Cunha et al., 2000; Heaton et al., 2005). Moreover, as noted above, this instrument is considered the gold standard for assessment of executive functioning (Rzezak et al. 2009).
- *Wechsler Adult Intelligence Scale (WAIS-III)*: validated as a measure of global intelligence, this scale provides a systematic and detailed assessment of the cognitive aspects of adolescents and adults (Cunha et al., 2000; Nascimento & Figueiredo, 2002; Wechsler, 1997). For this study, the Total IQ was calculated to evaluate the participants' overall cognitive ability. The Total IQ consists of a means of synthesizing the results from the intelligence scales from the evaluation of their subtests (Nascimento & Figueiredo, 2002).

Data collection procedures

Data collection with the participants was conducted in the Care Program for Bipolar Mood Disorder at the HCPA, which is connected to the Experimental Psychiatry Lab at the Research Center of the same hospital. For this purpose, prior to data collection, contact was made with the Hospital de Clínicas of Porto Alegre in order to define the procedures, such as scheduling of the assessments and care ethics. The bipolar participants were contacted from their registration in the Care Program for Bipolar Mood Disorder, and the control group participants through contact with persons who visit the Hospital de Clínicas of Porto Alegre who made themselves available to participate in research and were accepted after conducting the Structured Clinical Interview for the DSM-IV (SCID). The assessments of all participants were conducted in two sessions of approximately 90 minutes each at the Care Program for Bipolar Mood Disorder of the HCPA.

Data analysis procedure

Descriptive analyses were conducted by checking frequencies, means, and standard deviations. The student *t* test and ANOVA (followed by the Tukey multiple comparisons test) were conducted for statistical analysis to analyze the quantitative variables, and the chi-squared test for analysis of the categorical variables. The Cohen *d* was used to check the amplitude of the effect in the comparisons between the groups. The Pearson correlation coefficient was calculated to examine the variables for educational level, intelligence, number of manic episodes, and the measurement variables from the Wisconsin Test. When the correlation was significant, the Covariance analysis was used to compare means. The significant level used was .05.

All ethical procedures related to conducting research involving human beings were examined by the Ethics in Research Institute of the Institute of Psychology of the Federal University of Rio Grande do Sul (Research Protocol no. 2006/002).

Results

Sociodemographic data

The sociodemographic characteristics of the participants are summarized in Table 1, below. As can be seen, there was a predominance of women in the three groups. The participants diagnosed with bipolar disorder in depressive episodes were not differentiated from the euthymic participants in respect to age at onset of the disorder, but did present a significant difference in years of development of BD when compared with the euthymic participants. For Groups 1 (BD with depression) and 2 (BD in euthymia)

educational level for the majority of participants was high school, while in Group 3 (Control), the majority of participants had an educational level of college studies. As for professional activity, Group 3, was mostly working at the time of evaluation, unlike the other groups.

Participants from Group 1 had more mood episodes compared to those in Group 2. Both the average of manic episodes and depressive episodes was greater in Group 1. All bipolar participants used psychiatric medications, especially mood stabilizers and anti-psychotic drugs (typical and atypical), followed by antidepressants and benzodiazepines. In the comparison of the groups, however, there was no significant difference in the use of medication.

Performance of executive functions, intelligence, and mood symptomatology.

In regard to executive functioning, the main purpose of this study, the participants diagnosed with BD, whether depressed or euthymic, exhibited significantly different performance than the control group participants in most measures evaluated for executive functioning. As can be seen in Table 2, Group 1 had significantly inferior performance compared to Group 3 in the following measurements: *number of tests administered, total number of errors, perseverative responses, perseverative errors, conceptual level responses, number of categories completed, and attempts to complete first category*. In turn, Group 2 showed significantly inferior performance compared to Group 3 in *number of tests administered, total number of errors, and number of categories completed*. There were no significant differences between the 3 groups in respect to the *total number correct, failure to maintain context, and learning to learn*. Even without difference verified in the comparison between the groups for these last three measurements, moderate effects were identified for the variables *total number correct, and learning to learn*, in comparison between the depressive and control groups. All the same, in relation to the amplitude of the effect, describing the results between the euthymic participants the control group, the variables for *number of tests administered, total number of errors, and number of categories completed* also displayed moderate effects in comparison between the groups.

To examine the influence of the number of manic episodes on performance in the WCST variables, the Pearson correlation coefficients were calculated. No significant correlations were found in nine of the ten variables from the test between the groups. For Group 1, there was a significant correlation only for the *number of categories completed* ($r = .342$; $p = .035$), and for Group two, only for *attempts to complete the first category* ($r = .407$; $p = .032$).

The same procedure was conducted for academic level. However, academic level showed a significant correlation

Table 1
Sample characteristics

Variables	Groups			<i>p</i>
	Group 1 THB depressed (<i>n</i> =44)	Group 2 BD Euthymic (<i>n</i> =37)	Group 3 Controls (<i>n</i> =43)	
Gender				
Male	06	15	14	.020
Female	38	22	29	
Age M (SD)	43.80 (9.85)	41.95 (12.01)	39.53 (13.21)	.242
Age at onset of disorder	34.78 (10.99)	35.23 (11.66)	—	.864
Years of development	17.66 (11.38)	11.83 (9.66)	—	.020
Educational level				
Illiterate	—	1	—	
Elementary	15	12	11	.015
High School	21	13	09	
College	08	11	23	
Current Professional Activity				
Yes	08	15	36	< .001
No	36	22	07	
Number of Episodes Mood				
Depressed	11.84 (6.95)	7.48 (6.45)	—	.013
Manic	11.03 (6.86)	5.32 (4.03)	—	< .001
Current medication use				
Mood Stabilizer	41	35	—	.583
Typical antipsychotic	16	10	—	.256
Atypical antipsychotic	19	11	—	.154
Antidepressant	10	08	—	.561
Benzodiazepine	10	12	—	.233
Other medications	17	16	07	.019

with the measurements of executive function only in the assessment of the overall sample, with an exception for the measures for *total number correct* ($r = .100$; $p = .267$) and *failure to maintain context* ($r = -.152$; $p = .091$). As such, we conducted an analysis of covariance controlled for the educational level variable. The differences between the means for the scores on WCST and the various groups remained similar and statistically significant. In the assessment of the sample by groups, the main objective of the study, academic level did not present any correlation with executive function.

In respect to intelligence, the Total IQ variable showed a significant correlation with all measures from the WCST, except for in Group 1 for *learning to learn* ($r = .239$; $p = .211$), and for Group 2 in *total number correct* ($r = .282$; $p = .090$) and *failure to maintain context* ($r =$

$-.013$; $p = .938$). We chose the ANCOVA, then, which revealed no significant differences between the groups' scores when controlled for Total IQ. The corrected means were not demonstrated in this article, considering the assumption of a relation and of causality between the variables for intelligence and executive function. In this sense, the control for this variable may misrepresent the participants in the study, since the course of the disorder involves cognitive losses. Additionally, the complexity of executive function includes the ability of intelligence, among others.

With respect to general mood symptomatology, Groups 1 and 2 showed no statistically significant differences. In turn, the control groups showed scores significantly lower than participants with BD on variables related to anxiety, depression and mania.

Table 2

Means and standard deviations from the instruments for executive functioning, intelligence and mood symptoms, from both groups ($N = 124$)

Variables	Groups			p	Cohen D		
	Group 1 THB depressed ($n=44$)	Group 2 BD Euthymic ($n=37$)	Group 3 Controls ($n=43$)		1x2	1x3	2x3
WCST							
Num. Tests Administered	121.59 (15.09) ^A	118.65 (18.96) ^A	105.37 (24.15) ^B	.002 *	.17	.83	.61
Total Num. Correct	58.48 (18.04) ^A	61.62 (15.61) ^A	66.21 (12.59) ^A	.061	-.19	-.50	-.33
Num. Total Errors	63.11 (25.35) ^A	57.03 (27.03) ^A	39.16 (27.77) ^B	<.001*	.23	.90	.65
Perseverative responses	52.84 (36.88) ^A	42.97 (28.77) ^{AB}	29.14 (31.48) ^B	.040 *	.30	.69	.46
Perseverative errors	42.30 (26.91) ^A	35.49 (21.42) ^{AB}	24.56 (23.64) ^B	.040 *	.28	.70	.48
Conceptual Level Resp.	40.94 (24.55) ^A	47.65 (21.57) ^{AB}	55.94 (18.89) ^B	.024 *	-.29	-.69	-.41
Num. Categories Completed	2.73 (2.22) ^A	3.08 (2.03) ^A	4.33 (2.09) ^B	.002 *	-.16	-.74	-.61
Trail Completed 1st Cat	48.70 (49.73) ^A	33.65 (38.21) ^{AB}	23.33 (33.05) ^B	.023 *	.34	.61	.29
Weak. Maintain Context	.82 (1.02) ^A	1.16 (1.61) ^A	.58 (0.96) ^A	.103	-.26	.24	.46
Learning to learn	-10.37 (10.82) ^A	-9.55 (12.14) ^A	-5.60 (7.79) ^A	.094	-.07	-.51	-.40
WAIS							
QI Total	96.20 (9.21) ^A	98.70 (10.70) ^A	111.67 (11.14) ^B	<.001	-.25	-1.52	-1.19
HAM – D	15.64 (5.98) ^A	3.27 (2.51) ^A	1.57 (1.88) ^B	<.001	2.81	3.56	.78
HAM – A	17.14 (7.57) ^A	4.14 (3.89) ^A	1.80 (2.04) ^B	<.001	2.21	3.17	.81
YMRS	6.02 (4.80) ^A	1.24 (1.92) ^A	.29 (0.62) ^B	<.001	1.37	2.10	.78

Note: Means followed by the same letter in each row do not differ ($p = 0.05$), i.e, scores followed by the letter A do not differ; scores followed by the letter A differ from scores followed by the letter B (A = A and A# B). .20 = small; .50 = moderate; .80 = large. 0 or near zero effect

Discussion

Although the findings from this research are for a specific sample, with a transversal study method, the majority of the results found corroborate the data from the literature, which support that diagnosis of Bipolar Disorder is associated with transient and permanent cognitive deficits. This is evident given the finding that none of the markers for executive functioning differentiated the euthymic bipolar subjects from the depressed subjects. In this sense, the three markers that indicated differences between the control group and all of the bipolar subjects may be related to more sensitive measurements for permanent deficits, since they already show differences between the healthy control group and the bipolar subjects in asymptomatic stages of the disorder, which is also described in the literature (Goldberg & Chengappa, 2009; Mur et al., 2007; Rocca & Lafer, 2006). The transient deficits, in turn, may be observed through the WCST scores, which show differences between the depressed bipolar subjects and the control subjects.

In this area, various authors indicate that the executive functions are considered to be the most deficient cognitive functions in bipolar patients (Martínez-Arán et al., 2002),

are symptomatic (Maalouf et al., 2010) or euthymic (Goldberg & Chengappa, 2009; Rocca & Lafer, 2006). However, according to Martínez-Arán (2001), the executive dysfunction in euthymic period may be classified as mild. Results from Mur and cols. (2007) indicate that euthymic bipolar subjects have significantly lower performance than the control subjects in measures of executive functions, which is also verified in this study by the scores on the three WCST measurements.

According to the literature, the performance of the control subjects is comparatively better than that of the euthymic bipolar patients, followed by the bipolar subjects during a mood episode (Delaloye et al., 2009; Duncan, Burgess, & Emslie, 1995). Similar data were observed in this study, since the control groups presented significantly higher means, or, a generally higher performance, comparatively, than the euthymic bipolar subjects. These, in turn, showed greater performance than the depressed participants. Thus, the findings corroborate the findings that Rocca and Lafer (2006) developed through review of 53 studies (between 1990 and 2005). This review indicated that some cognitive difficulties persist in bipolar subjects, even during period of remission from symptomatology. Moreover, such difficulties are basically concentrated in the context of executive functions.

For Heaton et al. (2005) the two measurements from the WCST most used to evaluate executive functions are *perseverative errors* and *number of categories complete*, which also differentiate the control group from Group 1 in the sample studied. Frequent occurrence of perseverative errors in bipolar patients is defended by various authors (Martínez-Arán et al., 2002; Martínez-Arán et al., 2004a; Martínez-Arán et al., 2004b; (Zubieta, Huguélet, O'Neill, & Giordani, 2001). In this study, perseverative errors did not differentiate the control group from Group 2. For number of categories completed, however, the second most widely used measure from the WCST (Heaton et al., 2005) was one of the three measures that showed a significantly poorer performance in Group 2, compared with the control group.

It is known that academic achievement, even without any significant correlation with executive function in this study through evaluation by groups, plays a role in general intellectual ability, and that the latter makes an important contribution to neuropsychological performance (Jamrozinski, 2010; Obonsawin et al., 2002). In order to verify the influence of the intelligence variable on the correlation results obtained, new analyses were conducted from the control of this variable, revealing a lack of difference between the two groups in respect to executive function.

However, it is important to note here that the data from the literature appear divergent regarding the relationship between intelligence and executive function. For Jamrozinski (2010), the different cognitive data are seen as interrelated, and Duncan, Burgess and Emslie (1995) defend the idea that tests that evaluate functioning of the frontal lobe include a good measure of intelligence. Contrary to this position, other authors indicate that the WCST is not a good reference for the Total IQ variable (Ardila, Pineda, & Rosseli, 2000).

For this study, we assumed a strong association between intelligence and executive function. From this perspective, eliminating this factor would be equivalent to decharacterization of the bipolar patient, the course of whose disease indicates to cognitive deficits in general (Martínez-Arán et al., 2001).

For Rocca and Lafer (2006), there is a positive correlation between the number of mood episodes and cognitive deficits. This correlation was not observed in this study, however, since there was no significant correlation between the number of manic episodes (those most related to cognitive deterioration) and WCST performance in nine of the ten measurements. This result may be related to findings by Lebowitz et al (2001), who postulate that the performance of bipolar patients is also influenced by other factors.

Some authors postulate that the greater the number of episodes and duration of the illness, the worse the performance in mental flexibility, i.e. the lower the performance on tasks such as the WCST (Martínez-Arán et al. 2004a; Van Gorp et al., 1998). Although this association was not found (none of the markers for executive function

were differentiated between euthymic and depressed bipolar subjects), the data from this sample may be associated with a possible chronicity in the participants, since the group with the highest average of number of episodes (Group 1) had the worst performance, both for intellectual and executive functioning. The number of episodes variable may suggest that the Group 1 participants are more chronically affected by the disease than Group 2 participants, by having significantly more mood episodes. Furthermore, as expected, Group 3 showed significantly fewer mood symptoms than all of the bipolar subjects. Among these, the depressed scored highest in all mood scales.

The medications used most among the sample of bipolar subjects were mood stabilizers. It is worth mentioning the interference of medication on cognitive function (Martínez-Arán et al., 2001). However, the withdrawal of medication for participation in this research would not be an appropriate course of action, since it is known that mood stabilizers have a fundamental role in improvement for bipolar patients. For Haldane e Frangou (2005), the only predictor for cognitive functioning subject to change over the short term is the use of medication, especially the effects of antipsychotics. Although this is an important observation, it may not have a significant effect in our sample, as there were no significant differences regarding medication use in the comparison between groups, which would not justify the application of such a predictor. From the evaluation of executive functioning, Mur et al. (2007) also postulate that impairment in executive function and loss of inhibition may be important features in bipolar patients, regardless of the severity of the disease or drug effects.

As was the objective of Rocca and Lafer (2006), the intention of comparing euthymic bipolar subjects with control subjects in this study is based on the attempt to establish a relationship between remission and improvement in cognitive functioning. This comparison also allows assessment of whether or not this alteration is a trait of the disorder, or simply due to mood status. The fact that some markers do not detect differences between control subjects and euthymic bipolar patients in the sample from this study reinforces the premise from Rocca and Lafer that improvement in mood symptomatology may positively affect functionality.

Once confirmed that executive damage are present in both symptomatic and asymptomatic phases of bipolar disorder, these impairments could be related to both transient and permanent deficits that prevent the complete remission of symptoms and cause significant functional damages (Martínez-Arán et al., 2001). This may also be noted through the presence of professional activity in the majority of participants in the Control Group, unlike the other groups.

Although the results have indicated a tendency towards permanent executive deficits in bipolar subjects, it is necessary to emphasize the limitations of the sample and the method employed in this study, since this tendency was not confirmed in four measurements for executive

performance. Additionally, the correlation found between executive functioning and intelligence may be better discussed through studies intended specifically for this purpose. Still, in relation to the limitations of this study, the association between executive functioning and the number of manic episodes may be better explored, since in this study, such evidence was found in only two variables for executive functioning.

Regarding future practices and research in bipolarity, El-Mallakh and Ghaemi (2008) emphasized that the response to treatment, characterized by at least 50% improvement in symptoms, should no longer be the goal for BD. They stress that the focus should be on complete remission of symptomatology, even knowing that, even so, light to moderate symptoms are associated with ongoing functional impairment. As such, the authors report treatment of cognitive impairment as a guideline for care from mental health professionals. The results from this study indicate that symptomatic improvement in euthymic patients does not necessarily entail functional improvement, as corroborated by El-Mallakh and Ghaemi (2008).

Consequently, review of the literature and the limitations of this study suggest some topics for further research: the role of the number of mood episodes, academic level and intelligence in executive functions, longitudinal studies evaluating executive functioning after the first mood episode and throughout the course of the illness, chronicity and executive dysfunction, assessment of the efficacy of neuropsychological rehabilitation programs and functional neuro-imaging techniques for testing the relationship between executive deficits and levels of brain activity.

References

- Ardila, A., Pineda, D., & Rosseli, M. (2000). Correlation between intelligence test scores and executive function measures. *Archives of Clinical Neuropsychology, 15*, 31-36. doi:10.1016/S0887-6177(98)00159-0
- Borkowska, A., Leszczynska-Rodziewicz, A., Kapelski, P., Hauser, J., & Janusz, R. (2005). Eye movement disturbances and working memory deficit in bipolar affective disorder. *Psychiatria Polska, 39*, 481-495.
- Clark, L., Kempton, M., Scarna, A., Grasby, P., & Goodwin, G. (2005). Sustained attention-deficit confirmed in euthymic bipolar disorder but not in first-degree relatives of bipolar patients or euthymic unipolar depression. *Biological Psychiatry, 57*, 183-187. doi:10.1016/j.biopsych.2004.11.007
- Cunha, J. A. (2000). *Psicodiagnóstico V* [Psychodiagnostic V]. Porto Alegre, Brazil: Artes Médicas.
- Cunha, J. A., Trentini, C. M., Argimon, I. L., Oliveira, M. S., Werlang, B. G., & Prieb, R. G. (2005). *Teste Wisconsin de Classificação de Cartas – Adaptação e Padronização Brasileira* [Wisconsin Card Sorting Test – Brazilian adaptation and standardization]. São Paulo, Brazil: Casa do Psicólogo.
- Deckersbach, T., Dougherty, D., Savage, C., McMurrich, S., Fischman, A., Nierenberg, A., ... Rauch, S. (2006). Impaired recruitment of the dorsolateral prefrontal cortex and hippocampus during encoding in bipolar disorder. *Biological Psychiatry, 59*, 138-146. doi:10.1016/j.biopsych.2005.06.030
- Delaloye, C., de Bilbao, F., Moy, G., Baudois, S., Weber, K., Campos, L., ... Gold, G. (2009). Neuroanatomical and neuropsychological features of euthymic patients with bipolar disorder. *The American Journal of Geriatric Psychiatry, 12*, 1012-1021. doi:10.1097/JGP.0b013e3181b7f0e2
- Doyle, A., Wilens, T., Kwon, A., Seidman, L., Faraone, S., Fried, R., ... Biederman, J. (2005). Neuropsychological functioning in youth with bipolar disorder. *Biological Psychiatry, 58*, 540-548. doi:10.1016/j.biopsych.2005.07.019
- Duncan, J., Burgess, P., & Emslie, H. (1995). Fluid intelligence after frontal lobe lesions. *Neuropsychologia, 33*, 261-268. doi:10.1016/0028-3932(94)00124-8
- El-Mallakh, R., & Ghaemi (2008). *Depressão Bipolar: um guia abrangente* [Bipolar depression: a comprehensive guide]. Porto Alegre, Brazil: Artmed.
- Forlenza, O. (2000). *Neuropsiquiatria geriátrica* [Geriatric neuropsychiatry]. São Paulo, Brazil: Editora Atheneu.
- Frangou, S., Dakhil, N., Landau, S., & Kumari, V. (2006). Frontotemporal function may distinguish bipolar disorder from schizophrenia. *Bipolar Disorders, 8*, 47-55. doi:10.1111/j.1399-5618.2006.00274.x
- Goldberg, J., & Chengappa, K. (2009). Identifying and treating cognitive impairment in bipolar disorder. *Bipolar Disorders, 11*(2), 123-137. doi:10.1111/j.1399-5618.2009.00716.x
- Haldane, M., & Frangou, S. (2005). Maudsley Bipolar Disorder Project: insights sobre o papel do córtex pré-frontal em pacientes com transtorno de humor bipolar tipo I [Maudsley Bipolar Disorder Project: insights into the role of the prefrontal cortex in patients with bipolar disorder type I]. *Revista de Psiquiatria do Rio Grande do Sul, 27*(3), 241-250. doi:10.1590/S0101-81082005000300003
- Jamrozinski, K. (2010). Do euthymic bipolar patients have normal cognitive functioning? *Current Opinion in Psychiatry, 23*(3), 255-260. doi:10.1097/YCO.0b013e328338620a
- Joseph, R., McGrath, L., & Tager-Flusberg, H. (2005). Executive Dysfunction and Its Relation to Language Ability in Verbal School-Age Children With Autism. *Developmental Neuropsychology, 27*(3), 361-378. doi:10.1207/s15326942dn2703_4
- Kessler, R., Coccaro, E., Fava, M., Jaeger, S., Jin, R., & Walters, E. (2006). The prevalence and correlates of DSM-IV intermittent explosive disorder in the national comorbidity survey replication. *Archives of General Psychiatry, 63*, 669-678. doi:10.1001/archpsyc.63.6.669
- Kobak, K., Greist, J., Jefferson, J., Katzelnick, D., & Mundt, J. (2001). New Technologies to Improve Clinical Trials. Guest Editorial, *Journal of Clinical Psychopharmacology, 21*, 255-256. doi:10.1097/00004714-200106000-00001
- Lebowitz, B., Shear, P., Steed, M., & Strakowski, S. (2001). Verbal fluency in mania: relationship to number of manic episodes.

- Neuropsychiatry, Neuropsychology, & Behavioral Neurology*, 14(3), 177-182.
- Lezak, M. (2004). *Neuropsychological Assessment*. New York, NY: Oxford University Press.
- Lima, M., Tassi, J., Novo, I., & Mari, J. (2005). Epidemiologia do transtorno bipolar [Epidemiology of bipolar disorders]. *Revista de Psiquiatria Clínica*, 32, 15-20. doi:10.1590/S0101-60832005000700003
- Maalouf, F., Klein, C., Clark, L., Sahakian, B., Labarbara, E., Versace, A.,... Phillips, M. (2010). Impaired sustained attention and executive dysfunction: bipolar disorder versus depression-specific markers of affective disorders. *Neuropsychologia*, 48, 1862-1868. doi:10.1016/j.neuropsychologia.2010.02.015
- Martínez-Arán, A., Goodwin, G., & Vieta, E. (2001). El mito de la ausencia de disfunciones en el transtorno bipolar [The myth of the absence of dysfunction in bipolar disorder]. In Vieta, E. (org.). *Transtornos bipolares: avances clínicos y terapéuticos*. (1st ed.) Madrid, Spain: Médica Panamericana.
- Martínez-Arán, A., Pineda, R., Vieta, E., Colom, F., Reinares, M., Benabarre, A.,... Gasto, C. (2002). Executive function in patients with remitted bipolar disorder and schizophrenia in its relationship with functional outcome. *Psychotherapy and Psychosomatics*, 71, 39-46.
- Martínez-Arán, A., Vieta, E., Colom, F., Torrent, C., Sanchez-Moreno, J., Reinares, M.,... Salameo, M. (2004a). Cognitive impairment in euthymic bipolar patients: implications for clinical and functional outcome. *Bipolar Disorders*, 6, 224-232.
- Martínez-Arán, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sanchez-Moreno, J.,... Salameo, M. (2004b). Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *The American Journal of Psychiatry*, 161, 262-270.
- Merikangas, K., Akiskal, H., Angst, J., Greenberg, P., Hirschfeld, R., Petukhova, M., & Kessler, R. (2007). Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Archives of General Psychiatry*, 64, 543-552. doi:10.1001/archpsyc.64.5.543
- Meyer, T., & Deckersbach, T. (2005). No evidence for verbal memory impairment in individuals putatively at risk for bipolar disorder. *Comprehensive Psychiatry*, 46, 472-476. doi:10.1016/j.comppsy.2005.02.003
- Miller, E., & Cohen, J. (2001) Integrative theory of prefrontal cortex function. *Annual Reviews in the Neurosciences*, 24, 167-202.
- Morice, R. (1990). Cognitive inflexibility and pre-frontal dysfunction in schizophrenia and mania. *British Journal of Psychiatry*, 157, 50-54. doi:10.1192/bjp.157.1.50
- Mur, M., Portella, M., Martínez-Arán, A., Pifarré, J., & Vieta, E. (2007). Persistent neuropsychological deficit in euthymic bipolar patients: executive function as a core deficit. *Journal of Clinical Psychiatry*, 68, 1078-1086. doi:10.4088/JCP.v68n0715
- Nascimento, E., & Figueiredo, V. (2002). WISC-III e WAIS-III: alterações nas versões originais americanas decorrentes das adaptações para o uso no Brasil [WISC-III and WAIS-III: changes arising in the original American version of adaptations for use in Brazil]. *Psicologia: Reflexão e Crítica*, 15, 603-612. doi:10.1590/S0102-79722002000300014
- Obonsawin, M., Crawford, J., Page, J., Chalmers, P., Cochrane, R., & Low, G. (2002). Performance on tests of frontal lobe function reflects general intellectual ability. *Neuropsychologia*, 40, 970-977. doi:10.1016/S0028-3932(01)00171-3
- Rocca, C., & Lafer, B. (2006). Alterações neuropsicológicas no transtorno bipolar [Neuropsychological impairments in bipolar disorder]. *Revista Brasileira de Psiquiatria*, 28(3), 226-237. doi:10.1590/S1516-44462006000300016
- Rzezak, P., Fuentes, D., Guimarães, C., Thomé-Souza, S., Kuczynski, E., Guerreiro, M., & Valente, K. (2009). Executive dysfunction in children and adolescents with temporal lobe epilepsy: Is the Wisconsin Card Sorting Test enough? *Epilepsy and Behavior*, 15, 376-381. doi:10.1016/j.yebeh.2009.04.014
- Smith, D., Muir, W., & Blackwood, D. (2006). Neurocognitive impairment in euthymic young adults with bipolar spectrum disorder and recurrent major depressive disorder. *Bipolar Disorders*, 8, 40-46. doi:10.1111/j.1399-5618.2006.00275.x
- Spitzer, R., Williams, J., Gibbon, M., & First, M. (1992). Structured Clinical Interview for the DSM-III-R (SCID). *Archives of General Psychiatry*, 49, 624-629.
- Souza, F. (2005). Tratamento do transtorno bipolar: Eutímia [treatment of bipolar disorder: Eutímia]. *Revista de Psiquiatria Clínica*, 32, 63-70. doi:10.1590/S0101-60832005000700010
- Tabares-Seisdedos, R., Balanza-Martinez, V., Salazar-Fraile, J., Selva-Vera, G., Leal-Cercos, C., & Gómez-Beneyto, M. (2003). Specific executive/attentional deficits in patients with schizophrenia or bipolar disorder who have a positive family history of psychosis. *Journal of Psychiatric Research*, 37, 479-486.
- Tavares, M. (2000). Entrevista Clínica Estruturada para o DSM-IV [structured clinical interview for DSM-IV]. In J. Cunha, et al. *Psicodiagnóstico V*. Porto Alegre, Brazil: Artes Médicas.
- Totic-Poznanovic, S., Marinkovic, D., Pavlovic, D., & Paunovic, V.R. (2005). Neuropsychological profile of patients with bipolar depression in remission. *Vojnosanitetski Pregled*, 62, 543-550. doi:10.2298/VSP0508543T
- Toulopoulou, T., Quraishi, S., Mc Donald, C., & Murray, R.M. (2006). The Maudsley Family Study: premorbid and current general intellectual function levels in familial bipolar I disorder and schizophrenia. *Journal of Clinical and Experimental Neuropsychology*, 28, 243-259. doi:10.1080/13803390500360513
- Van Gorp, W., Altshuler, L., Theberge, D., Wilkins, J., & Dixon, W. (1998). Cognitive impairment in euthymic bipolar patients with and without prior alcohol dependence: A preliminary study. *Archives of General Psychiatry*, 55, 41-46. doi:10.1001/archpsyc.55.1.41
- Wechsler, D. (1997). *WAIS – III – administration and scoring manual*. San Antonio, TX: Psychological Corporation.
- Young, R., Biggs, J., Ziegler, V., & Meyer, D. (1978). A rating scale for mania: reliability, validity and sensitivity. *British Journal of Psychiatry*, 133, 429-435. doi:10.1192/bjp.133.5.429

Zubieta, J., Huguelet, P., O'Neil, R., & Giordani, B. (2001).
Cognitive function in euthymic bipolar I disorder. *Psychiatry
Research, 102*, 9-20. doi:10.1016/S0165-1781(01)00242-6

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