

VISUAL AND VERBAL MEMORY IN EUTHYMIC BIPOLAR PATIENTS:
IMPACTS OF SUBTYPE, PSYCHOTIC SYMPTOMS AND SUICIDE BEHAVIOR

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Abstract

Objective: Recent studies point out to the existence of neuropsychological deficits in patients with bipolar disorder even in euthymic periods. Episodic memory deficits are frequently described in patients with bipolar disorder (BD). This study aims to evaluate the performance of patients with BD compared with health controls on tests of verbal and visual episodic memory. We further considered the bipolar subtype, lifetime history of psychotic symptoms and suicide attempts.

Method: Sixty euthymic BD patients and sixty normal individuals with same age and scholarship were involved in the study. All subjects were submitted to the MINI Neuropsychiatric interview, Raven's Progressive Matrices, Rey Auditory Verbal Learning Test and Rey Complex Figure Test.

Results: Regardless the absence of intelligence differences between BD and Control subjects, the former are impaired in both verbal and visual memory measures. Comparing groups according BD subtype, we found that visual memory presents worse results in Type I patients than in Type II. No differences were found considering history of psychotic symptoms and suicide attempts.

Conclusions: Our results suggests that episodic memory impairments is important in euthymic bipolar patients and not influenced by the subtype and history of psychotic symptoms, and suicide attempts.

Key Words: bipolar disorder, episodic memory, neuropsychology, psychosis, suicide.

Declaration of interest: none

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Introduction

Considered the sixth leading cause of disability worldwide, bipolar disorder (BD) is a chronic, clinically severe and common psychiatric disorder that accounts for significant economic, familial and individual burden (Woods 2000). Prevalence rates for BD have been acknowledged to approximate 1 to 2% (Hirschfeld 2001) in the general population. These estimates are probably conservative since when the diagnosis is broadened to include bipolar spectrum disorders, the rate increases to 6 to 7% (Pini et al. 2005, Akiskal 1996).

BD is associated with several psychiatric comorbidities and a range of serious comorbid medical conditions, which leads to a higher mortality rate in untreated BD than in the general population (Oquendo et al. 2000). Furthermore, BD is the psychiatric diagnosis most closely associated with suicidal behavior (Baldessarini et al. 2006). BD patients are also more prone to have forensic problems (about 10% of them), to have very low employment and higher pension or disability benefits. A large proportion never marry and a vast majority of married patients divorce or experience marital problems (Morgan et al. 2005), reflecting their

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overall poor social functioning.

Cognitive deficits are associated with poor recovery in these patients since even when euthymic they have altered functions such as memory, attention, executive functions and processing speed (Olley et al. 2005) to such an extent that current employment status is significantly associated with cognitive status (Dikerson et al. 2004). Moreover, cognitive deficits, including those in verbal memory, are a stronger predictor of poor self-reported life quality (Brissos et al. 2008) and overall functional outcome in bipolar patients (Martinez-Aran et al. 2007).

Episodic memory deficit results in BD are rather contradictory since there are positive (Bora et al. 2009, Delaloye et al. 2009, Kiesepä et al. 2005) and negative associations regarding visual episodic memory (Ferrier et al. 1999), performance of BD type II (Hsiao et al. 2009) and bipolar patients not using psychotic medication (Jamrozinski et al. 2009).

An explanation for the disparate findings is the fact that BD is a heterogeneous clinical condition and some subgroups of patients exhibit more severe cognitive impairments than others (Jamrozinski 2010, Selva et al. 2007). BD subtype (Harkavy-Friedman et al. 2006), lifetime history of psychotic illness (Martinez-Aran et al. 2008) and history of suicide attempt (Malloy-Diniz et al. 2009) are among the clinical features that could affect bipolar patients' performance on cognitive assessments.

The present study aimed to compare the performance of bipolar patients and normal controls on neuropsychological tests of episodic memory for both visual and verbal content. It was hypothesized that clinical variables like subtype, suicide behavior and history of psychotic symptoms could present different patterns of memory functioning.

Methods and Subjects

Study participants included 60 BD patients recruited from the Núcleo de Transtornos Afetivos from the Psychiatric Service of the Hospital das Clínicas of the Universidade Federal de Minas Gerais. Inclusion criteria consisted of: a) BD diagnosis identified using a structured interview (MINI-PLUS) according to DSM-IV. b) An euthymic state at the time of the neuropsychological assessment as determined by the Brazilian adaptation of the Beck Depression Inventory (BDI) (Gorenstein and Andrade 1998) and the Young Mania Rating Scale (YMRS) (Vilela et al. 2005). Subjects were classified as euthymic if they had both a BDI score lower than 12 points and a YMRS lower than 13. c) At least eight years of formal education. d) Normal intelligence as measured by the Test of Raven's Progressive Matrices (percentile >10) (General Scale, Raven 2002).

Patients were further interviewed by a psychiatrist using a semi-structured interview to collect information regarding socio-demographic and clinical parameters. Episodic memory was evaluated using the Brazilian version of the Rey Auditory Verbal Learning Test (RAVLT) (Malloy-Diniz et al. 2007) and the Rey-Osterreich Complex Figure (ROCF) (Strauss et al. 2006).

The control group consisted of 60 normal subjects recruited from the community. No subject had a history of an axis-I psychiatric illness according to DSM-IV criteria as assessed by the MINI-LUS. The controls had at least eight years of formal education and normal intelligence as measured by the Test of Raven's Progressive Matrices.

Statistical Analysis

Since certain variables exhibited non-normal distributions, groups (bipolar x healthy controls; BD I x BD II; bipolar with psychotic symptoms x no psychotic symptoms) were compared according to polarity of the first episode using the Mann-Whitney test for quantitative variables.

Area under curve measure in Receiver Operator Characteristic Curve (ROC) was used to assess accuracy in comparison between Bipolar and Healthy subjects concerning memory measures. Since our data had nonparametric distribution, we use Cliff's Delta to assess effect size of group's differences (Leech and Onwuegbuzie 2002). We also use Bonferroni's correction for multiple comparison and, therefore results were considered significant when $p < 0.006$. To assess the effects of humor in memory measures in comparisons according to lifetime history of psychotic illness and bipolar subtype, we use Generalized Linear Model considering BDI's and YMRS's results as covariates. Categorical variables were analyzed using chi-square tests.

Results

Sixty bipolar patients were studied (36 BD I; 14 with lifetime history of psychotic symptoms; 14 with lifetime history of suicide attempt). All patients were euthymic at the time of assessment (BD I mean=7.5 and SD=2.5; YMRS mean=4.7 and SD=3.0). Patients and controls did not differ on socio-demographic parameters (age, gender distribution, educational level) or intelligence, but the neuropsychological examination of episodic memory revealed that individuals in the BD group showed less efficient performance in both verbal and visual components. Considering the measures of area under ROC curve we found significant results concerning ROCF retrieval, RAVLT A1, LOT, Proactive interference and Recognition Memory. All results were between 0.7 and 0.9 (Table 1) pointing to a moderate and useful accuracy in discriminate bipolar and comparison control group (Swet 1988). Considering these measures, Cliff's effect size ranging from 0.42 to 0.79 indicated lack of overlap between bipolar and control group. We did not find significant differences for the visuoconstruction score (copy of ROCF), RAVLT's forget speed and retroactive interference (Table 1)

Bipolar patients were also analyzed by subtype (BD I or II). Socio-demographic parameters as well intelligence were comparable between the groups. The sole significant difference on the neuropsychological evaluation was found regarding visual memory (BD I mean=13.3 and SD=11.2; BD II mean=19.2 and

Table 1. Comparison between bipolar and healthy controls in sociodemographic and neuropsychological measures

	Group													
	Bipolar Disorder							Comparison Control						
	Mean	Standard Deviation	Count	Column N %	Mean	Standard Deviation	Count	Column N %	z our x2	p	Cliff's delta	Area under ROC curve	Standard Error	p
Age	39.78	12.99			38.57	9.07			-2.202	.840				
Formal Education			35	58.3%			37	61.7%						
			25	41.7%			23	38.3%	0.139	.709				
Gender			19	31.7%			24	40.0%						
			41	68.3%			36	60.0%	0.906	.341				
Raven raw score	45.00	5.58			46.00	2.79			-1.648	.099				
Rey Complex Figure Copy	28.81	7.76			30.93	4.60			-1.095	.273	.558	.053	.275	
Rey Complex Figure retrieval after 3 minutes	15.68	10.91			26.43	5.96			-5.801	.000	.807	.042	.000	
RAVLT A1 (immediate memory)	5.32	1.28			6.22	1.38			-4.067	.000	.710	.048	.000	
RAVLT Learning over trials	12.87	6.71			18.80	7.21			-4.341	.000	.729	.046	.000	
RAVLT Proactive Interference	0.79	0.27			1.02	0.31			-4.295	.000	.726	.047	.000	
RAVLT Retroactive interference	0.88	0.43			0.95	0.12			-2.567	.010	.636	.053	.010	
RAVLT Forget Speed	0.99	0.29			0.91	0.17			-1.212	.225	.437	.053	.232	
RAVLT Recognition Memory	11.20	2.33			12.87	1.62			-4.250	.000	.722	.046	.000	

SD=9.5; $z=2.257$; $p=0.024$). There were no differences on socio-demographic measures (age, education, gender), intelligence and verbal memory between BD I and II patients.

Patients were further analyzed according to lifetime history of psychotic symptoms ($n=14$) and history of suicide attempt ($n = 14$). In both analyses, socio-demographic parameters, intelligence levels, visuo construction, verbal and visual memory were comparable.

Considering the effect of humor status on memory measures, we did not find any significant relationship in comparisons according subtype and lifetime history of psychotic illness.

Discussion

The objective of the present study was to evaluate verbal and visual memory in bipolar patients compared to healthy controls as well as to analyze the impact of bipolar type (I or II), history of psychotic symptoms and suicide attempts.

Differences were found between bipolar patients and healthy controls in learning, storage and auditory-verbal recall as well as in visual modality. The results appear to be specific since no differences were found between the groups with regard to general intelligence, visuo construction and socio-demographic data. Some authors argue that poor memory in bipolar patients could be of a motivational nature, particularly in depression since recognition memory is usually preserved in these patients (Ilsley et al. 1995). In the current study, recognition memory was worse in the euthymic bipolar patients compared to controls, and was also worse in BD I and patients with a lifetime history of psychotic symptoms. Therefore, it can be argued that memory difficulties are not related to motivational aspects, persisting even in the stage when memory is assessed on clues given by the examiner.

Regarding the relationship between deficits in verbal and visual episodic memory according BD subtype, a difference was only seen on the retrieval of Rey Complex Figure, which revealed greater visual memory impairment in BD I patients compared to type II. These results are similar to those described in the literature that point to subgroups of BD I patients having impaired cognitive performance compared to BD II (Savitz et al. 2009, Selva et al. 2008). However, the present results differ from those of Hsiao et al (2009), which did not find differences between BD I, II and controls on visual memory. Those authors described worse performance of BD I in verbal memory, perceptual motor skills and executive functions. It is important to note that Rey Complex Figure copy and retrieval are both influenced by executive functions (Watanabe et al. 2009). Therefore, future studies should investigate the relationship between executive function impairment and Rey Complex Figure scores in bipolar patients to elucidate whether visual memory deficits are genuine or are reflections of executive impairment.

As in previous studies, the present one did not find differences between episodic memory in bipolar patients according to lifetime history of psychotic illness (Bora et al. 2007, Kiesepä et al. 2005, Savitz

et al. 2005, Savitz et al. 2009) and therefore these results reinforce the hypothesis that memory impairment in BD is independent of this clinical feature. The same conclusion can be extended to the comparison between suicide attempters and non-attempters. As was reported in a previous study performed by the current research group with a sample of BD I outpatients (Malloy-Diniz et al. 2009), the present study did not reveal any differences in verbal and visual memory tests according to lifetime history of suicide attempt.

A methodological strength of the current study was the comparison of bipolar patients and healthy controls of the same age, educational and intelligence levels. Furthermore, the bipolar patients were euthymic during the period of assessment and therefore mood effect in evaluation can be excluded. However, certain limitations must be noted. The sample could be considered small, which reduces statistical power when performing comparisons between subgroups like psychotic symptoms or suicide behavior and a β -error cannot reliably be excluded. Nonetheless, considering the Area under curve ROC, differences between bipolar and control groups had moderate and useful accuracy. Furthermore, Cliff's Delta points to the lack of overlap between bipolar and control groups in those measures that reach statistically significant differences. Second, all subjects were submitted to pharmacological therapy during the study and these treatments may have influenced the results. But, Ancín et al. (2010) suggested that cognitive alterations in bipolar patients cannot be explained by medication because the alterations remained after controlling for medication variables in the statistical analysis of several studies (for example, Fleck et al. 2001) as well as in drug-free euthymic bipolar patients (Goswami et al. 2009). Future studies are needed to clarify the specific effect of medication in episodic memory in bipolar patients.

The nature of memory impairment in BD and its probable role as a possible endophenotype should be investigated further and consider neuropsychological variables and genetic polymorphisms in affected bipolar patients and their unaffected relatives. Furthermore, variables such as age of first hospitalization, number of manic and depressive episodes, comorbidities and other clinical variables should be included in the research agenda. Findings from these studies would lead to better understanding BD and improved clinical practices with this population.

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