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## Research report

# Insight, quality of life and cognitive functioning in euthymic patients with bipolar disorder

Vasco Videira Dias<sup>a,\*</sup>, Sofia Brissos<sup>b</sup>, Benicio N. Frey<sup>c</sup>, Flávio Kapczinski<sup>d</sup>

<sup>a</sup> Autonomous University of Lisbon (UAL), Lisbon, Portugal

<sup>b</sup> Centro Hospitalar Psiquiátrico de Lisboa, Lisbon, Portugal

<sup>c</sup> McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, QC, Canada

<sup>d</sup> Bipolar Disorders Program and Molecular Psychiatry Unit, Hospital de Clínicas, Federal University, UFRGS, Porto Alegre, Brazil

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## Abstract

**Introduction:** The relationship between insight, quality of life and cognition in bipolar disorder has not been clearly established.

**Method:** A neuropsychological battery assessing attention, mental control, perceptual-motor skills, executive functions, verbal fluency, abstraction and visuo-spatial attention was administered to 70 remitted bipolar patients and 50 healthy controls. Insight was assessed using the Scale to Assess Unawareness of Mental Disorder; Quality of Life was assessed using the Portuguese version of the WHO Quality of Life Assessment – Abbreviated version (WHOQOL–BREF–PT).

**Results:** No differences in QoL and cognitive performance were observed between bipolar patients with ‘impaired’ and ‘preserved’ insight. Insight was found to be correlated with poorer psychological and environmental QoL. A multiple regression model showed that depressive symptoms were significant predictors of physical, psychological and environmental QoL.

**Conclusion:** The present study adds to the notion that depressive symptoms, even of low intensity, are strong predictors of QoL. The present study suggests that the impact of insight on self-reported QoL may be subtle during remission and may be more substantially affected in the presence of manic symptoms.

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**Keywords:** Awareness; Bipolar disorder; Executive functions; Frontal; Insight; Cognition; Quality of life

## 1. Introduction

Impaired insight is a common phenomenon in bipolar disorder (BD), especially during the manic phases (Ghaemi et al., 1996). Although insight is clearly affected by mood-related psychopathology, mood symptoms and

insight seem to relate to differential phenomenological domains (Varga et al., 2006), since insight does not seem to improve as it would be expected with the resolution of mood symptoms (David et al., 1992; Amador et al., 1993).

Preserved insight has been suggested to be at least partially dependent on intact frontal-executive functioning (Amador and David, 2004). It is noteworthy that even remitted BD patients present neuropsychological deficits related to attention/processing speed, memory, and particularly to executive function (for reviews see Robinson et al., 2006; Torres et al., 2007). Even though some studies

\* Corresponding author. Rua Ilha dos Amores, Lote 4.12, Bloco C, 1.º esq, 1990-122, Lisbon, Portugal. Tel.: +351 213 144 425; fax: +351 213 144 426.

E-mail address: v.dias@netcabo.pt (V.V. Dias).

have found no association between the level of insight and performance on several neuropsychological measures (Yen et al., 2002; Varga et al., 2006), in a previous study, we found that insight was impaired in 60% of BD patients in remission, and patients presented significantly worse cognitive performance compared to healthy control, leading to the hypothesis that insight may be partially dependent on intact cognition (Dias et al., 2008).

The study of insight and its correlates is important because awareness of illness may have diagnostic, nosological, and prognostic value (Amador et al., 1991), and may affect treatment and rehabilitation efforts (Lysaker and Bell, 1995). Currently, effective treatment in BD implies mood stabilization, along with attaining good psychosocial functioning, and achieving a subjective feeling of well-being, which is closely related to the concept of QoL (Awad et al., 1995).

QoL is markedly impaired in BD patients during the depressive phase (Leidy et al., 1998; Vojta et al., 2001; Russo et al., 1997; Yatham et al., 2004; Sierra et al., 2005; Gazalle et al., 2006), and depressive symptoms have been associated with greater impairment in work, family, and social life, appearing to be the primary determinant of impaired QoL in BD (Bauer et al., 2001; Vojta et al., 2001). Other factors such as manic symptoms (Gazalle et al., 2007a), female sex (Robb et al., 1998), and time undiagnosed (Gazalle et al., 2005) have also been put forward as playing an important role in the self-perception of QoL.

Even though euthymic patients tend to self-report higher QoL than acutely ill patients (Namjoshi and Buesching, 2001; Chand et al., 2004; Piccinni et al., 2007), impairments in QoL have also been shown to persist in remitted patients (Robb et al., 1997; Michalak et al., 2005; Sierra et al., 2005; Gazalle et al., 2007b), indicating that other factors besides mood symptoms may be involved in the determination of QoL in BD. Kauer-Sant'Anna et al. (2007) showed that higher rates of comorbidity with anxiety disorders may be an important factor associated with poorer QoL among BD patients.

Previously, we have reported that neurocognitive function, insight, and QoL are all impaired in BD patients while in remission, and that deficits in executive functioning and verbal abstraction were strong predictors of poor self-reported QoL (Dias et al., 2008; Brissos et al., in press); however, the interaction between impaired insight, impaired neurocognitive function and poorer self-reported QoL have not yet been fully assessed.

## 2. Aims of the study

This cross-sectional study further explores the relationship between insight, quality of life and cognitive

functioning in bipolar I patients in remission, and uses a linear regression model to investigate predictive factors of QoL. We hypothesized that cognitive impairment would be related to worse insight and to worse self-reported QoL in BD patients, and that remitted patients, independently of their insight level, are capable of subjectively assess QoL.

## 3. Materials and methods

### 3.1. Participants

Seventy bipolar type I outpatients (28 men and 42 women), aged 17–63, were recruited from the Department of Psychiatry of Santarém's Hospital, Júlio de Matos' Psychiatric Hospital, and from the Association of Bipolar and Depressive Patients (ADEB). Patients were diagnosed according to DSM-IV criteria (American Psychiatric Association, 1994), ascertained from personal interview and using the Mini International Neuropsychiatric Interview – MINI (Sheehan and Lecrubier, 1994).

Bipolar patients were in remission, defined as a Young Mania Rating Scale – YMRS (Young et al., 1978) score  $\leq 6$  and a Hamilton Depression Rating Scale – HDRS (Hamilton, 1960) score  $\leq 7$ . Patients were using a stable medication regimen for at least 4 weeks preceding the assessment, ascertained by interview, self-assessment (written diaries), and/or family information.

Patients with organic impairment, previous head trauma or neurological disorders, history of moderate or severe learning difficulties, substance abuse or dependence, or an ECT course in the previous 6 months were excluded. No attempts were made to control for medication treatments. At the time of evaluation all but 1 patient were taking medication. Patients were predominantly taking mood stabilizers ( $n=60$ ), namely valproate ( $n=39$ ), lithium ( $n=24$ ), lamotrigine ( $n=20$ ), and carbamazepine ( $n=2$ ). Patients were also taking oral antipsychotics ( $n=41$ ), long-acting antipsychotics ( $n=4$ ), antidepressants ( $n=26$ ), benzodiazepines ( $n=21$ ), topiramate ( $n=6$ ), and gabapentin ( $n=2$ ). Fifteen patients were receiving mood stabilizers only, and 4 patients were medicated with antipsychotics only.

Fifty healthy individuals (16 men and 34 women) aged 17–61 recruited by word of mouth consisting of the patients' acquaintances and hospital personnel were included in the study as the control group. Controls were screened for personal and first-degree family axis I psychiatric disorders by personal interview and using the MINI. No attempt was made to match controls with patients for age, gender, or education. The local ethics

committee approved the study, and all participants provided informed consent prior to study entry.

#### 4. Assessment instruments

##### 4.1. Scale to Assess Unawareness of Mental Disorder (SUMD) – shortened version

The shortened version of SUMD (Amador et al., 1994) consists of 9 items grouped in two parts, and assesses awareness of mental disorder on several dimensions, using a 5-point Likert scale, varying from 1 (awareness) to 5 (no awareness); higher scores indicate less insight. The first part assesses awareness of mental disorder (range: 1–5), social consequences of illness (range: 1–5), and effects of medication (range: 1–5); the sum of these three dimensions consists of the overall illness awareness (range: 3–15). The second part (6 items) evaluates the level of symptom awareness and symptom attribution. The present study focused only on present state of awareness (i.e. at the time of testing), namely on current awareness of mental disorder, social consequences of illness, and effects of medication. SUMD ratings were made by the psychiatrist, who was blind to the neurocognitive test results.

##### 4.2. World Health Organization Quality of Life – Brief Form

QoL has been described as a multidimensional concept encompassing the physical, emotional, social, and spiritual well-being aspects (WHOQOL Group, 1998). The subjective well-being and QoL were assessed using the validated Portuguese version of the WHO Quality of Life Assessment – abbreviated version (WHOQOL–BREF–PT). The WHOQOL is a generic QoL instrument designed to be applicable to people living under different circumstances, conditions, and cultures (Fleck et al., 1993). We used the 26-item version (WHOQOL Group, 1998), WHOQOL–BREF for brevity, useful in clinical evaluations, and thought to be sensitive to health-related QoL status of people with long-term mental illness. WHOQOL–BREF provides unweighted measurement on four domains: physical, psychological, social relationships, and environment. The physical domain has questions related to daily activities, treatment compliance, pain and discomfort, sleep and rest, energy and fatigue. The psychological domain assesses positive and negative feelings, self-esteem, body image and physical appearance, personal beliefs, and attention. The social relationship domain is related to personal relationships, social support, and sexual activity. The environmental domain

explores physical security, financial resources, health and social care and their availability, opportunities for acquiring new information and skills, and participation in and opportunities for recreation and transport. Higher scores indicate better QoL.

##### 4.3. Assessment of cognitive function

The neurocognitive test battery was directed at the following cognitive domains: Attention and mental control (Wechsler Memory Scale [WMS]: Mental Tracking and the Digit Span); Perceptual-motor skills (Symbol Digit Modalities Test [SDMT], and Trail Making Test part A [TMT-A]); Executive functions (Stroop Colour Test [SCT], and Stroop Colour-Write Test [SCWT], Trail Making Test part B [TMT-B], and Hanoi Towers Test [ToH]); Verbal fluency (Controlled Oral Word Association [COWA]); Verbal abstraction (Wechsler Intelligence Scale for Adults – Revised [WAIS-R]: Comprehension and similarities sub-tests); Visuo-spatial attention (Bell's Test), and Memory function (WAIS-R: Information sub-test, WMS: Logical memory). These are well-established tests and detailed descriptions of them are found in standard texts (Strauss et al., 2006; Lezak et al., 2004). Neuropsychological assessment lasted from 1 to 3 h, and was carried out by the neuropsychologist, who was blind to the insight ratings.

#### 5. Statistical analysis

Bipolar patients were divided into two groups based on their overall illness awareness (SUMD total score); 25 (35.7%) patients (6 men and 19 women) were considered to have 'preserved' insight (score  $\leq 3$ ), whereas 45 (64.3%) patients (20 men and 25 women) failed to recognize one or more aspects of their mental disorder (score  $> 3$ ), and were considered to have 'impaired' insight. The three groups were compared regarding sociodemographic and clinical variables. Gender, age, educational level, and mood symptoms (HDRS and YMRS ratings) were used as covariates – ANCOVA – to compare the results on neuropsychological variables of the two patient groups, and controls. Dependant variables (QoL domains) were shown to be normally distributed. Relationships between insight, QoL, and clinical and neuropsychological variables in bipolar patients were calculated using Pearson's rank-order correlation coefficient, with a significance level of  $P < 0.05$ . The clinical and neurocognitive variables with significant correlations with each QoL domain were considered as possible explanatory variables in a multiple linear regression model (variances provided as adjusted

$R^2$ ), and entered simultaneously into multiple regression equations to determine the overall amount of variance in every QoL domain, together with the overall illness awareness. The criterion for entry into an equation was set at 0.03 to provide reasonable protection against type I error. Statistical analysis was carried out using the SPSS 15.0 (SPSS Inc., Chicago, Illinois).

## 6. Results

### 6.1. Sociodemographic, clinical, and neurocognitive characteristics of bipolar patients

We found no significant differences between the three groups regarding gender, age or educational level (Table 1). Patients with ‘impaired’ insight scored very low on measures of depressive (HDRS: mean=3.1, SD=2.52) and manic symptoms (YMRS: mean=1.2, SD=1.84), which were not significantly different from patients with ‘preserved’ insight (HDRS: mean=2.3, SD=2.66; YMRS: mean=0.8, SD=1.30), albeit both patient groups differed from controls ( $F=18.835$ ,  $P=0.000$ , and  $F=9.118$ ,  $P=0.000$  on depressive and manic symptoms, respectively). Patients with ‘preserved’ insight did not differ from patients with ‘impaired’ insight in terms of age of illness onset and duration, number of hospital

admissions, and number of manic or depressive episodes (Table 1).

Bipolar patients with ‘impaired’ insight performed significantly worse than controls on several neuropsychological tests, namely in mental tracking, the Digit Span, SDMT, TMT-A, TMT-B, SCT (perseverations), ToH, Comprehension and Similarities sub-tests of the WAIS-R, and in logical memory (Table 2). Patients with ‘impaired’ insight performed quantitatively worse than patients with ‘preserved’ insight on all neurocognitive tests, except on the Bells test, but the differences were not statistically significant (Table 2). Patients with ‘preserved’ insight performed worse than controls on all neurocognitive tests, but these differences were only statistically significant in six (Digit Span, SDMT, Comprehension and Similarities sub-tests of the WAIS-R, Bell’s test, and logical memory) out of sixteen tests (Table 2).

### 6.2. Insight and QoL of bipolar patients

Bipolar patients with ‘impaired’ insight demonstrated lower scores on all domains of the WHOQOL-BREF as compared to patients with ‘preserved’ insight, although the differences were not statistically significant (Table 1). Moreover, both patient groups demonstrated lower QoL scores as compared to healthy

Table 1  
Sociodemographic and clinical characteristics of bipolar patients with ‘impaired’ and ‘preserved’ insight, and healthy comparison subjects

Variables	1. Bipolar patients with ‘impaired’ insight ( $n=45$ )		2. Bipolar patients with ‘preserved’ insight ( $n=25$ )		3. Healthy subjects ( $n=50$ )		ANOVA		Scheffé post hoc test
	Mean	SD	Mean	SD	Mean	SD	$F$	$P$	
Gender (male:female) <sup>a</sup>	20:25	–	6:19	–	16:34	–	3.648	0.161	
Age (year)	38.96	10.15	36.32	12.36	34.76	11.10	1.728	0.182	
Educational level (year)	10.62	4.03	11.68	3.97	12.58	5.50	2.062	0.132	
QoL Physical domain	60.33	15.67	63.16	14.09	80.12	12.60	26.087	<0.000	1=2; 1<3; 2<3
QoL Psychological domain	54.16	15.36	61.52	16.60	76.84	9.71	34.125	<0.000	1=2; 1<3; 2<3
QoL Social domain	60.02	18.99	62.20	20.36	78.64	16.14	14.192	<0.000	1=2; 1<3; 2<3
QoL Environmental domain	57.49	12.97	64.60	13.26	67.96	9.83	9.472	<0.000	1=2; 1<3; 2=3
							$t$	$P$	
Age at onset (year) <sup>b</sup>	25.80	9.73	24.92	8.70	–	–	0.376	0.708	
Illness duration (year) <sup>b</sup>	12.62	8.25	11.44	8.95	–	–	0.557	0.579	
Number of admissions <sup>b</sup>	1.87	2.26	1.52	1.98	–	–	0.641	0.524	
Number of depressive episodes <sup>b</sup>	6.97	6.62	7.35	6.99	–	–	0.205	0.839	
Number of manic episodes <sup>b</sup>	5.69	5.58	4.52	4.44	–	–	0.830	0.410	
Awareness of a mental disorder <sup>b</sup>	1.69	0.70	1.00	0.00	–	–	57.641	<0.000	
Awareness of medication effects <sup>b</sup>	1.91	0.63	1.00	0.00	–	–	24.878	<0.000	
Awareness of social consequences <sup>b</sup>	2.20	0.66	1.00	0.00	–	–	48.571	<0.000	
Overall awareness <sup>b</sup>	5.80	1.49	3.00	0.00	–	–	48.571	<0.000	

Significance level  $P<0.05$ .

<sup>a</sup> Chi-square test.

<sup>b</sup> Student’s  $t$ -test.

Table 2

Neuropsychological variables of bipolar patients with ‘impaired’ and ‘preserved’ insight, and healthy comparison subjects (gender, age, educational level, HDRS, and YMRS as covariates)

Variables	1. Bipolar patients with ‘impaired’ insight (n=45)		2. Bipolar patients with ‘preserved’ insight (n=25)		3. Healthy subjects (n=50)		ANCOVA		
	Mean	SD	Mean	SD	Mean	SD	F	P	Scheffé post hoc test <sup>a</sup>
Mental control									
Mental tracking	5.71	2.46	6.76	1.86	7.21	1.77	3.199	<b>0.045</b>	1=2; 1<3; 2=3
Digit span (WMS)	8.27	2.07	8.72	1.34	10.14	1.90	5.212	<b>0.007</b>	1=2; 1<3; 2<3
Perceptual-motor skills									
SDMT	37.91	14.73	46.56	10.79	56.88	14.26	14.027	<0.000	1=2; 1<3; 2<3
TMT-A (sec)	55.40	32.37	50.16	25.49	35.38	12.83	5.030	<b>0.008</b>	1=2; 1<3; 2=3
Executive functions									
SCWT (sec)	61.91	18.01	58.48	18.02	56.59	8.92	0.891	0.413	
SCWT (perseverations)	0.51	1.25	0.36	0.95	0.12	0.39	2.087	0.129	
SCT (sec)	166.20	57.50	143.40	42.93	124.55	30.80	2.106	0.127	
SCT (perseverations)	6.31	8.84	3.64	3.48	2.47	2.81	3.830	<b>0.025</b>	1=2; 1<3; 2=3
TMT-B (sec)	190.36	139.71	127.20	96.26	84.48	36.50	5.729	<b>0.004</b>	1=2; 1<3; 2=3
ToH (moves)	22.37	9.49	17.16	8.18	12.37	6.91	10.782	<0.000	1=2; 1<3; 2=3
Verbal fluency									
COWA	15.44	5.08	17.20	5.48	18.52	4.48	2.304	0.105	
Verbal abstraction									
Comprehension (WAIS-R)	13.49	6.32	14.56	6.48	19.71	6.46	10.754	<0.000	1=2; 1<3; 2<3
Similarities (WAIS-R)	8.87	5.96	10.84	6.02	15.31	7.15	13.071	<0.000	1=2; 1<3; 2<3
Visuo-spatial attention									
Bell’s Test (omissions)	2.42	2.78	3.88	3.36	1.14	1.94	6.857	<b>0.002</b>	1=2; 1=3; 2<3
Memory function									
Information (WAIS-R)	17.58	5.40	19.24	5.29	20.41	5.46	1.041	0.356	
Logical memory (WMS) <sup>b</sup>	4.82	1.91	6.38	2.24	8.82	2.55	11.847	<0.000	1=2; 1<3; 2<3

Legend: COWA: Controlled Oral Word Association; SCT: Stroop Colour Test; SCWT: Stroop Colour-Write Test; SDMT: Symbol Digit Modalities Test; ToH: Hanoi Towers Test; TMT-A: Trail Making Test part A; TMT-B: Trail Making Test part B; WAIS-R: Wechsler Intelligence Scale for Adults – Revised; WMS: Wechsler Memory Scale.

The signs (>, <) indicate better or worse functioning and not actual scores on the tests.

<sup>a</sup> Significance level  $P<0.05$ .

<sup>b</sup> Bipolar patients with ‘impaired’ insight  $n=27$ , Bipolar patients with ‘preserved’ insight  $n=20$ , healthy subjects  $n=39$ .

controls, and these differences were statistically significant on the physical, psychological, and social domains; on the environmental domain, this difference was only statistically significant between patients with ‘impaired’ insight and healthy controls (Table 1).

Patients with ‘preserved’ insight had the minimum score on all the SUMD domains; patients with ‘impaired’ insight scored a little higher on all domains, specifically in the item related to awareness of having a disorder (mean=1.69, SD=0.7), on the awareness of the effects of medication (mean=1.91, SD=0.6), of the social consequences of the disorder (mean=2.20, SD=0.7), and on the overall degree of awareness (mean=5.80, SD=1.5). Interestingly, patients showed more impaired insight for the social consequences of the disorder, followed by the awareness of the medication effects and awareness of having a mental disorder (Table 1).

### 6.3. Insight and sociodemographic and clinical variables, and neurocognition

Bipolar patients’ age correlated positively with overall illness awareness ( $r=0.243$ ,  $P<0.05$ ), and with the awareness of the medication effects ( $r=0.281$ ,  $P<0.05$ ), indicating that older patients have significantly less insight in those dimensions.

The educational level of bipolar patients correlated negatively with the awareness of medication effects ( $r=-0.270$ ;  $P<0.05$ ), indicating that patients with higher education show significantly better insight in that dimension.

The presence of psychotic symptoms in the past correlated negatively with the awareness of having a mental disorder ( $r=-0.318$ ,  $P<0.01$ ), indicating that bipolar patients with past psychotic symptoms have significantly less insight in that dimension.

Table 3  
Significant Pearson's correlations between neuropsychological variables in bipolar I patients and overall illness awareness (SUMD)

Neurocognitive variable	SUMD dimension
	Overall awareness
Mental tracking	-0.230
SDMT	-0.389**
TMT-A (sec)	0.344**
TMT-B (sec)	0.400**
SCT (perseverations)	0.288*
ToH (moves)	0.292*
Similarities (WAIS-R)	-0.265**
Logical memory (WMS)	-0.408**

Legend: SCT: Stroop Colour Test; SDMT: Symbol Digit Modalities Test; ToH: Hanoi Towers Test; TMT-A: Trail Making Test part A; TMT-B: Trail Making Test part B; WAIS-R: Wechsler Intelligence Scale for Adults – Revised; WMS: Wechsler Memory Scale. Correlation significance level: \* $P < 0.05$ , \*\* $P < 0.01$  (two-tailed).

Manic symptoms were also positively associated with the awareness of having a mental disorder ( $r = 0.302$ ,  $P < 0.05$ ), indicating that patients with more manic symptoms possess significantly less insight in that dimension. However, the number of manic and or depressive episodes was not significantly correlated with any changes in insight.

Concerning overall illness awareness, we found a statistically significant correlation of seven out of sixteen neurocognitive tests, indicating that patients with worse cognitive performance on the SDMT, TMT-A, TMT-B, SCT (perseverations), ToH, Similarities sub-test of the WAIS-R, and in logical memory, have significantly less insight in that dimension (Table 3).

#### 6.4. Insight and QoL

In bipolar patients, the physical and social domains of QoL did not correlate significantly with any dimension of insight (Table 4); however the psychological domain of QoL was negatively associated with all insight dimensions, indicating that better insight is significantly associated with better self-reported QoL in that domain

(Table 4). The environmental domain of QoL was also negatively associated with all insight dimensions with the exception of the awareness of social consequences of the disorder, indicating that patients with better overall awareness, especially of a mental disorder, and of the medication effects presented a better self-reported QoL in the environmental domain (Table 4).

#### 6.5. Predictors of QoL in bipolar patients

A multiple regression model was created with the clinical and neurocognitive variables which were found to correlate with QoL domains, and with the overall illness awareness dimension. The clinical variables were entered in the first block of the model because previous research has uniformly supported the role of these variables in QoL, neurocognitive variables were entered in a second step, as there is less available evidence supporting the unique contribution of these variables to QoL, and lastly we entered overall illness awareness, because we wanted to investigate the role of illness awareness in predicting the four domains of QoL.

All domains of QoL were predicted by at least one clinical and one neurocognitive variable, except the social domain, which was better explained by clinical variables only. Overall illness awareness was a significant predictor of the psychological and environmental domains of QoL.

The best explanatory model of physical QoL was composed by age, educational level, depressive symptoms, and performance on the SCT, which accounted for 31.1% of physical QoL variance ( $R = 0.634$ , adj  $R^2 = 0.360$ ;  $F [4,43] = 9.631$ ,  $P = 0.000$ ). The psychological domain was predicted by depressive symptoms, awareness of social consequences, and scores on the Comprehension sub-test of the WAIS-R, which accounted for 36.0% of psychological QoL variance ( $R = 0.630$ , adj  $R^2 = 0.354$ ;  $F [3,43] = 9.411$ ,  $P = 0.000$ ). The social domain was predicted by scores on the comprehension sub-test of the WAIS-R, which accounted for 17.1% of the variance in social QoL ( $R = 0.432$ , adj  $R^2 = 0.171$ ;

Table 4  
Significant Pearson's correlations between WHOQOL-BREF domains and insight dimensions (SUMD) in bipolar I patients

	WHOQOL-BREF domains			
	Physical domain	Psychological domain	Social domain	Environmental domain
Awareness of mental disorder	-0.107	-0.303*	-0.096	-0.341**
Awareness of medication effects	-0.182	-0.250*	-0.068	-0.294*
Awareness of social consequences	-0.026	-0.286*	-0.025	-0.220
Overall awareness	-0.118	-0.328**	-0.071	-0.329**

Correlation significance level: \* $P < 0.05$ , \*\* $P < 0.01$  (two-tailed).

$F [1,53]=12.137, P=0.001$ ). Lastly, the best explanatory model for environmental domain of QoL was composed by educational level, depressive symptoms, and scores on the similarities sub-test of the WAIS-R, accounting for 35.9% of the variance ( $R=0.628$ , adj  $R^2 0.359$ ;  $F [3,51]=11.084, P=0.000$ ).

## 7. Discussion

The present study was designed to assess the influence of insight and neurocognitive function in subjective QoL in Bipolar patients. We found that bipolar subjects with ‘impaired insight’ reported similar subjective QoL and exhibited similar performance in a battery of prefrontal cognitive tasks as compared to patients with ‘preserved insight’. These results suggest that even those with impaired “awareness of mental disorder, awareness of medication status, and awareness of social consequences of the illness” are able to acknowledge and report lower QoL than healthy controls. This finding is important in the light of recent studies suggesting that impaired insight may question the validity of self-reported measures in individuals with BD (Ghaemi and Rosenquist, 2004; Burdick et al., 2005; Gazalle et al., 2007b). Gazalle et al. (2007b) investigated subjective QoL scores in bipolar I patients during mania, depression and remission, and found that acutely manic patients reported overall QoL rates similar to euthymic patients and healthy controls. The authors suggested that during mania subjective measures may be affected by lack of insight or unawareness of their own illness. This is in agreement with the present study where we found that manic symptoms did not correlated with ability to be aware of having a mental disorder. This indicates that patients with manic symptoms tend to have less insight into having a mental disorder. Accordingly, a two-year follow-up of bipolar I patients further supports that insight may deteriorate along with repeated manic but not depressive episodes (Yen et al., 2007).

Although the neurocognitive performance in patients with ‘impaired insight’ and patients with ‘preserved insight’ was not statistically different, one can appreciate that those with ‘impaired insight’ performed poorer than healthy controls in 10 out of the 16 tasks, while patients with ‘preserved insight’ performed poorly in 6 out of the 16 tasks. Consistently, in the correlation analysis we found that overall awareness scores significantly correlated with 7 neurocognitive tasks, suggesting that less overall insight may be associated with poorer prefrontal cognitive performance. This is in line with our recent study (Dias et al., 2008) and others (Young et al., 1998;

Varga et al., 2006) showing that poorer insight may be related to prefrontal dysfunction in individuals with BD. Here it is important to mention that the present study was performed in a well-characterized sample of euthymic bipolar patients, meaning that the power to differentiate prefrontal functioning between individuals with ‘impaired’ vs. ‘preserved’ insight under remission may have suffered from a “floor effect”. Although it has been suggested that impaired insight may be associated with decreased right dorsolateral prefrontal cortex volume in schizophrenia (Shad et al., 2004), cerebral correlates of insight in bipolar patients have not been investigated.

In the multiple regression models, physical, psychological and environmental domains of QoL were all predicted by the level of depressive symptoms. These results are in line with a recent study that compared QoL scores between bipolar patients that were currently depressed vs. those with subsyndromal depressive symptoms vs. patients in remission (Gazalle et al., 2006). In this latter study, depressive scores negatively correlated with all QoL domains and the authors observed a dose–response association between patients’ depressive state where remitted patients scored better than subsyndromal patients, followed by those currently depressed, in all QoL domains, except for social QoL. In fact, there is compelling evidence that the levels of depressive symptoms have a significant negative impact on QoL in bipolar patents during major depressive episodes (Russo et al., 1997; Vojta et al., 2001; Berlim et al., 2004; Yatham et al., 2004; Gazalle et al., 2006, 2007b) and here we report that this may be also true in euthymic subjects. In addition, our finding suggests that the treatment of subsyndromal symptoms in individuals in remission is not only important in decreasing the risk for future episodes, but it may positively affect subjects’ quality of life. The results of the present study should be interpreted in light of some limitations. The failure to differentiate the groups on depressive or manic symptoms may be due to an artifact of the cut off scores used rather than a reflection of the characteristics of the groups. However, it is also possible that the lack of differences may be due to the fact that we investigated individuals under remission. Given that a number of studies have suggested that both insight and QoL are substantially affected by the presence of manic and depressive symptoms, future studies addressing the interaction between insight, QoL and neurocognition in acute mania and acute bipolar depression would provide valuable information to this field. As previously reported (Gazalle et al., 2007b), there is no QoL scale developed specifically for the bipolar disorder population; thus it is possible that some aspects of QoL that may be particularly affected by bipolar illness may be missing.

Finally, cross-sectional studies can generate and test associative hypotheses only and cannot provide information of causality.

In conclusion we found that during remission, bipolar patients with ‘impaired’ insight report similar QoL scores and exhibit similar prefrontal cognitive performance as compared to patients with ‘preserved’ insight. The present study supports previous reports suggesting that the presence of manic symptoms may be a critical determinant in the clinical presentation of reduced insight in BD and highlights the importance of the treatment of subsyndromal symptoms.

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#### Conflict of interest

Dr. Frey and Dr. Vasco Dias declare no conflicts of interest. Dr. Sofia Brissos is a consultant for Janssen-Cilag Portugal.

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#### References

- Amador, X.F., David, A.S., 2004. *Insight and Psychosis: Awareness of Illness in Schizophrenia and Related Disorders*, 2nd ed. Oxford University Press, Oxford.
- Amador, X.F., Strauss, D.H., Yale, S.A., Gorman, J.M., 1991. Awareness of illness in schizophrenia. *Schizophr. Bull.* 17, 113–132.
- Amador, X.F., Strauss, D.H., Yale, S.A., Flaum, M.M., Endicott, J., Gorman, J.M., 1993. Assessment of insight in psychosis. *Am. J. Psychiatry* 150, 873–879.
- Amador, X.F., Flaum, M., Andreasen, N.C., Strauss, D.H., Yale, S.A., Clark, S.C., Gorman, J.M., 1994. Awareness of illness in schizophrenia and schizoaffective and mood disorders. *Arch. Gen. Psychiatry* 51, 826–836.
- American Psychiatric Association, 1994. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV*. Washington, D.C.
- Awad, A.G., Hogan, T.P., Voruganti, L.N., Heslegrave, R.J., 1995. Patients’ subjective experiences on antipsychotic medications: implications for outcome and quality of life. *Int. Clin. Psychopharmacol.* 10, 123–132.
- Bauer, M.S., Kirk, G.F., Gavin, C., Williford, W.O., 2001. Determinants of functional outcome and healthcare costs in bipolar disorder: a high-intensity follow-up study. *J. Affect. Disord.* 65, 231–241.
- Berlim, M.T., Pargendler, J., Caldieraro, M.A., Almeida, E.A., Fleck, M.P., Joiner, T.E., 2004. Quality of life in unipolar and bipolar depression: are there significant differences? *J. Nerv. Ment. Dis.* 192, 792–795.
- Brissos, S., Dias, V.V., Carita, A.I., Martinez-Arán, A., in press. Quality of life in bipolar type-I disorder and schizophrenia in remission: clinical and neurocognitive correlates. *Psychiatry Res.*
- Burdick, K.E., Endick, C.J., Goldberg, J.F., 2005. Assessing cognitive deficits in bipolar disorder: are self-reports valid? *Psychiatry Res.* 136, 43–50.
- Chand, P.K., Mattoo, S.K., Sharan, P., 2004. Quality of life and its correlates in patients with bipolar disorder stabilized on lithium prophylaxis. *Psychiatry Clin. Neurosci.* 58, 311–318.
- David, A., Buchanan, A., Reed, A., Almeida, O., 1992. The assessment of insight in psychosis. *Br. J. Psychiatry* 161, 599–602.
- Dias, V.V., Brissos, S., Carita, A.I., 2008. Clinical and neurocognitive correlates of insight in patients with bipolar I disorder in remission. *Acta Psychiatr. Scand.* 117, 28–34.
- Fleck, M.P., Louzada, S., Xavier, M., Chachamovich, E., Vieira, G., Santos, L., Pinzon, V., 1993. Application of the Portuguese version of the instrument for the assessment of quality of life of the World Health Organization (WHOQOL-100). *Rev. Saude Publica* 33, 198–205.
- Gazalle, F.K., Andreazza, A.C., Ceresér, K.M., Hallal, P.C., Santin, A., Kapczinski, F., 2005. Clinical impact of late diagnosis of bipolar disorder. *J. Affect. Disord.* 86, 313–316.
- Gazalle, F.K., Andreazza, A.C., Hallal, P.C., Kauer-Sant’anna, M., Ceresér, K.M., Soares, J.C., Santin, A., Kapczinski, F., 2006. Bipolar depression: the importance of being in remission. *Rev. Bras. Psiquiatr.* 28, 93–96.
- Gazalle, F.K., Hallal, P.C., Andreazza, A.C., Frey, B.N., Kauer-Sant’Anna, M., Weyne, F., da Costa, S.C., Santin, A., Kapczinski, F., 2007a. Manic symptoms and quality of life in bipolar disorder. *Psychiatry Res.* 153, 33–38.
- Gazalle, F.K., Frey, B.N., Hallal, P.C., Andreazza, A.C., Cunha, A.B., Santin, A., Kapczinski, F., 2007b. Mismatch between self-reported quality of life and functional assessment in acute mania: a matter of unawareness of illness? *J. Affect. Disord.* 103, 247–252.
- Ghaemi, S.N., Hebben, N., Stoll, A.L., Pope, H.G.J., 1996. Neuropsychological aspects of lack of insight in bipolar disorder: a preliminary report. *Psychiatry Res.* 65, 113–120.
- Ghaemi, S.N., Rosenquist, K.J., 2004. Is insight in mania state-dependent? A meta-analysis. *J. Nerv. Ment. Dis.* 192, 771–775.
- Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatr.* 23, 56–62.
- Kauer-Sant’Anna, M., Frey, B.N., Andreazza, A.C., Ceresér, K.M., Gazalle, F.K., Tramontina, J., da Costa, S.C., Santin, A., Kapczinski, F., 2007. Anxiety comorbidity and quality of life in bipolar disorder patients. *Can. J. Psychiatry* 52, 175–181.
- Leidy, N.K., Palmer, C., Murray, M., Robb, J., Revicki, D.A., 1998. Health-related quality of life assessment in euthymic and depressed patients with bipolar disorder. Psychometric performance of four self-report measures. *J. Affect. Disord.* 48, 207–214.
- Lezak, M.D., Howieson, D.B., Loring, D.W., Hannay, H.J., Fischer, J.S., 2004. *Neuropsychological Assessment*. Oxford University Press, Oxford.
- Lysaker, P., Bell, M., 1995. Work rehabilitation and improvements in insight in schizophrenia. *J. Nerv. Ment. Dis.* 183, 103–106.
- Michalak, E.E., Yatham, L.N., Wan, D.D.C., Lam, R.W., 2005. Perceived quality of life in patients with bipolar disorder. Does group psychoeducation have an impact? *Can. J. Psychiatry* 50, 95–100.

- Namjoshi, M.A., Buesching, D.P., 2001. A review of the health-related quality of life literature in bipolar disorder. *Qual. Life. Res.* 10, 105–115.
- Piccinni, A., Catena, M., Del Debbio, A., Marazziti, D., Monje, C., Schiavi, E., Mariotti, A., Bianchi, C., Palla, A., Roncaglia, I., Carlini, M., Pini, S., Dell’Osso, L., 2007. Health-related quality of life and functioning in remitted bipolar I outpatients. *Compr. Psychiatry* 48, 323–328.
- Robb, J.C., Cooke, R.G., Devins, G.M., Young, L.T., Joffe, R.T., 1997. Quality of life and lifestyle disruption in euthymic bipolar disorder. *Psychiatry Res.* 31, 509–517.
- Robb, J.C., Young, L.T., Cooke, R.G., Joffe, R.T., 1998. Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. *J. Affect. Disord.* 49, 189–193.
- Robinson, L.J., Thompson, J.M., Gallagher, P., Goswami, U., Young, A.H., Ferrier, I.N., Moore, P.B., 2006. A meta-analysis of cognitive deficits in euthymic patients with bipolar disorder. *J. Affect. Disord.* 93, 105–115.
- Russo, J., Roy-Byrne, P., Reeder, D., Alexander, M., Dwyer-O’Connor, E., Dagadakis, C., Ries, R., Patrick, D., 1997. Longitudinal assessment of quality of life in acute psychiatric inpatients: reliability and validity. *J. Nerv. Ment. Dis.* 185, 166–175.
- Shad, M.U., Mudassani, S., Sahni, S.D., Keshavan, M.S., 2004. Insight and prefrontal cortex in first-episode schizophrenia. *Neuroimage* 22, 1315–1320.
- Sheehan, D.V., Lecrubier, Y., 1994. Mini-International Neuropsychiatric Interview (MINI). Tampa, FL, University of South Florida, Institute for Research in Psychiatry; Paris, INSERM-Hopital de la Salpetriere.
- Sierra, P., Livianos, L., Rojo, L., 2005. Quality of life for patients with bipolar disorder: relationship with clinical and demographic variables. *Bipolar. Disord.* 7, 159–165.
- Strauss, E., Sherman, E., Spreen, O., 2006. *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary*, (3rd ed.). Oxford University Press, New York.
- Torres, I.J., Boudreau, V.G., Yatham, L.N., 2007. Neuropsychological functioning in euthymic bipolar disorder: a meta-analysis. *Acta Psychiatr. Scand.* 116, 17–26.
- Varga, M., Magnusson, A., Flekkoy, K., Ronneberg, U., Opjordsmoen, S., 2006. Insight, symptoms and neurocognition in bipolar I patients. *J. Affect. Disord.* 91, 1–9.
- Vojta, C., Kinosian, B., Glick, H., Altshuler, L., Bauer, M.S., 2001. Self-reported quality of life across mood states in bipolar disorder. *Compr. Psychiatry* 42, 190–195.
- Yatham, L.N., Lecrubier, Y., Fieve, R.R., Davis, K.H., Harris, S.D., Krishnan, A.A., 2004. Quality of life in patients with bipolar I depression: data from 920 patients. *Bipolar. Disord.* 6, 379–385.
- Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. *Br. J. Psychiatry* 133, 429–435.
- Young, D.A., Zakzanis, K.K., Bailey, C., Davila, R., Griese, J., Sartory, G., Thom, A., 1998. Further parameters of insight and neuropsychological deficit in schizophrenia and other chronic mental disease. *J. Nerv. Ment. Dis.* 186, 44–50.
- Yen, C.-F., Chung, L.-C., Chen, C.-S., 2002. Insight and neuropsychological functions in bipolar outpatients in remission. *J. Nerv. Ment. Dis.* 190, 713–715.
- Yen, C.F., Chen, C.S., Ko, C.H., Yen, J.Y., Huang, C.F., 2007. Changes in insight among patients with bipolar I disorder: a 2-year prospective study. *Bipolar. Disord.* 9, 238–242.
- WHOQOL Group, 1998. Development of the World Health Organization WHOQOL–BREF quality of life assessment. *Psychol. Med.* 28, 551–558.