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Title:

Predictors of psychosocial functioning in euthymic patients with bipolar disorder: a model selection approach

Running title: Predictors of functioning in bipolar disorder

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Abstract:

Background. Functional impairment is a major target in the treatment of bipolar disorder (BD), but the magnitude and type of functional difficulties differ across patients. Findings on predictors of overall functioning and specific functional areas are inconsistent. We aimed to characterize functional difficulties and identify factors associated with global functioning and individual domains in euthymic patients.

Methods. The Functional Assessment Short Test (FAST) was used to assess overall psychosocial functioning and specific functional domains in 80 euthymic participants with BD. Participants also completed a clinical interview and a cognitive assessment. Model selection with elastic net regression was performed to identify predictors of global functioning. We then examined the association of these predictors with individual functional domains using correlation.

Results. FAST scores indicated moderate or severe impairment for 54% of the sample, with occupational functioning showing the highest impairment rate. Elastic net regression selected a model with three variables (higher residual depressive symptoms, lower executive functioning, more perceived cognitive deficits) as predictors of overall functioning. No significant associations were found between these predictors. Depressive symptoms were associated with interpersonal relationships and leisure time, executive skills with occupational functioning, and perceived deficits with cognitive functioning.

Conclusions. Residual depressive symptoms were the strongest predictor of overall functioning which highlights the importance of assessing and targeting subthreshold symptoms for recovery. Executive difficulties were associated with functioning, particularly occupational skills, independently of depressive symptoms. Interventions targeting these difficulties, such as cognitive and functional remediation, may be key treatment options towards facilitating functional recovery.

Keywords: bipolar disorder; functioning; FAST; model selection; elastic net; residual symptoms; executive functioning; subjective complaints.

Introduction

Bipolar disorder (BD) is a chronic affective condition with significant impact on multiple areas of functioning, including work, family, and social life (Sanchez-Moreno et al., 2009). Functional difficulties often persist beyond the acute phases of the illness, while functional recovery is not always achieved after mood episodes (or achieved with a significant time-lag behind remission of mood symptoms) even for patients receiving adequate mood stabilization treatment (Vieta et al., 2018). An observational study following-up patients two years after treatment for an acute episode showed that although 64% had achieved clinical remission, only 34% had achieved functional recovery (Haro et al., 2011). This indicates a substantial gap between remission and recovery which has recently ignited research interest in assessment and treatment options for functional outcomes (Sanchez-Moreno, Martinez-Aran, & Vieta, 2017).

An important issue related to functional recovery is how to define and measure it in a standardized way (Harvey, 2006). Although several different tools have been used to assess psychosocial functioning, the Functional Assessment Short Test (FAST) is probably the first scale specifically examining difficulties experienced by patients with BD (Rosa et al., 2007) and has been recommended for clinical research in BD (Miskowiak et al., 2017). Although the original validation of the FAST established a single cut-off score to differentiate between impaired and non-impaired patients (Rosa et al., 2007), a recent study provided multiple severity thresholds and classified euthymic patients across different categories of functional impairment severity based on their FAST score: no impairment (44%), mild (15%), moderate (35%) or severe impairment (6%) in global functioning (Bonnin et al., 2018). This classification may be useful for assessing the effects of interventions targeting psychosocial functioning in more homogeneous patient subgroups, but these interventions could be more tailored towards specific therapeutic targets and potentially more effective if we had a better understanding of the factors contributing to functional impairment and delaying recovery. Informing tailored interventions could further benefit from exploring impairment in specific functional domains and the correlates of difficulties in these domains.

Depressive symptoms and cognitive deficits are the only variables consistently showing an association with functional outcomes in euthymic patients (Gitlin & Miklowitz, 2017). Residual depressive symptoms affect multiple functional domains, including occupational outcomes (Gilbert & Marwaha, 2013; O'Donnell et al., 2017) and poor quality of life (Bonnin et al., 2019). Several studies have suggested that cognition may also predict psychosocial functioning (Ehrminger et al., 2019; López-Villarreal et al., 2020), with verbal memory and executive functions found to be significantly associated with employment outcomes (Tse, Chan, Ng, & Yatham, 2014). Although the impact of these factors on functional outcomes is well-supported, more evidence is required on the relationship between these two variables in association with functioning. Studies have suggested a mediating role of cognition on the effect of residual depressive symptoms on functioning (Bonnin et al., 2014) or relative independence of mood symptoms (Roux et al., 2018).

Reviews also suggest that other factors contribute to functioning, including clinical course and illness severity characteristics (Léda-Rêgo, Bezerra-Filho, & Miranda-Scippa, 2020), but findings are inconsistent between studies, probably due to the variety of factors considered and the choice of analytic methods. Most studies select *a priori* certain candidate predictors without considering others or test multivariable linear models which creates multiple comparison problems and increases the risk of model overfitting (i.e., high variance, low predictive value). A potential solution is using advanced statistical procedures, such as regularized regression (Zou & Hastie, 2005), on a larger number of potential predictors in order to select factors to be further investigated, as these approaches allow

the inclusion of multiple predictors (e.g., sociodemographic, clinical, and cognitive variables) without the limitations of power and overfitting.

Aims of the study

This study will a) characterize functional difficulties in euthymic patients with bipolar disorder with reference to global functioning and specific functional domains of the FAST, and b) identify factors associated with the FAST total and different domain scores using a model selection approach. We anticipated replicating the well-documented association with residual depressive symptoms and cognition, as well as identifying further factors associated with psychosocial functioning.

Methods

Study design

This is a cross-sectional secondary analysis of baseline data (prior to randomization) from the Cognitive Remediation in Bipolar (CRiB) feasibility RCT which compared cognitive remediation to treatment-as-usual in patients with BD (Strawbridge et al., 2021). Written informed consent was obtained from all participants prior to inclusion. The trial was reviewed and approved by the City Road & Hampstead NHS Research Ethics Committee (reference 15/LO/1557).

Participants

The sample comprised 80 outpatients with a DSM-5 diagnosis of BD, recruited via primary and secondary care services, as well as community advertisement (online, public places, mental health organizations). Participants were aged between 18 and 65 years, with sufficient fluency in English. The subtype of BD and overall eligibility were confirmed using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998). Participants were free of acute mood symptoms for at least one month prior to inclusion. Remission at screening stage was defined using cut-off scores of ≤ 7 on the Hamilton Depression Rating Scale 17-item (HAM-D) (Hamilton, 1960) and Young Mania Rating Scale (YMRS) (Young, Biggs, Ziegler, & Meyer, 1978). Exclusion criteria included history of a neurological disorder, a personality disorder diagnosis, and abuse of or dependency on alcohol or illicit substances over the past six months.

Measures

Clinical and functional assessment

A structured interview was used to collect information on sociodemographic characteristics (e.g., age, gender, education) and illness-history variables (e.g., age of onset, BD subtype, illness duration, previous episodes, family history of affective disorders and history of psychosis). Current use of psychotropic medication was recorded for different classes (lithium, anticonvulsants, antipsychotics, antidepressants, and anxiolytics) using a binary variable (i.e., yes/no). Residual mood symptoms were assessed using the HAM-D for depression and the YMRS for (hypo)mania.

Psychosocial functioning was assessed using the Functional Assessment Short Test (FAST) (Rosa et al., 2007), a validated, interviewer-rated instrument designed for assessing daily-life difficulties. FAST has 24 items examining six functional domains (autonomy, occupation, cognition, financial issues, interpersonal relationships, leisure time) with higher scores representing greater levels of functional impairment. Each item is rated on a 4-point scale ranging from 0 (no difficulties) to 3 (severe

difficulties). The global functioning score is computed by adding all individual items and ranges from 0 to 72. Scores for specific functional domains are calculated in the same way.

Cognitive assessment

Participants completed a battery of cognitive tests in a standardized order administered by a trained psychologist. The test battery included tests assessing four cognitive domains:

- *Processing speed*, using the *Digit-symbol coding* and *Symbol search* from the Wechsler Adult Intelligence Scale 4th edition (Wechsler, 2014)
- *Attention and working memory*, using the *Digit span* (sum of forward, backward, and sequencing conditions) from the Wechsler Adult Intelligence Scale 4th edition (Wechsler, 2014)
- *Verbal learning and memory*, using the *Verbal paired associates I* (VPA1) and the *Verbal paired associates II* (VPA2) from the Wechsler Memory Scale 4th edition (Wechsler, 2009)
- *Executive functioning*, using the *Hotel test* (Manly, Hawkins, Evans, Woldt, & Robertson, 2002), the *Matrix reasoning* subtest from the Wechsler Abbreviated Scale of Intelligence 2nd Edition (Dumont, Willis, Veizel, & Zibulsky, 2014), and the *FAS letter fluency* from the Delis-Kaplan Executive Function System (Delis, 2001)

The self-report *Perceived Deficits Questionnaire* (PDQ) (Sullivan, Edgley, & Dehoux, 1990) examined subjective cognitive complaints, providing an overall score for perceived difficulties in attention, memory, planning and organization.

Statistical analysis

Analyses were conducted using SPSS (version 25; IBM, New York), the Amos SPSS extension (version 25; IBM, New York), and R software (version 3.6, www.r-project.org). All variables were checked for normality of distributions using the Shapiro-Wilk test and log transformation was applied where necessary. Statistical significance was set at $p < 0.05$ (two-tailed) for all tests.

Standardizing cognitive variables

Raw scores were transformed to age- and education-corrected standardized scores (z scores; $Mean = 0$, $SD = 1$) based on the normative data provided by the test manuals and test scores were reversed if necessary, so that lower scores indicate poorer performance. Composite scores were computed for each of the four cognitive domains by averaging the z scores of the individual tests, and for global cognition by averaging the domain composite scores.

Characterizing functional difficulties

Participants were classified in two ways, based on their FAST total score and individual domain scores:

1. Global functional impairment (Bonnín et al., 2018): scores of 11 or lower representing no functional impairment; scores from 12 to 20 indicating mild impairment; scores from 21 to 40 describing moderate impairment, while scores above 40 reflecting severe impairment.
2. Impairment in individual functional domains was calculated using recommended cut-offs for each FAST subscale (Rosa et al., 2007): scores > 1 in autonomy; > 1 in occupation; > 2 in cognition; > 1 in financial issues; > 3 in interpersonal relationships; and > 3 in leisure time.

Identifying predictors of functioning

We conducted an elastic net regression using the GLMNET package in R (Friedman, Hastie, & Tibshirani, 2010) which permitted consideration of multiple potential predictors in the same model (Supplementary Table 1). Elastic net is a hybrid shrinkage method combining two regularized regression approaches, the LASSO and the Ridge regression, thus allowing variable selection and coefficient shrinking (Zou & Hastie, 2005). Potential predictors were entered in the model with FAST total score as the outcome. A repeated 10-fold cross-validation of elastic net was carried out to identify the values of the tuning parameters *alpha* (type of shrinkage) and *lambda* (amount of shrinkage) minimizing the mean squared prediction error (*MSE*) and providing a stable model with reduced risk of over-fitting (Friedman et al., 2010). The final model shrank predictor coefficients and selected only variables with penalized coefficients not equal to zero. To evaluate whether and to what extent variables selected by the elastic net regression were associated with the different subscales of the FAST we used Pearson's correlation. The level of significance was adjusted to account for multiple correlations (corrected *alpha* = 0.008).

Variables retained by the elastic net regression were further investigated in a path model to examine whether the association of these factors with functioning is independent or secondary to others. Path analysis is an extension of linear regression allowing the modelling of multiple variables simultaneously acting as predictors and outcomes (Streiner, 2005). The path analysis was performed using Amos software version 25 with maximum likelihood estimation method. Regarding power considerations, an adequate sample size for path analysis requires at least 15 participants per free parameter in the model for unbiased estimation of path coefficients and standard errors (Bentler & Chou, 1987; Kline, 2015). This allowed the estimation of up to five parameters. Model fit was evaluated with commonly used statistics and recommended cut-offs for good fit (Hooper, 2008): the chi-square statistic for the entire model ($p > 0.05$), the Comparative Fit Index (CFI; ≥ 0.90), the Goodness of Fit Index (GFI; ≥ 0.95), the Root Mean Square Error of Approximation (RMSEA; < 0.08), and the Standardized Root Mean Square Residual (SRMR; < 0.08). The model allowed the residual variances of cognitive variables to be correlated. Age and education were included as covariates.

Results

Sample characteristics

Eighty euthymic participants were included in this study. Sample characteristics, cognitive and FAST scores are reported in Table 1. Clinical variables, cognitive tests and the FAST had no missing data.

-- Table 1 around here --

Functional difficulties

Rates of functional impairment based on the FAST scores are presented in Figure 1 for global functioning and individual domains. Using pre-selected cut-offs for global functioning, only 15% presented without any impairment and 54% experienced at least moderate functional impairment.

-- Figure 1 around here --

For individual domains, most participants had problems with occupational functioning (94%) which is further supported by employment rates within the sample: 54% were not currently working, 24% were working part-time, and 22% full-time (including full-time education; Table 1). In the six months prior to study participation, almost half (43%) of those in full- or part-time employment had to take at least

two weeks off due to health problems. Cognitive functioning showed a comparably high impairment rate (88%).

Predictors of functioning

The optimal cross-validated model retained three variables associated with functional difficulties on the FAST: higher residual depressive symptoms (HAMD), more perceived cognitive complaints (PDQ) and lower performance in executive functioning ($\alpha = 0.61$, $\lambda = 3.59$, minimum $MSE = 79.77$; Supplementary Table 2).

For the FAST subscales, autonomy and financial issues were not correlated with any predictors after adjusting for multiple correlations (Table 2). Depressive symptoms were significantly correlated with interpersonal relationships and leisure activities. Executive skills were only correlated with occupational, while subjective cognitive complaints only with cognitive functioning.

-- Table 2 around here --

A path analysis was conducted to assess whether cognitive variables (executive skills and subjective cognitive complaints) were independently associated with functioning or secondary to residual depressive symptoms. The examined model showed a good fit to the data: chi-square was not significant [$\chi^2(3) = 3.28$, $p = 0.35$], the CFI and GFI indices had respective values of 0.97 and 0.98, while the RMSEA and SRMR were both lower than 0.08 (Supplementary Table 3).

Standardized path coefficients are presented in Figure 2. All predictors were significantly associated with the FAST total score and the model accounted for 38% of the FAST variance. Higher residual depressive symptoms (HAMD score; $\beta = 0.43$) and more perceived deficits (PDQ score; $\beta = 0.22$) were associated with increased functional difficulties. Poorer executive skills were associated with poorer functioning ($\beta = -0.30$). HAMD was not significantly associated with subjective complaints or executive skills, indicating that cognitive variables did not mediate the effect of residual symptoms on the FAST, but were independently associated with functioning (details in Supplementary Table 4). Executive skills and perceived deficits were also not correlated ($r = -0.13$, $p > 0.2$).

-- Figure 2 around here --

Discussion

This study characterized functional difficulties in euthymic people with BD and examined the factors associated with psychosocial functioning using a model selection approach. More than half of the sample presented with moderate or severe functional difficulties, with occupational and cognitive functioning showing the greatest impairment rates. Elastic net regression selected residual depressive symptoms (HAMD), higher subjective cognitive complaints (PDQ), and poorer performance in executive functioning as predictors of greater functional difficulties. Each of these variables were associated with different functional domains. A *post-hoc* path analysis indicated that perceived cognitive deficits and poor executive skills might account for a proportion of the variation in functioning independently of residual depressive symptoms. In total, this model explained almost 40% of the FAST variance. Factors associated with functioning may represent therapeutic targets for interventions attempting to tackle functional difficulties.

What is the profile of functional difficulties?

Impairment rates in our cohort replicated previous findings for moderate and severe impairment categories (Bonnín et al., 2018), but we detected a substantially higher rate for mild impairment and a threefold lower rate for non-impaired patients. Our cohort reported an average FAST score of 22, indicating moderate functional difficulties for patients not suffering from acute mood symptoms. This provides support to the notion that remission of acute clinical symptoms does not necessarily translate into functional recovery or improved well-being, and that therapeutic interventions targeting functional difficulties are imperative to enhance these outcomes (Bonnín et al., 2019).

In line with meta-analytic evidence, the individual domains presenting the highest impairment rates were occupational and cognitive functioning (Léda-Rêgo et al., 2020). To some extent, this is not surprising for the occupational domain given that a substantial proportion of the sample was unemployed at study entry. However, unemployment (54%) did not fully account for the extent of impairment (94%) observed in this domain, suggesting that even employed participants may face significant occupational difficulties. Likewise, increased impairment rates in certain domains indicate that even patients with a FAST total score corresponding to no or mild impairments in global functioning may experience significant domain-specific difficulties, as previously suggested for the occupational domain (Solé et al., 2018). Similar to that study, leisure activities and financial difficulties were the least affected domains across our sample. Performance in these domains may be highly dependent on mood state, with difficulties presenting during acute or episodic phases (e.g., excessive spending during mania or lack of interest in activities during depression).

Which are the factors associated with overall functioning and specific functional difficulties?

Residual depressive symptoms was the factor most strongly associated with overall functional difficulties which replicates previous evidence pointing to residual symptoms as the strongest contributing factor of functional impairment during inter-episodic or euthymic periods (Samalin, de Chazeron, Vieta, Bellivier, & Llorca, 2016) and longitudinal studies showing that clinical or subclinical depressive symptoms are the primary predictors of poor functioning (Demmo et al., 2018; Godin et al., 2020). This association was detected despite the conservative criteria for euthymia employed in this study and the low mean HAMD score indicating that even subsyndromal depressive symptoms may contribute to functional difficulties for a substantial proportion of patients. In line with previous evidence (Samalin et al., 2016), residual depressive symptoms were associated with the interpersonal and leisure domains. These FAST domains evaluate the patient's ability to participate in and enjoy social activities or interests which taps into constructs also assessed by depression scales. This might partially explain the observed association. Targeting subthreshold symptoms in remitted patients may foster improvements in both overall functioning and specific functional difficulties.

Executive functioning was also identified as a predictor which highlights the importance of executive skills for functional recovery and the potential of interventions addressing these deficits to facilitate functional improvement. Patients with lower executive skills have been previously shown to have poor functional outcomes (O'Donnell et al., 2017; Roux et al., 2018). Importantly, occupational functioning was the FAST subscale correlated with executive skills. A previous meta-analysis also supported the role of executive functioning as a predictor of favorable employment outcomes, even stronger than depressive symptoms (Tse et al., 2014). However, unlike this meta-analysis and other studies (Bonnin et al., 2014; Roux et al., 2018), we did not detect a significant association between psychosocial functioning and verbal memory, even though this was the most impaired domain in our cohort. This was an unexpected finding and it is possible that this discrepancy was due to differences in the verbal memory measures.

Subjective cognitive complaints have been extensively explored in relation to objective cognitive measures but have received limited attention as a potential predictor of psychosocial functioning. Recent findings support a significant association between cognitive complaints and functional outcomes (Luo, Zhu, Lu, Zong, & Lin, 2020; L. Samalin et al., 2017). Our study builds on these findings suggesting that perceived cognitive deficits are significantly associated with FAST scores even when accounting for the effect of objective cognitive measures. Given the weak association between objective cognitive measures and subjective cognitive complaints (Jensen et al., 2015), these two variables might represent independent sources of the FAST variation. It is also notable that cognitive complaints (PDQ score) was correlated with the FAST cognitive subscale. Cognitive difficulties in the context of daily-life activities are possibly more accurately reflected by self-report cognitive measures compared to objectives one.

The lack of a significant association between residual depressive symptoms and both executive skills and perceived deficits demonstrates the independence of these variables from clinical symptoms as predictors of functioning. Although a mediating effect of cognition on the relationship between depressive symptoms and functioning might be apparent for patients experiencing more severe or persistent symptoms (John et al., 2019), our findings do not support this mediating role in euthymic patients. This is consistent with previous evidence (Roux et al., 2018) and further supported by our findings for individual functional domains. Residual depressive symptoms were correlated with difficulties in interpersonal relationships and leisure activities, while executive skills and subjective complaints were correlated with occupational and cognitive functioning, respectively. The independence of executive skills and perceived deficits from mood symptoms possibly arises because these variables contribute to different areas of functioning.

Limitations

Although our sample consisted of euthymic participants, these people showed interest in taking part in a cognitive remediation trial which may introduce a self-selection bias, so our functional impairment rates might have been under- or over-estimated. Accurate estimation is further limited by the relatively small sample size. However, our sample was comparable to previous studies estimating functional impairment in euthymic patients (Rosa et al., 2007). Although participants currently abusing or dependent on alcohol or illicit substances were excluded from the study, our analysis could not control for the potentially confounding effect of past alcohol or substance use.

It would be useful to examine factors associated with psychosocial functioning within the different severity categories (no impairment, mild, moderate, severe impairment). Our sample was not powered for this subgroup analysis, but it represents an interesting perspective for future research. The cross-sectional analysis hampers the interpretation of our findings in terms of causality and the direction of the association between identified predictors and functioning. Variables not considered in this study may also have an effect on functioning, for example sleep disturbances (Samalin et al., 2017), emotional processing (Aparicio et al., 2017), impulsivity (Jiménez et al., 2012) or psychiatric comorbidities (Cotrena, Damiani Branco, Milman Shansis, & Paz Fonseca, 2020). Finally, our analysis did not control for medication adherence as a factor potentially affecting residual symptoms, cognitive variables and psychosocial functioning.

What are the clinical implications?

Modifying factors contributing to functioning may improve functional outcomes. Patients who achieve clinical remission may still experience residual symptoms and assessing the magnitude and type of these symptoms might be challenging using conventional depression scales. Developing and

implementing specific tools for subthreshold mood symptoms might be required (Romera et al., 2013). A large observational study monitoring patients with BD for two years found that improvement in global functioning during the follow-up period was associated with a reduction of residual mood symptoms, as well as with reduced comorbidities, improved sleep and better medication adherence, which might represent further intervention targets to improve functioning (Henry et al., 2017). Previous research also suggests that using psychological therapies, such as mindfulness-based interventions, in conjunction to pharmacotherapy may both alleviate these residual symptoms and facilitate functional recovery for remitted patients (Bojic & Becerra, 2017).

Psychological interventions targeting functional outcomes have shown promising results, with functional remediation, an intervention focusing on cognitive skills and strategies useful for daily-life activities, demonstrating significant benefits even in patients with subsyndromal symptomatology (Sanchez-Moreno et al., 2017; Torrent et al., 2013). Cognitive remediation is another intervention targeting functional recovery through cognitive improvement for which recent evidence suggest significant benefits in functioning (Strawbridge et al., 2021). Our findings point to the significance of executive skills both for general functioning and specifically for the occupational domain. Emphasizing the improvement of these skills may increase the benefits derived from these interventions. Subjective cognitive complaints may be an important additional component for psychological interventions. Findings from people with schizophrenia show that considering subjective cognitive difficulties is important for good therapeutic engagement which in turn may improve therapeutic outcomes (Cella, Swan, Medin, Reeder, & Wykes, 2014).

Finally, occupational functioning was the domain most strongly contributing to the FAST total score and showed the highest impairment rate. Previous research highlights the importance of employment for the well-being of people with mental illness (Eklund, Hansson, & Ahlqvist, 2004). Improvement of occupational skills (e.g., identifying job opportunities, preparing for interview, managing time) may benefit euthymic patients across severity categories. Hence, remediation programmes should consider integrating or further emphasizing these components to tackle relevant difficulties. Combining psychological interventions with supported employment programmes may be a successful treatment approach for long-term improvement in work outcomes (McGurk et al., 2015).

Conclusions

A substantial proportion of euthymic participants present with moderate or severe functional difficulties, primarily in occupational functioning. Higher residual depressive symptoms and subjective cognitive complaints and poorer executive skills may be central factors contributing to greater functional impairments. For euthymic patients with BD, cognitive variables possibly represent independent predictors of functioning. Interventions aiming to improve functional and daily-life outcomes should consider these factors. Patients may particularly benefit from adaptations to address poor occupational skills or from combination strategies to enhance employment outcomes.

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Tables

Table 1. Baseline characteristics of the sample (N = 80).

Characteristics	Mean	SD	Range
<i>Sociodemographic/clinical</i>			
Age	42.2	12.8	19 – 65
Education (in years)	15.9	2.1	11 – 21
Age BD diagnosed	30.9	11.7	16 – 61
Diagnosis duration (in years)	10.8	8.9	0 – 34
Duration of untreated illness (in years)	10.7	9.6	0 – 44
Number of depressive episodes	11.8	11.9	1 – 48
Number of (hypo)manic episodes	8.5	7.2	1 – 32
Number of hospitalizations	2.4	22.9	0 – 14
Current euthymia (in months)	13.8	24.6	1 – 168
Number of psychotropic medications	2.4	1.5	0 – 7
Psychological therapies undertaken	1.9	1.54	0 – 8
HAMD	3.8	2.6	0 – 7
YMRS	2.3	2.4	0 – 7
<i>Cognitive</i>			
Processing speed	-0.14	0.7	-1.67/1.50
Working memory	-0.09	0.7	-1.33/1.67
Verbal learning and memory	-0.26	1.1	-2.50/1.67
Executive functioning	-0.22	0.7	-1.78/1.22
Global cognitive composite	-0.17	0.6	-1.56/1.17
Subjective cognitive complaints (PDQ)	35.9	13.9	2 – 68
<i>Functional</i>			
FAST total	21.8	9.8	3 – 43
FAST autonomy	2.4	2.5	0 – 11
FAST occupational	7.5	4.4	0 – 15
FAST cognitive	5.7	2.6	0 – 12
FAST financial	0.9	1.8	0 – 4
FAST interpersonal	4.1	3.2	0 – 17
FAST leisure	1.3	1.4	0 – 5
	n	%	
<i>Sociodemographic/clinical</i>			
Gender (female)	57	71	
Employed	37	46	
Full-time	19	24	
Part-time	18	22	
BD type (type I)	53	66	
Family history of affective disorders	43	54	
History of psychosis	52	65	
<i>Current medications</i>			
Mood stabilizers	60	75	
Antipsychotics	59	74	
Antidepressants	39	49	
Anxiolytics	13	16	

Notes: BD: Bipolar Disorder; FAST: Functional Assessment Short Test; HAMD: Hamilton Depression Rating Scale 17 items; PDQ: Perceived deficits questionnaire; YMRS: Young Mania Rating Scale.

Table 2. Pearson correlations between functional domains and predictors of functioning (N = 80).

FAST subscales	HAMD		Executive skills		PDQ	
	r	p	r	p	r	p
Autonomy	0.30	0.01	-0.08	> 0.2	0.21	0.06
Occupational functioning	0.25	0.03	-0.43	< 0.001	0.24	0.03
Cognitive functioning	0.30	0.01	-0.27	0.02	0.49	< 0.001
Financial issues	0.20	0.08	-0.02	> 0.2	-0.01	> 0.2
Interpersonal relationships	0.41	< 0.001	-0.08	> 0.2	0.03	> 0.2
Leisure activities	0.35	0.002	-0.21	0.07	0.23	0.05

Notes: FAST: Functional Assessment Short Test; HAMD: Hamilton depression rating scale; PDQ: Perceived Deficits Questionnaire. Significant correlation coefficients **in bold**, after adjusting the significance level for multiple comparisons (corrected $\alpha = 0.008$).

Figure legend

Figure 1. Functional impairment rates according to FAST scores for global functioning (A) and individual functional domains (B).

Figure 2. Path model for significant FAST predictors.

Rectangles denote observed variables, arrows indicate regression paths, and values represent the standardized path coefficients. Squared multiple correlation values (R^2) are reported for dependent variables. HAMD: Hamilton depression scale; PDQ: Perceived deficits questionnaire; FAST: Functioning assessment short test. * $p < 0.05$, ** $p < 0.001$

Figure 1

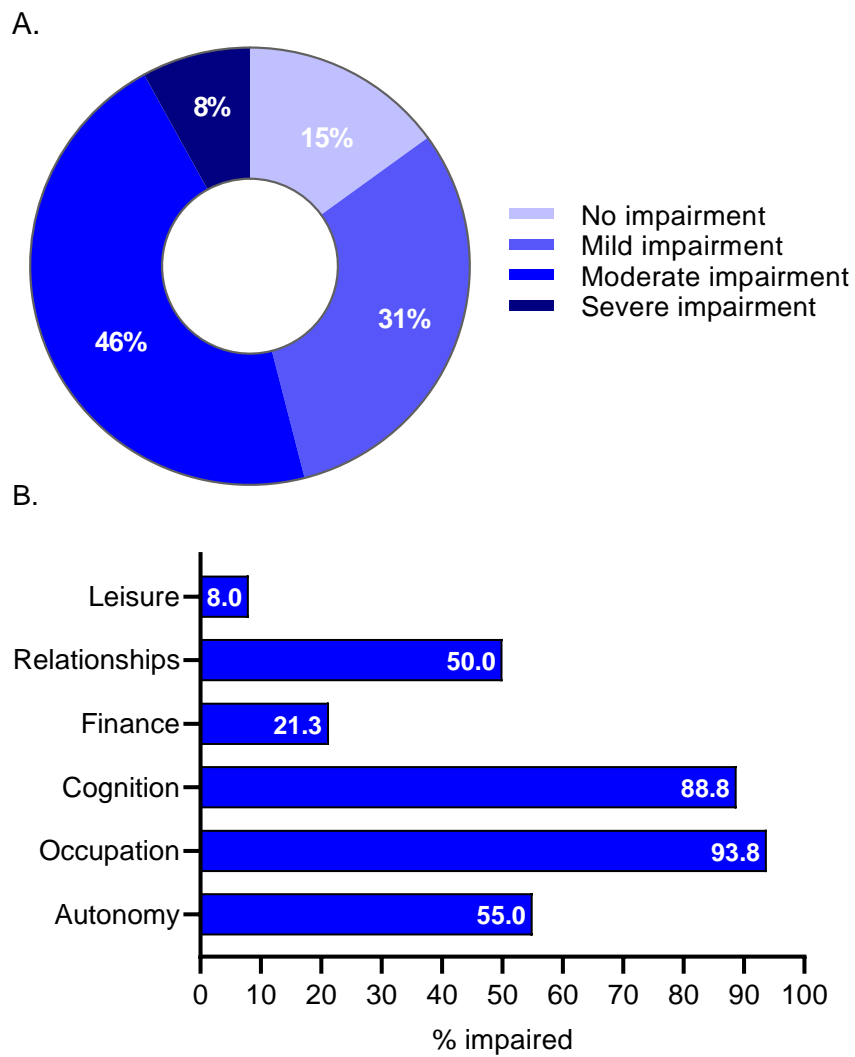


Figure 2

