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# Quality of life, functioning and cognition in bipolar disorder and major depression: A latent profile analysis



Charles Cotrena<sup>a</sup>, Laura Damiani Branco<sup>a,\*</sup>, Renata Kochhann<sup>a</sup>, Flávio Milman Shansis<sup>b</sup>, Rochele Paz Fonseca<sup>a,\*</sup>

<sup>a</sup> Department of Psychology, Pontifical Catholic University of Rio Grande do Sul, Brazil

<sup>b</sup> Program for the Study and Research of Mood Disorders (PROPESTH), São Pedro Psychiatric Hospital, Brazil

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## ABSTRACT

This study aimed to identify profiles of functioning and quality of life (QOL) in depression (MDD), bipolar disorder (BD) and healthy adults, as well as the clinical, demographic and cognitive variables associated with each of these profiles. Participants completed the WHODAS 2.0 and WHOQOL-BREF, which were submitted to latent profile analysis. The four cluster solution provided the best fit for our data. Cluster 1 consisted mostly of healthy adults, and had the highest functioning and QOL. Clusters 2 contained older patients with subclinical depressive symptoms and psychiatric comorbidities, whose impairments in QOL and functioning were associated with mood symptoms and several cognitive abilities. Patients with MDD, BDI or BDII with mild to moderate depression, such as those in cluster 3, may benefit more significantly from interventions in cognitive flexibility, inhibition, planning, and sustained attention. Lastly, patients with mood disorders and clinically significant levels of depression, as well as a history of suicide attempts, like those in cluster 4, may benefit from interventions aimed at working memory, inhibitory control, and cognitive flexibility; that is, the three core executive functions. These findings should be further investigated, and used to guide treatments for patients with mood disorders and different patterns of functional impairment.

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## 1. Introduction

The World Health Organization (WHO) defines quality of life as a state of physical, mental and social wellbeing, according to self-perceptions of one's position in life in the context of the culture and value system in which they live, and in relation to their goals, expectations, standards and concerns (The WHOQOL Group, 1995). This construct can be divided into four aspects, which correspond to physical health, psychological functioning, social relationships, and environment (Fleck et al., 2000). Impairments in quality of life can be caused by general medical conditions (Bakker et al., 2013), neurological disorders (Haley et al., 2011), or mental health issues such as obsessive-compulsive disorder (Kugler et al., 2013), schizophrenia (Ojeda et al., 2012), bipolar disorder (BD) (Rosa et al., 2010) and major depressive disorder (MDD) (IsHak et al., 2011). In the latter case, quality of life has proved so relevant for the prevention of mood episodes, that some authors have recommended

its use as a measure of treatment efficacy (IsHak et al., 2011). This observation is bolstered by preliminary evidence of the association between quality of life and cognitive impairment (Mackala et al., 2014), a major outcome variable in the study of mood disorders.

Quality of life, which refers to *perceived* well-being in different areas of life, is often evaluated in combination with individual functioning, which taps into *actual* performance on everyday tasks. Functioning is also affected in patients with mood disorders such as MDD and BD, both of which are associated with high rates of functional disability and psychosocial difficulties (Hammar and Ardal, 2009; Judd et al., 2014). According to the literature, functional impairment is strongly associated with cognitive deficits, both in general medical conditions (Alosco et al., 2013) and psychiatric disorders such as BD and MDD (Malhi et al., 2007).

Despite the known impact of these conditions on patient functioning and occupational productivity, and the association between these factors and cognitive impairment, few studies have evaluated the association between functioning, quality of life and cognitive deficits in patients with mood disorders (Evans et al., 2013). The existing literature on the topic has produced contradicting results. While some studies identify a significant relationship between these factors (Godard et al., 2011), others find little to no association between them (Baune et al., 2010).

\* Corresponding author at: Department of Psychology, Pontifical Catholic University of Rio Grande do Sul, Av. Ipiranga, 6681, building 11, rm 932, Porto Alegre 90619-900, Rio Grande do Sul, Brazil. Tel./fax: +55 51 3320 3500.

E-mail addresses: [lauradbranco@gmail.com](mailto:lauradbranco@gmail.com) (L.D. Branco), [rochele.fonseca@gmail.com](mailto:rochele.fonseca@gmail.com) (R.P. Fonseca).

Nevertheless, several programs have been developed to promote improvements in quality of life and functioning through cognitive stimulation and training (Lee et al., 2013; Vieta et al., 2014). While some have successfully achieved their goal, improving the cognitive functioning as well as the daily life of patients with mood disorders (Torrent et al., 2013), others have fallen short of this goal, and found that cognitive improvements failed to generalize to other aspects of patients' lives (Naismith et al., 2010). Given the sensitivity of cognitive training to individual differences, this is not a surprising finding (Jaeggi et al., 2014). The transfer of cognitive gains to daily life may be facilitated by a more precise description of associations between different aspects of cognitive function and domains of quality of life and disability. This information may help identify cognitive functions which relate more strongly to daily functioning and would therefore be more likely to be generalized, as well as maximize improvements in real-life settings in addition to formal testing. Given the aforementioned absence of a consensus in the literature as to the association between cognition and functioning in mood disorder, additional studies on the topic are required to settle this issue and allow for the development of more adequate interventions for these populations, which address both cognitive impairments and their functional consequences (Bowie et al., 2013).

One of the reasons why such relationships have been so difficult to define may be the existence of individual variability in the extent to which cognition, disability and quality of life are related in patients with mood disorders. Similar intradiagnostic variability has been identified with regards to cognitive profiles, and to this end, statistical clustering approaches have been successfully used to delineate subprofiles of cognitive functioning within populations with MDD (Hermens et al., 2011) and BD (Martino et al., 2014). Although this approach has not been applied to disability and quality of life, it is reasonable to expect that, if distinct cognitive profiles exist within populations with mood disorders, there may also be some within-sample variability regarding the extent to which cognition, disability and quality of life are related.

Therefore, the goal of the present study was to identify profiles of quality of life and functioning in patients with MDD, BDI and BDII, assessing the relationship between these factors and individual differences in clinical, demographic and cognitive features. In the process, we hope to address current knowledge gaps regarding quality of life and functioning in BD, and the association between these factors and specific subcomponents of attention and the executive functions in patients with mood disorders.

## 2. Methods

### 2.1. Subjects

The sample consisted of 142 participants, of whom 28 had been diagnosed with BDI, 21 with BDII, and 29 with MDD. The remaining 64 subjects were control participants with no mood disorders.

Patients were consecutively recruited from the mood disorders outpatient unit of a psychiatric hospital, a university teaching clinic, and private practice, from September 2013 to October 2014. Control participants were recruited by convenience from work and university settings, as well as the community at large.

The sample included native Brazilians of both genders aged between 18 and 67 years, with 1–31 years of formal education. Participants with uncorrected sensory impairments which would interfere with task performance, a history of neurological conditions, and/or who were currently pregnant or lactating were excluded from the sample. Additionally, patients with psychotic symptoms at the time of testing or who reported substance abuse within the previous month were excluded from the clinical sample. The control group was selected using the same criteria, and was screened for mood disorders, cognitive impairment and intellectual disability.

### 2.2. Procedures

All participants provided written consent for participation, and the present study was approved by the research ethics committee of the university where it was performed. Participants were assessed individually, and evaluated based on DSM-5 criteria (American Psychiatric Association, 2013). Diagnoses were established by consensus with a clinical psychologist with expertise in mood disorders. Participants underwent three assessment sessions lasting approximately one and a half hours each. Individuals were first administered a sociocultural and health questionnaire adapted from Fonseca et al. (2012) to screen for inclusion and exclusion criteria, and evaluate socioeconomic status (SES) and the frequency of reading and writing habits (FRWH). SES was evaluated based on the Brazil Classification Criteria (Associação Brasileira de Empresas de Pesquisa (ABEP), 2008), which provides scores ranging from 0 to 46, while the FRWH was assessed using a previously described inventory (Cotrena et al., 2015; Pawlowski et al., 2012) which verifies the weekly frequency with which respondents read and write different types of materials, and yields a total score ranging from 0 to 28.

All participants also completed a comprehensive neuropsychological assessment battery, whose tests were administered in a pseudo-randomized order to avoid the influence of one test over the other. Assessment instruments were selected based on the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus battery (Green and Nuechterlein, 2004), a widely-used and internationally-validated method for the neuropsychological assessment of patients with schizophrenia, which has also been found to be sensitive to executive impairments in BD (Burdick et al., 2011). According to Yatham et al. (2010), the applicability of this neuropsychological battery to BD can be increased by the inclusion of additional measures of executive functioning such as the Trail Making Test, the Wisconsin Card Sorting Test, and the Stroop Color-Word Test. Therefore, we have also included these instruments in our assessment protocol.

Our assessment battery consisted of the following measures: i) Mini-Mental State Examination (MMSE) (Chaves and Izquierdo, 1992; Folstein et al., 1975), using the cutoffs proposed by Kochhann et al. (n.d.), ii) Block Design and Vocabulary Subtests from the Wechsler Adult Intelligence Scales (WAIS-III) (Nascimento, 2004; Wechsler, 1997), whose scores were converted to estimated IQ using the tables provided by Jeyakumar et al. (2004), iii) Iowa Gambling Task (IGT) (Bechara et al., 1994; Schneider and Parente, 2006) as a measure of affective decision making, iv) Hayling Sentence Completion Test (HSCT) (Burgess and Shallice, 1997; Fonseca et al., 2010), as a measure of processing speed (Part A speed), inhibition (Part B speed, accuracy) and cognitive flexibility (discrepancy between speed A and B), vi) Trail Making Test (TMT) (Reitan and Wolfson, 1995; Zimmermann et al., 2015), as a measure of processing speed (Part A speed), inhibition (Part B speed, accuracy) and cognitive flexibility (ratio of speed A to B), vi) Semantic, phonemic and unconstrained verbal fluency tasks (Montreal Assessment of Communication Battery – MAC) (Fonseca et al., 2008; Joannette et al., 2004), vii) Modified Wisconsin Card Sorting Test (MWCST) (Nelson, 1976; Zimmermann et al., 2015), viii) Sentence-Word Span subtest, from the Brazilian Brief Neuropsychological Battery NEUPSILIN (Fonseca et al., 2009) as a measure of working memory (total score and largest block remembered), ix) Digit span subtest from the Wechsler Memory Scale – Revised (Wechsler, 2002; Zimmermann et al., 2015), as a measure of focused attention (direct order) and working memory (inverse order), x) Divided Attention Test (DAT) (Sisto et al., 2006), xi) Sustained Attention Test (SAT) (Sisto et al., 2006), xii) Stroop Color Word Test (SCWT) (Stroop, 1935; Zimmermann et al., 2015).

Clinical assessments were performed using the Mini International Neuropsychiatric Interview (MINI) (Amorim, 2000; Sheehan et al., 1998), complemented with DSM-5 criteria for MDD and BD. The presence of depressive or manic symptoms was investigated using the Hamilton Depression Rating Scale (HDRS) (Gorenstein et al., 2000; HAMILTON, 1960) and the Young Mania Rating Scale (YMRS) (Vilela and Loureiro, 2000; Young et al., 1978).

Lastly, functional capacity and quality of life were evaluated using the World Health Organization Disability Assessment Schedule (Silveira et al., 2013; Ustun et al., 2010), which assesses five domains of functioning (cognition, mobility, self-care, social relationships, occupational activity and participation), and the World Health Organization Quality of Life Assessment (Fleck et al., 2000; The WHOQOL Group, 1995), which evaluates four domains of quality of life (physical health, psychological health, social relationships and environment).

### 2.3. Data analysis

Participant scores on all subscales of the WHOQOL and WHODAS 2.0 were examined by latent profile analysis, with the presence or absence of comorbidities and scores on the HDRS and YMRS entered as covariates. Model selection was performed using the Bayesian Information Criteria, as recommended by Nyland et al. (2007), as well as the principles of interpretability, parsimony, and similarity of cluster size. Demographic and clinical variables were compared between the resulting clusters using ANOVA or ANCOVA, followed by Bonferroni post-hoc tests. Categorical variables were compared using chi-square tests.

To control for the influence of demographic variables such as age and education, Z-scores were calculated for all neuropsychological measures using normative data ( $Z\text{-score} = (\text{participant score} - \text{normative mean}) / \text{standard-deviation}$ ). The

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