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Letter to the editor: Longitudinal stability of neurocognitive subtypes in bipolar disorder

Dear editor,

It is well known that patients with bipolar disorder exhibit deficits in verbal memory, attention, and executive functions even during periods of euthymia (Arts et al., 2007; Bora et al., 2009; Mann-Wrobel et al., 2011). Notwithstanding this general profile, different studies showed that deficits could be heterogeneous, with some patients showing a neurocognitive functioning indistinguishable from that of healthy controls, while others presented global impairments (Martino et al., 2008, 2014; Reichenberg et al., 2009; Iverson et al., 2011; Burdick et al., 2014). However, to the best of our knowledge, to date no studies have been conducted evaluating the longitudinal stability of these neurocognitive subtypes. Therefore, the purpose of this sub-analysis is to evaluate changes in the number of cognitive domains affected over a long period of follow-up in a sample of patients with euthymic BD. A second aim was to evaluate the longitudinal relationship between the neurocognitive subtypes and psychosocial outcome.

The present sample comprised 50 patients diagnosed with BD type I or II using the Structured Clinical Interview for DSM-IV. Patients were included if they were aged between 18 and 65, euthymic (Hamilton Depression Rating Scale –HDRS- <8 and Young Mania Rating Scale –YMRS- <6) during at least 8 weeks, and had two cognitive assessments separated by a period of at least 48 months. Exclusion criteria were: history of substance abuse, neurological disease, or any other unstable clinical condition that could affect cognitive performance. Patients completed a neuropsychological tests described in detail in previous studies of our group using other patient samples (Martino et al., 2008, 2014). Briefly, it included the following tests selected to assess 5 cognitive domains: 1) Attention: Forward Digit Span, and Trail Making Test part A; 2) Verbal memory: Memory Battery of Signoret; 3) Language: Boston Naming Test; 4) Executive functions: Backward Digit Span; Wisconsin Card Sorting Test; Trail Making Test part B; and Phonological Fluency; 5) Facial Affect Recognition: Ekman-60. Raw-score of neurocognitive performance were transformed into Z-scores based on normative data for each test. A cognitive domain was defined as affected when at least one of the tests that evaluated it had a performance below 1.5 SD of the mean. Psychosocial functioning was assessed with the General Assessment of Functioning (GAF). The Hospital Ethics Committee approved the study and all subjects gave written informed consent for their participation after receiving a complete description of the study.

At study entry, patients had a mean age of 45.57 (14.23) years (range = 22-65), 42% were BD type I and they had a length of illness of 14.61 (10.60) years with 3.90 (2.36) previous depressive episodes and 2.53 (1.92) previous hypomanic/manic episodes. The period between baseline (T1) and the re-assessment (T2) of cognitive and psychosocial functioning was 74.98 (20.55) months. There were no differences between T1 and T2 in terms of subclinical symptoms (T1-HDRS: 1.88 (2.14), T2-HDRS: 1.27 (12.10), Wilcoxon Signed Rank Test Z = -1.51, p = 0.13; T1-YMRS: 0.65 (1.31), T2-YMRS: 0.37 (1.31), Z = -1.17, p = 0.24) or exposure to benzodiazepines (20% vs 27%, McNemar test p = 0.25), antidepressants (46% vs 32%, p = 0.12), mood stabilizers (98% vs 96%, p = 1.0), and antipsychotics (54% vs 46%, p = 0.50). There was no overall difference in the number of affected cognitive domains between T1 and T2 (Wilcoxon Signed Rank Test Z = -1.71, p = 0.085). Likewise, there were no differences between T1 and T2 at the level of the individual cognitive domains: attention (34% vs 32%, McNemar test p = 1.00); verbal memory (24% vs 14%, p = 0.18); language (18% vs 14%, p = 0.73); executive functions (24% vs 26%, p = 1.0); facial affect recognition (36% vs 32%, p = 0.73). Based on previous studies, we grouped the sample of patients at study entry into 3 subtypes: cognitive indemnity (0 cognitive domain affected, 32%), selective deficits (1-2 cognitive domains affected, 50%), and global deficits (3 or more cognitive domains affected, 18%). These neurocognitive subtypes were associated with different levels of psychosocial functioning both at baseline (Kruskal-Wallis $X^2 = 11.12$, p = 0.004) and at the end of follow-up (Kruskal-Wallis $X^2 = 12.04$, p = 0.002) (Fig. 1). In contrast, there were no differences between groups regarding changes in GAF throughout follow-up (Kruskal-Wallis $X^2 = 0.92$, p = 0.63).

Our results suggest that cognitive heterogeneity, as reported in previous studies (Martino et al., 2008, 2014; Reichenberg et al., 2009; Iverson et al., 2011; Burdick et al., 2014; Lewandowski et al, 2014), would tend to be stable over time. In fact, there were no changes in the overall number of cognitive domains affected or in the commitment of each particular domain over a mean follow-up period of more than 6 years. Likewise, it has been reported that cognitive subtypes might contribute to explain variability in psychosocial functioning (Martino et al, 2008, 2014). Another cross-sectional study identified two subtypes of bipolar patients: a functionally and cognitively impaired group and a functionally and cognitively preserved group (Reinares et al., 2013). Results of this sub-analysis extend longitudinally these findings, suggesting stable profiles of patients with preserved or impaired cognitive and psychosocial functioning. Further studies should elucidate whether these patient profiles (or subtypes) respond only to a continuum of severity or, conversely, reflect the existence of pathophysiological differences within the nosographic construct of BD.

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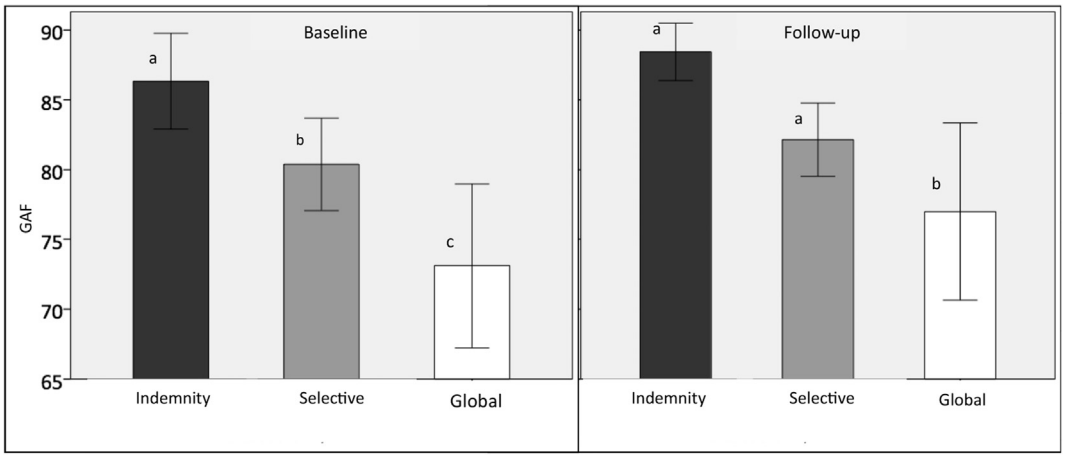

Fig. 1. Psychosocial functioning at baseline and at the end of follow-up by cognitive subtype (Cognitive indemnity, selective deficits and global deficits). Different letters mean Mann-Whitney $p < 0.05$ between groups. Error bars represent 95%IC.

Conflict of interest

The authors report no financial or personal relationships, interests, and affiliations relevant to the subject matter of the manuscript.

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