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# Emotional Intelligence: A comparison between patients after First Episode Mania and those suffering from chronic Bipolar Disorder type I

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| **Corresponding Author:** | Eduard Vieta, MD, PhD<br>University Hospital Clinic of Barcelona, CIBERSAM, IDIBAPS<br>Barcelona, SPAIN |
| **Corresponding Author Secondary Information:** | |
| **Corresponding Author's Institution:** | University Hospital Clinic of Barcelona, CIBERSAM, IDIBAPS |
| **Corresponding Author's Secondary Institution:** | |
| **First Author:** | Cristina Varo, M.Sc. |
| **First Author Secondary Information:** | |
| **Order of Authors:** | Cristina Varo, M.Sc. |
| | Silvia Amoretti, M.Sc., Ph.D. |
| | Giulio Sparacino, M.D. |
| | Esther Jiménez, M.Sc., Ph.D. |
| | Brisa Solé, M.Sc., Ph.D. |
| | Caterina del Mar Bonnin, M.Sc., Ph.D. |
| | Laura Montejo, M.Sc. |
| | Maria Serra, M.Sc. |
| | Carla Torrent, M.Sc., Ph.D. |
| | Estela Salagre, M.D. |
| | Antoni Benabarre, M.D., Ph.D. |
| | Pilar Salgado-Pineda, Ph.D. |
| | Irene Montoro Salvatierra, M.Sc. |
| | Pilar A Sáiz, M.D., Ph.D. |
| | María P García-Portilla, M.D., Ph.D. |
| | Vanessa Sánchez-Gistau, M.D., Ph.D. |
| | Edith Pomarol-Clotet, M.D., Ph.D. |
| | Josep Antoni Ramos-Quiroga, M.D., Ph.D. |
| | Isabella Pacchiarotti, M.D., Ph.D. |
| | Clemente Garcia-Rizo, M.D., Ph.D. |
| | Juan Undurraga, M.D., Ph.D. |
| | María Reinares, M.Sc., Ph.D. |
| | Anabel Martinez-Aran, M.Sc., Ph.D. |
| | |

| | |
|---|---|
| | Eduard Vieta, MD, PhD |
| | Norma Verdolini, M.D., Ph.D. |
| **Order of Authors Secondary Information:** | |
| **Manuscript Region of Origin:** | SPAIN |
| **Abstract:** | Background: Deficits in emotional intelligence (EI) were detected in patients with Bipolar Disorder (BD), but little is known about whether these deficits are already present in patients after presenting a first episode mania (FEM). We sought (i) to compare EI in patients after a FEM, chronic BD and healthy controls (HC); (ii) to examine the effect exerted on EI by socio-demographic, clinical and neurocognitive variables in FEM patients.<br>Methods: The Emotional Intelligence Quotient (EIQ) was calculated with the Mayer-Salovey-Caruso Intelligence Test (MSCEIT). Performance on MSCEIT was compared among the three groups using generalized linear models. In patients after a FEM, the influence of socio-demographic, clinical and neurocognitive variables on the EIQ was examined using a linear regression model.<br>Results: 184 subjects were included (FEM n=48, euthymic chronic BD type I n=75, HC n=61). BD patients performed significantly worse than HC on the EIQ (Mean Difference MD=10.09, Standard Error SE=3.14, p=0.004) and on the Understanding emotions branch (MD=7.46, SE=2.53, p=0.010). FEM patients did not differ from HC and BD on other measures of MSCEIT. In patients after a FEM, EIQ was positively associated with female sex (β=-0.293, p=0.034) and verbal memory performance (β=0.374, p=0.008). FEM patients performed worse than HC but better than BD on few neurocognitive domains.<br>Conclusions: Patients after a FEM showed preserved EI, while patients in later stages of BD presented lower EIQ, suggesting that impairments in EI might result from the burden of disease and neurocognitive decline, associated with the chronicity of the illness. |

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**TITLE: Emotional Intelligence: A comparison between patients ~~with~~ after First Episode Mania and those suffering from chronic Bipolar Disorder type I**

**Authors:** Cristina Varo, M.Sc.[a,b*], Silvia Amoretti, M.Sc., Ph.D.[b,c,d,e*], Giulio Sparacino, M.D.[f], Esther Jiménez, M.Sc., Ph.D.[a,b], Brisa Solé M.Sc., Ph.D.[a,b], Caterina del Mar Bonnin, M.Sc., Ph.D.[a,b], Laura Montejo, M.Sc.[a,b], Maria Serra, M.Sc.[a], Carla Torrent, M.Sc., Ph.D.[a,b], Estela Salagre, M.D.[a,b], Antoni Benabarre, M.D., Ph.D.[a,b], Pilar Salgado-Pineda, Ph.D.[b,g], Irene Montoro Salvatierra, M.Sc.[b,h], Pilar A Sáiz, M.D., Ph.D.[b,i], María P García-Portilla, M.D., Ph.D.[b,i], Vanessa Sánchez-Gistau, M.D., Ph.D.[b,h], Edith Pomarol-Clotet, M.D., Ph.D.[b,g], Josep Antoni Ramos-Quiroga, M.D., Ph.D.[b,d,e,l], Isabella Pacchiarotti, M.D., Ph.D.[a,b], Clemente Garcia-Rizo, M.D., Ph.D.[b,c], Juan Undurraga, M.D., Ph.D.[m,n], María Reinares, M.Sc., Ph.D.[a], Anabel Martinez-Aran, M.Sc., Ph.D.[a,b**], Eduard Vieta, M.D., Ph.D.[a,b**], Norma Verdolini, M.D., Ph.D.[a,b]

[a] Bipolar and Depressive Disorders Unit, Institute of Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, 170 Villarroel st, 12-0, 08036, Barcelona, Spain
[b] Biomedical Research Networking Center for Mental Health Network (CIBERSAM), Barcelona, Spain
[c] Barcelona Clinic Schizophrenia Unit, Institute of Neurosciences, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain
[d] Psychiatric Genetics Unit, Vall d'Hebron Research Institute (VHIR), Barcelona, Catalonia, Spain.
[e] Department of Psychiatry, Hospital Universitari Vall d'Hebron, Barcelona, Catalonia, Spain
[f] Department of Health Sciences, Università degli Studi di Milano, Milan, Italy
[g] FIDMAG Germanes Hospitalàries Research Foundation, c/ Dr. Pujades 38, 08830, Sant Boi de Llobregat, Barcelona, Spain
[h] Hospital Universitari Institut Pere Mata, Institut d'Investigació Sanitària Pere Virgili (IISPV), Universitat Rovira i Virgili, CIBERSAM, Reus, Tarragona, Spain
[i] Deparment of Psychiatry, University of Oviedo, Instituto de Investigación Sanitaria del Principado de Asturias, ISPA, Mental Health Services of Principado de Asturias, SESPA, Oviedo, Spain
[l] Department of Psychiatry and Legal Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain
[m] Department of Neurology and Psychiatry, Faculty of Medicine, Clinica Alemana Universidad del Desarrollo, Santiago, Chile
[n] Early Intervention Program, Instituto Psiquiátrico Dr. J. Horwitz Barak, Santiago, Chile

* The first two authors contributed equally to this work

****Corresponding authors:**
Prof. Eduard Vieta, e-mail: EVIETA@clinic.cat
Prof. Anabel Martinez-Aran, e-mail: AMARTIAR@clinic.cat

Telephone: +34 932275400 ext. 3130, Fax: +34 932279228

Address: Bipolar and Depressive Disorders Unit, Hospital Clinic, University of Barcelona, Institute of Neuroscience, IDIBAPS, CIBERSAM, 170 Villarroel st, 12-0, 08036, Barcelona, Catalonia, Spain

**Location of work and address for reprints:** Bipolar and Depressive Disorders Unit, Hospital Clinic, University of Barcelona, Institute of Neuroscience, IDIBAPS, CIBERSAM, 170 Villarroel st, 12-0, 08036, Barcelona, Catalonia, Spain

**Abstract**

~~**Introduction**~~**Background:** Deficits in emotional intelligence (EI) were detected in patients with Bipolar Disorder (BD), but little is known about whether these deficits are already present in patients **after** presenting a first episode mania (FEM). We sought (i) to compare EI in patients **after a** FEM, chronic BD and healthy controls (HC); (ii) to examine the effect exerted on EI by socio-demographic, clinical and neurocognitive variables in FEM patients.

**Methods:** The Emotional Intelligence Quotient (EIQ) was calculated with the Mayer-Salovey-Caruso Intelligence Test (MSCEIT). Performance on MSCEIT was compared among the three groups using generalized linear models. In patients **after** a FEM, the influence of socio-demographic, clinical and neurocognitive variables on the EIQ was examined using a linear regression model.

**Results:** 184 subjects were included (FEM n=48, euthymic chronic BD type I n=75, HC n=61). BD patients performed significantly worse than HC on the EIQ (Mean Difference MD=10.09, Standard Error SE=3.14, p=0.004) and on the Understanding emotions branch (MD=7.46, SE=2.53, p=0.010). FEM patients did not differ from HC and BD on other measures of MSCEIT. In patients **after a** FEM, EIQ was positively associated with female sex (β=-0.293, p=0.034) and verbal memory performance (β=0.374, p=0.008). FEM patients performed worse than HC but better than BD on few neurocognitive domains.

**Conclusions:** Patients ~~**with**~~ **after** a FEM showed preserved EI, while patients in later stages of BD presented lower EIQ, suggesting that impairments in EI might result from the burden of disease and neurocognitive decline, associated with the chronicity of the illness.

**Key words:** emotional intelligence, first episode mania, bipolar disorder, verbal memory, MSCEIT

**Introduction**

Neurocognitive impairment is a well-established feature in bipolar disorder (BD), even in the early stages of disease (Pope, Mazmanian, & Sharma, 2016). It is present also in many cases during euthymic periods and is an important determinant of psychosocial functioning (Pope et al., 2016). Although neurocognition has been more exhaustively studied, over the past decades there has been an increased interest in the study of social cognition (SC) (Varo et al., 2019a, 2020) which is defined as the ability to detect, process, and use social information to manage interpersonal functioning and social behavior. SC deficits may produce significant daily difficulties given the crucial importance of SC for social relations and well-being (Miskowiak & Varo, 2021). SC encompasses five distinct areas, namely (i) Emotional processing, (ii) Theory of Mind, (iii) Attributional bias, (iv) Social perception, (v) Social knowledge (Green, Horan, & Lee, 2019). In BD research, the study of SC has focused mainly on emotional processing, which has been also conceptualized as emotional intelligence (EI) (Samamé, Martino, & Strejilevich, 2015), and generally measured by means of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) (Mayer, Salovey, Caruso, & Sitarenios, 2003).

Deficits in EI have been detected in patients with chronic BD (Aparicio et al., 2017; Beatrice Frajo-Apor et al., 2020; McClure et al., 2005; Samamé et al., 2015; Varo et al., 2019a, 2020). However, the evolution of EI throughout the course of BD is unclear due to the paucity of studies that have examined the deficits in EI in patients experiencing a first episode mania (FEM) (Daros, Ruocco, Reilly, Harris, & Sweeney, 2014; Szmulewicz, Lomastro, Valerio, Igoa, & Martino, 2019) and the lack of longitudinal studies on EI of these patients. It remains to be solved whether the deficits are present since the beginning of the disease (i.e., as primary deficits) and remain stable from early stages to chronicity, or whether they emerge and worsen as a result of the burden of disease related with the chronicity of the illness (i.e., as secondary deficits). Moreover, to the best of our knowledge, no study so far has assessed EI in FEM patients in comparison with those in later stages of BD.

Previous evidence for the role of EI for patients suffering from a non-affective first episode psychosis (FEP) has been reported (Sanchez–Gistau et al., 2020). EI was found to be altered in non-affective FEP patients at onset and its impairment represents a stable pattern and a relevant feature of early schizophrenia (Green et al., 2012). Schizophrenia and BD share a chronic clinical course with impairments in neurocognitive and clinical features, although with different levels of severity (Lee et al., 2013). As a consequence, patients with a FEM might present a similar but subtler pattern of EI abnormalities than non-affective FEP patients. To date, no study has investigated the association between socio-demographic, clinical, neuropsychological variables and EI among patients with a FEM. A better comprehension of the relationship between these variables and EI performance would have implications in understanding the nature, trajectory and clinical relevance of the difficulties on this SC domain in the early stages of BD. Considering these gaps in the literature, the main aim of the present study was to explore EI using the full version of the MSCEIT in patients ~~with~~ **after** a FEM in comparison with patients with chronic BD and HC. Also, **the secondary aim** **was** provided insight on the potential contribution of socio-demographic, clinical and neurocognitive variables on EI performance in patients ~~with~~ **after** a FEM. We hypothesized that FEM patients would present intermediate EI performance between HC and chronic BD, and their performance would be influenced by neurocognitive performance, clinical and socio-demographic variables.

## Material and Methods

*Participants*

Data was pooled from two projects developed by our research group. The first project recruited FEM patients as part of a two-year longitudinal multicentric study including the Bipolar and Depressive disorders Unit of IDIBAPS-Hospital Clinic in Barcelona, FIDMAG Research Foundation and the University Hospital Institut Pere Mata. The second project

recruited cross-sectionally chronic BD patients both at the Hospital Clinic in Barcelona and at mental health services in Oviedo. HC were recruited through advertisement at the Hospital Clinic in Barcelona. The four centers cooperate under the umbrella of the Spanish Research Network on Mental Health (CIBERSAM) (Salagre et al., 2019).

The inclusion criteria for FEM patients, evaluated at baseline, were: (i) aged between 18 and 45 years old at the time of first evaluation; (ii) having experienced their FEM (with or without psychotic symptoms) over the previous three years; (iii) being in full or partial remission (Hamilton Depression Rating Scale 17-item [HDRS-17] (HAMILTON, 1960; Ramos-Brieva & Cordero-Villafafila, 1988) **≤14** and Young Mania Rating Scale [YMRS] (Colom et al., 2002; Young, Biggs, Ziegler, & Meyer, 1978) ≤14, ~~respectively~~). The inclusion criteria for patients with BD were: (i) aged over 18 years old; (ii) fulfilling DSM-IV-TR criteria for BD type I (BD-I) and (iii) being euthymic (HDRS-17≤8, YMRS≤6), at least in the 3 months before the inclusion. **Patients could have experienced more than one affective episode over the previous three years, could then be considered within their early stage BD illness.**

Exclusion criteria for both FEM and BD patients were the presence of (i) a mental intellectual disability (defined as intelligence quotient [IQ]<70); (ii) presence of any medical condition affecting neuropsychological performance; (iii) alcohol/substance dependence in the previous year to study inclusion; (iv) having received electroconvulsive therapy (ECT) in the 12 months before participation.

**All patients were under stable treatment regimen.**

HC without current or past psychiatric history, meeting the same exclusion criteria as patients, were recruited via advertisement. ~~None of the HC had first-degree relatives with psychiatric disorders.~~ **In addition, HC were asked if they had first-degree relatives with psychiatric disorders".**

The study was carried out following the latest version of the Declaration of Helsinki, and it was reviewed by the ethical committee of the four institutions. Written informed consent was obtained from all participants.

*Clinical assessment*

In order to gather clinical data, all patients were assessed by means of ~~a semi-structured interview based on~~ the Structured Clinical Interview for DSM Disorders (SCID-I-II) **(First, M.; Gibbon, M.; Spitzer, R.; Williams, J.; Benjamin, 1997a, 1997b)**. The YMRS and HDRS-17 scores were used to evaluate the severity of manic and depressive symptomatology, respectively. All the participants also completed the Functional Assessment Short Test (FAST) (Rosa et al., 2007), a scale designed to assess psychosocial functional impairment in psychiatric patients, with higher scores indicating poorer psychosocial functioning. The full description of other clinical variables is reported in the Supplementary Material.

*Emotional intelligence assessment*

EI was evaluated using the Spanish version of the MSCEIT, V2.0 (Mayer et al., 2003). This instrument consists of 141 items and provides eight task scores that measure the four branches of EI: (i) Perceiving Emotions: to recognize and to appraise emotions accurately; (ii) Using Emotions: to access or generate feelings when they facilitate thoughts; (iii) Understanding Emotions: to understand complex emotions and how emotions transition from one stage to another, to recognize the causes of emotions, and to understand relationships among emotions; (iv) Managing Emotions: to stay aware of one's emotions, and to solve emotion-laden problems. The Perceiving Emotions and Using Emotions branches are assigned to the Experiential Area, while the Understanding Emotions and Managing Emotions branches are assigned to the Strategic Area. The test provides an overall score, the EI quotient (EIQ), and also scores in the two areas, in the four branches and in each of the specific tasks. Lower

scores indicate poorer performance in EI. The average range of EIQ is 100, with a standard deviation (SD) of 15.

*Neuropsychological assessment*

All participants were evaluated using a comprehensive neuropsychological battery exploring different cognitive domains: Processing Speed, Working Memory, Verbal Learning and Memory, Visual Memory, Executive Functions and Attention. The neuropsychological battery comprised the Digit-symbol Coding, Symbol Search, Arithmetic, Digits, and Letter-Number sequencing subtests from Wechsler Adult Intelligence Scale (WAIS-III) (Wechsler, 1997), Phonemic (F-A-S) and Categorical (Animal naming) components of the Controlled Oral Word Association Test (COWAT) (Patterson, 2018), the Trail Making Test-A (TMT-A) and Trail Making Test-B (TMT-B) (Reitan, 1958), the California Verbal Learning Test (CVLT) (Delis, Kramer, Kaplan, & Over, 1987), the Rey Osterrieth Complex Figure (ROCF) (Rey, 1958), the computerized version of the Wisconsin Card Sorting Test (WCST) (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), the Stroop Color-Word Interference Test (Golden, 1994), and the Continuous Performance Test–II (CPT-II), version 5 (Conners, 2002). Finally, estimated IQ was assessed with the (WAIS-III) vocabulary subtest (Wechsler, 1997).

*Statistical analysis*

Comparison of socio-demographic and clinical characteristics among groups (FEM, BD, and HC) was carried out using Chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. The Tukey's test was carried out for post-hoc comparisons to identify pair-wise differences between groups. Effect sizes (Glass's d) were also calculated to estimate the magnitude of the differences between the groups. Neurocognitive tests raw scores were standardized to z-scores based on HCs' performance (for further information on the calculation of the composites of neurocognitive domains see Supplementary Material).

Performance on MSCEIT and the neurocognitive domains was compared across the three groups using generalized linear models (GLM). All models were adjusted for those clinical and socio-demographic variables for which the three groups differed significantly. Then, a Bonferroni post-hoc correction was applied when significant main effects were present when comparing the three groups, in order to identify pair-wise differences between groups. Estimated Marginal Means, adjusted for the other variables in the model, were reported for each variable of interest (i.e. EIQ), as well as the 95% Confidence Interval (CI), their Mean Difference (MD) and its Standard Error (SE).

**Moreover, exploratory analyses were conducted to satisfy our secondary aim**. In order to assess which socio-demographic, clinical and neuropsychological variables were associated with IEQ in the FEM and in the BD groups, we first performed Pearson bivariate correlations to identify those continuous variables significantly associated with EIQ. For categorical variables (i.e. sex), Student's t-test was run to evaluate the distribution of EIQ. Only those variables with a p value ≤0.05 were then entered into a hierarchical multiple regression model, aimed at evaluating the association between socio-demographic, clinical and neuropsychological variables and EIQ.

All statistical analyses were conducted using IBM SPSS Statistics version 23.0. Statistical significance was set at $p<0.05$.

**Results**

The total sample included 184 participants: 48 patients with a FEM in full or partial clinical remission, 75 euthymic BD patients and 61 HC. Socio-demographic variables among groups are reported in Table 1.

*Clinical features among the groups*

Regarding clinical variables, there were significant differences between patient groups (FEM and chronic BD) and HC in the total HDRS-17 ($p<0.001$) and YMRS scores ($p<0.001$), as well as in the overall psychosocial functioning ($p<0.001$). Both patient groups presented more subsyndromal depressive symptoms than HC (BD versus HC $p<0.001$, FEM versus HC $p<0.001$, respectively), whereas chronic BD patients exhibited more subsyndromal manic symptoms than HC ($p<0.001$). No statistically significant differences were found in subsyndromal symptoms between patient groups. Significant group differences in the FAST total score were observed for both the patient groups, presenting significantly decreased functioning compared to HC ($p<0.001$). In addition, chronic BD patients showed poorer psychosocial function than patients in the FEM group ($p<0.001$).

Significant differences were observed in the comparison between chronic BD and FEM patients in age at first hospitalization ($p=0.009$), being lower in the case of the FEM group ($p=0.009$), but not regarding the polarity at onset ($p=0.265$) or the presence of family history for either BD ($p=1.000$) or major depressive disorder ($p=0.986$). Groups differed in terms of duration of illness ($p<0.001$) and total number of episodes ($p<0.001$). **Patients after a FEM experienced an average of 1.19 episodes of mania whilst BD chronic patients an average of 3.62.**

*Emotional intelligence performance*

Patients in the FEM group performed similarly to HC on MSCEIT Total score (**Supplementary Table 1,** ~~**Table 2,**~~ figure 1) an all measures of MSCEIT (**Supplementary Table 1**, ~~**Table 2**~~, Figure ~~**1**~~ **2**).

Significant differences were found for EIQ ($p=0.005$) and in the MSCEIT Understanding Emotions branch ($p=0.007$), even after controlling for age, subsyndromal manic and depressive symptoms. Bonferroni post-hoc testing revealed that BD patients presented significantly lower EIQ than HC (MD=10.09, SE=3.14, $p=0.004$) but no difference was found neither between HC

and FEM patients (MD=2.69, SE=3.56, p=1.000) nor between FEM and chronic BD patients (MD=7.40, SE=3.61, p=0.121).

In addition, BD patients performed more poorly than HC on the Understanding Emotions branch (MD=7.46, SE=2.53, p=0.010). A trend-level difference was reported between patient groups, with BD patients showing lower scores than those in the FEM group (MD=-6.84, SE=2.93, p=0.056). No significant difference was reported between FEM patients and HC (MD=0.62, SE=2.87, p=1.000).

*Neurocognitive performance*

Concerning neurocognitive domains, there was a main effect of group in terms of processing speed (p<0.001), verbal memory (p<0.001), working memory (p<0.001), executive functions (p<0.001), visual memory (p=0.033) and attention (p<0.001), after controlling for age, subsyndromal depressive and manic symptoms (**Supplementary Table 1~~Table 2~~**, Figure ~~2~~ **3**).

Bonferroni post-hoc pair-wise comparisons between groups revealed that FEM patients performed worse than HC on processing speed (MD=0.96, SE=0.24, p<0.001), executive functions (MD=0.83, SE=0.30, p=0.015) and attention (MD=1.02, SE=0.26, p<0.001), but not on verbal, working and visual memory. On the contrary, FEM patients performed better than chronic BD patients on processing speed (MD=0.97, SE=0.25, p<0.001), executive functions (MD=1.02, SE=0.30, p=0.002) and attention (MD=1.79, SE=0.28, p<0.001), but not on verbal memory, working memory and visual memory. Chronic BD patients performed significantly worse than HC on all neurocognitive domains: processing speed (MD=1.93, SE=0.22, p<0.001), verbal memory (MD=1.00, SE=0.24, p<0.001), working memory (MD=0.72, SE=0.18, p<0.001), executive functions (MD=1.85, SE=0.26, p<0.001), visual memory (MD=0.51, SE=0.20, p=0.035) and attention (MD=2.81, SE=0.21, p<0.001).

*Socio-demographic, clinical and neurocognitive variables associated with EIQ in FEM patients*

In FEM patients, lower EIQ correlated with poorer performance in verbal memory (r=0.371, p=0.011). Also, male patients showed lower scores in EIQ than females (t=2.054, p=0.046) (see table 3). No other clinical variable correlated with EIQ.

After including the variables significant in bivariate analyses in a hierarchical regression model ($F(2,43)=6.202$, adjusted $R^2=0.188$, p=0.004), both male sex (β=-0.293, p=0.034) and the verbal memory domain (β=0.374, p=0.008) were significantly associated with EIQ, with a higher effect exerted by verbal memory performance.

Results for the chronic BD groups are reported in Supplementary **Tables 3 and 4.** ~~**Tables 1and 2.**~~

**Discussion**

To the best of our knowledge, this is the first study to comprehensively assess EI in **patients after a FEM** using the full MSCEIT version. The present study of EIQ in fully or partially remitted FEM (n=48) versus chronic BD-I (n=75) and HC (n=61) showed three main findings. While **patients after a FEM** presented intermediate EIQ scores between HC and chronic BD, with EIQ scores significantly lower in BD than HC, in the MSCEIT branches, FEM patients' performance was globally comparable to HC. In addition, lower performance in Understanding Emotions branch was found for chronic BD patients in comparison with HC. Whilst EI appeared to be preserved in FEM patients, neurocognition, and particularly processing speed, attention and executive functions performance was already impaired at the early stages of the illness. Lower EIQ in FEM was associated with male sex and lower performance in verbal memory.

Although EI has been widely studied in patients in later stages of BD (Aparicio et al., 2017; Beatrice Frajo-Apor et al., 2020; Samamé et al., 2015; Varo et al., 2019a), little is known about the EI performance of patients after a FEM and the course of EI impairment across the clinical stages of BD and the evidence is seldom conflicting. So far, only two studies assessed some level of EI patients **after** a FEM (Daros et al., 2014; Szmulewicz et al., 2019). Nonetheless, these

studies were characterized by small sample size, which limited the generalizability of results, and only evaluated the lower levels of EI abilities such as labeling, discrimination, and appraising emotions. Daros and colleagues assessed 24 non-affective FEP and 16 FEM patients in comparison with 35 HC both during acute psychosis and after seven weeks of treatment (Daros et al., 2014). Both groups of patients presented difficulties recognizing facial expressions that did not resolve with treatment and clinical stabilization. In a small sample of 26 FEM patients, Szmulewicz and colleagues found that in comparison with HC, FEM patients presented a compromised cognitive theory of mind performance characterized by a reduced ability to infer intentions from others whilst the affective theory of mind performance was preserved, indicating that FEM patients were capable to detect other's emotions and feelings (Szmulewicz et al., 2019). In the present study, FEM patients, in comparison with HC, did not present difficulties in EI, assessed through the full version of MSCEIT, which evaluates both lower and higher EI abilities.

Although EI appeared to be overall preserved among the patients **after a FEM** assessed in our study, their neurocognitive performance on processing speed, attention and executive functions was mildly impaired. These findings are in line with a recent study assessing cognitive groups of patients after recovery from a FEM (Chakrabarty et al., 2021). The authors identified that almost the 50% of FEM patients reported selective cognitive impairment after recovery, with pronounced deficits in processing speed and lower performance in verbal memory, working memory and executive functioning in comparison with HC. Furthermore, in line with our results, these deficits seemed to be stable over time in those patients that experienced a recurrence. Particularly, Kozicky and colleagues (2014) found that this impairment in cognitive performance was mostly evident in those who experienced longer manic or hypomanic episodes (Kozicky et al., 2014).

Patients suffering from chronic BD, included in this study, presented impairment in all the cognitive domains and lower EIQ and difficulties in the MSCEIT Understanding emotions

branch. Our results are in line with previous studies, supporting the presence of less severe impairment in SC compared to neurocognitive domains in patients with BD (Bilderbeck et al., 2016). Deficits of EI were not observed in FEM patients. This might suggest that more severe SC deficits might be associated with other conditions, such as schizophrenia, instead of BD since in non-affective FEP patients EI impairment was found to start early in the course of illness and to remain stable (Green et al., 2012). **Given that EI is more severely affected in psychosis than in mania, one may argue that patients reporting psychotic symptoms during the first episode of mania might show greater difficulties in EI than patients without psychotic symptoms. Despite this, we did not find any difference in terms of EIQ between FEM patients who presented Psychotic Symptoms at Onset and those who did not.** Our findings suggest that neurocognition seemed to be already altered at the first symptomatic manic presentation, whilst EI started out intact in the FEM patients and then slightly worsened with illness course. One recurring question is whether neurocognition and SC in BD are sufficiently distinct to be considered separately. **Previous studies investigating the relationship between neurocognition and EI have yielded mixed and inconclusive results. While there are studies that reported that lower levels of EI may be mediated by neurocognitive abilities (Aparicio et al., 2017; Frajo-Apor et al., 2017), others have not found a relationship between the two constructs** (Fanning, Bell, & Fiszdon, 2012)**.** Our results highlight the connection between EI and neurocognition and the idea that they are two complementary but separated constructs (DeTore, Mueser, & McGurk, 2018), **with partial overlap and** with a different degree of impairment. Thus, **our findings were in line with many other works supporting the idea that neurocognitive ability may represent a "necessary, but not sufficient" prerequisite for social cognitive abilities, especially in those that contain an emotional component (Bora, Veznedaroğlu, & Vahip, 2016; Lee et al., 2013; Varo et al., 2019).** This view is consistent with studies from neuroimaging in social neuroscience (Mitchell, 2008). **Nonetheless, the role of neurocognitive impairments on social cognition and EI in**

**euthymic BD patients remains somewhat unclear. Therefore, the nature of this association should be the focus of further investigation.**

Whilst in the present study the two groups of patients did not differ in terms of severity of symptoms at the time of evaluation, BD group performed worse than FEM group in measures of indicators assessing the burden of disease, such as longer duration of illness and higher total number of lifetime episodes, psychosocial functioning, and in the neurocognitive performance. Thus, our findings support the hypotheses that EI difficulties might be a result of the burden of disease and neurocognitive decline associated with the chronicity of the illness.

As for the socio-demographic, neurocognitive and clinical variables associated with EIQ in **patients after a FEM**, lower EIQ scores were found to be associated with male sex and lower verbal memory performance. Regarding sex differences in EI, our findings are in line with previous studies in which men performed worse than women on EI in non-clinical samples (Pardeller, Frajo-Apor, Kemmler, & Hofer, 2017) and BD patients (Varo et al., 2019a). As for the role played by verbal memory in EI, our finding is in line with previous literature underlining how EI performance might be associated with cognitive abilities (Eack et al., 2010; Beatrice Frajo-Apor et al., 2020; Varo et al., 2019). In a previous study assessing BD patients, all neurocognitive domains were associated with EI (Varo et al., 2019). **However, to date, it is difficult to ascertain which neuropsychological domain (among verbal memory, executive functions, psychomotor speed, working memory and attention) has a greater influence on social cognition, especially on EI. In the current study verbal memory resulted to be the central domain involved in EI ability. EI was assessed by MSCEIT which demands an accurate interpretation of the semantic meaning of the social situation. It involves exercises related to verbal memory skills, such as association, categorization and mental imagery.** In another study assessing EI and cognitive abilities in healthy adults, verbal fluency was the only cognitive domain associated with EIQ (Pardeller, Frajo-Apor, Kemmler, & Hofer, 2017).

In the present study, being men with worse performance in verbal memory arose as risk factors for worse EI ability. In consequence, an exhaustive assessment of SC and EI in this population would be recommended in order to tailor specific early intervention strategies (Vieta et al., 2018).

The findings of the present study should be interpreted in light of the following limitations. First, since our study used data from two separate projects, the groups were not matched and there were uneven sample sizes. Moreover, some inclusion criteria differ between studies. In order to partially overcome this limitation, we decided to add age and both depressive and manic subsyndromal symptoms as covariates in the statistical models. Second, the cross-sectional design of this study did not enable us to determine causal inferences between EI, clinical symptomatology, and neurocognition, nor to examine the changes in EI ability associated with neuroprogression in BD. Since the FEM sample size was derived from a longitudinal study, we will be able to provide insight on the course of EI in the early phases of BD, for the patients included in the present study, as soon as the follow-up will be ended. Similarly, the description of influence of treatment should be further detailed. Also, the ability of MSCEIT test to discriminate individuals at the mean and high level of EI has been questioned (Fiori et al., 2014).

Despite these limitations, the strength of the present study is to provide insight on **EI in patients in the early stage of the illness**, an almost unexplored aspect in this group of patients and is the first investigation aimed at understanding which socio-demographic, clinical, and neurocognitive factors may contribute to EI levels in the early stages of BD. Furthermore, the present study can rely on a quite big sample size for both FEM and BD patients, allowing for a cross-sectional comparison of the EI abilities in two different phases of BD using the four branches of MSCEIT. In particular, BD patients have difficulties in EI but not patients that experienced their FEM **over last three years**. Therefore, our findings suggest that EI is preserved in early stages, which represents an optimistic result. However, this might worsen in

later stages of the disease. Difficulties in EI performance might be possibly associated with the increasing burden of disease, and neuroprogression in chronic BD, although this hypothesis will need to be confirmed in longitudinal studies. On the contrary, neurocognition and psychosocial functioning seemed to be impaired at an earlier stage than EI. These findings have important implications in terms of early interventions, which should address not only neurocognitive performance but also social cognitive functioning at the early stages in order to prevent or mitigate the cognitive decline often associated with BD in the long-term (Vieta et al., 2018). Both EI and neurocognitive performance should be assessed in the early stages of the disease. While neurocognitive performance could be already impaired in the early stages and thus represents a target of secondary preventive intervention, EI could be not impaired in the early stages of the disease and should be addressed with primary preventive interventions aimed at possibly avoiding EI difficulties in these patients.

**Disclosures**

**Role of the Funding Source:** The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Conflicts of interest**

EV has received grants and served as consultant, advisor or CME speaker for the following entities (unrelated to the present work): AB-Biotics, Abbott, Allergan, Angelini, Dainippon Sumitomo Pharma, Ferrer, Gedeon Richter, Janssen, Lundbeck, Otsuka, Sage, Sanofi-Aventis, and Takeda. AMA has received funding for research projects and/or honoraria as a consultant or speaker for the following companies and institutions (work unrelated to the topic of this manuscript): Otsuka, Pfizer, AstraZeneca, Bristol-Myers Squibb, Lundbeck, the Spanish Ministry of Economy and Competitiveness and Instituto de Salud Carlos III. AB has received grants and served as consultant, advisor or CME speaker for the following entities in the last five years (unrelated to the present work): Janssen, Lundbeck, Otsuka and Pfizer. PAS has been a consultant to and/or has received honoraria or grants from Adamed, CIBERSAM, European Comission, Government of the Principality of Asturias, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, Plan Nacional sobre Drogas and Servier. MPGP has been a consultant to and/or has received honoraria/grants from Angelini, Alianza Otsuka-Lundbeck, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, and SAGE Therapeutics.
IP has received CME-related honoraria, or consulting fees from ADAMED, Janssen-Cilag and Lundbeck. CGR has received honoraria/travel support from Angelini, Adamed, Janssen-Cilag and Lundbeck. NV has received financial support for CME activities and travel funds from the following entities (unrelated to the present work): Angelini, Janssen, Lundbeck, Otsuka. The rest of authors report no biomedical financial interests or potential conflicts of interest related to the present article.

**Data Availability Statement**

The data that support the findings of this study are available on request from the corresponding authors.

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**Figure legends**

**Figure 1: Emotional Intelligence Quotient with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

**Figure 2: Mean MSCEIT scores with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

**Figure 3. Neuropsychological composite mean scores with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; PS=Processing Speed Composite; VM=Verbal Memory Composite; WM=Working Memory Composite; EF=Executive Functions Composite; VisM=Visual Memory Composite; AT= Attention composite

**TITLE PAGE**

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**TITLE: Emotional Intelligence: A comparison between patients after First Episode Mania and those suffering from chronic Bipolar Disorder type I**

**Authors:** Cristina Varo, M.Sc.[a,b*], Silvia Amoretti, M.Sc., Ph.D.[b,c,d,e*], Giulio Sparacino, M.D.[f], Esther Jiménez, M.Sc., Ph.D.[a,b], Brisa Solé M.Sc., Ph.D.[a,b], Caterina del Mar Bonnin, M.Sc., Ph.D.[a,b], Laura Montejo, M.Sc.[a,b], Maria Serra, M.Sc.[a], Carla Torrent, M.Sc., Ph.D.[a,b], Estela Salagre, M.D.[a,b], Antoni Benabarre, M.D., Ph.D.[a,b], Pilar Salgado-Pineda, Ph.D.[b,g], Irene Montoro Salvatierra, M.Sc.[b,h], Pilar A Sáiz, M.D., Ph.D.[b,i], María P García-Portilla, M.D., Ph.D.[b,i], Vanessa Sánchez-Gistau, M.D., Ph.D.[b,h], Edith Pomarol-Clotet, M.D., Ph.D.[b,g], Josep Antoni Ramos-Quiroga, M.D., Ph.D.[b,d,e,l], Isabella Pacchiarotti, M.D., Ph.D.[a,b], Clemente Garcia-Rizo, M.D., Ph.D.[b,c], Juan Undurraga, M.D., Ph.D.[m,n], María Reinares, M.Sc., Ph.D.[a], Anabel Martinez-Aran, M.Sc., Ph.D.[a,b**], Eduard Vieta, M.D., Ph.D.[a,b**], Norma Verdolini, M.D., Ph.D.[a,b]

[a] Bipolar and Depressive Disorders Unit, Institute of Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, 170 Villarroel st, 12-0, 08036, Barcelona, Spain
[b] Biomedical Research Networking Center for Mental Health Network (CIBERSAM), Barcelona, Spain
[c] Barcelona Clinic Schizophrenia Unit, Institute of Neurosciences, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain
[d] Psychiatric Genetics Unit, Vall d'Hebron Research Institute (VHIR), Barcelona, Catalonia, Spain.
[e] Department of Psychiatry, Hospital Universitari Vall d'Hebron, Barcelona, Catalonia, Spain
[f] Department of Health Sciences, Università degli Studi di Milano, Milan, Italy
[g] FIDMAG Germanes Hospitalàries Research Foundation, c/ Dr. Pujades 38, 08830, Sant Boi de Llobregat, Barcelona, Spain
[h] Hospital Universitari Institut Pere Mata, Institut d'Investigació Sanitària Pere Virgili (IISPV), Universitat Rovira i Virgili, CIBERSAM, Reus, Tarragona, Spain
[i] Deparment of Psychiatry, University of Oviedo, Instituto de Investigación Sanitaria del Principado de Asturias, ISPA, Mental Health Services of Principado de Asturias, SESPA, Oviedo, Spain
[l] Department of Psychiatry and Legal Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain
[m] Department of Neurology and Psychiatry, Faculty of Medicine, Clinica Alemana Universidad del Desarrollo, Santiago, Chile
[n] Early Intervention Program, Instituto Psiquiátrico Dr. J. Horwitz Barak, Santiago, Chile

* The first two authors contributed equally to this work

****Corresponding authors:**
Prof. Eduard Vieta, e-mail: EVIETA@clinic.cat
Prof. Anabel Martinez-Aran, e-mail: AMARTIAR@clinic.cat

Telephone: +34 932275400 ext. 3130, Fax: +34 932279228

Address: Bipolar and Depressive Disorders Unit, Hospital Clinic, University of Barcelona, Institute of Neuroscience, IDIBAPS, CIBERSAM, 170 Villarroel st, 12-0, 08036, Barcelona, Catalonia, Spain

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**Abstract**

**Background:** Deficits in emotional intelligence (EI) were detected in patients with Bipolar Disorder (BD), but little is known about whether these deficits are already present in patients after presenting a first episode mania (FEM). We sought (i) to compare EI in patients after a FEM, chronic BD and healthy controls (HC); (ii) to examine the effect exerted on EI by socio-demographic, clinical and neurocognitive variables in FEM patients.

**Methods:** The Emotional Intelligence Quotient (EIQ) was calculated with the Mayer-Salovey-Caruso Intelligence Test (MSCEIT). Performance on MSCEIT was compared among the three groups using generalized linear models. In patients after a FEM, the influence of socio-demographic, clinical and neurocognitive variables on the EIQ was examined using a linear regression model.

**Results:** 184 subjects were included (FEM n=48, euthymic chronic BD type I n=75, HC n=61). BD patients performed significantly worse than HC on the EIQ (Mean Difference MD=10.09, Standard Error SE=3.14, p=0.004) and on the Understanding emotions branch (MD=7.46, SE=2.53, p=0.010). FEM patients did not differ from HC and BD on other measures of MSCEIT. In patients after a FEM, EIQ was positively associated with female sex (β=-0.293, p=0.034) and verbal memory performance (β=0.374, p=0.008). FEM patients performed worse than HC but better than BD on few neurocognitive domains.

**Conclusions:** Patients after a FEM showed preserved EI, while patients in later stages of BD presented lower EIQ, suggesting that impairments in EI might result from the burden of disease and neurocognitive decline, associated with the chronicity of the illness.

**Key words:** emotional intelligence, first episode mania, bipolar disorder, verbal memory, MSCEIT

**Introduction**

Neurocognitive impairment is a well-established feature in bipolar disorder (BD), even in the early stages of disease (Pope, Mazmanian, & Sharma, 2016). It is present also in many cases during euthymic periods and is an important determinant of psychosocial functioning (Pope et al., 2016). Although neurocognition has been more exhaustively studied, over the past decades there has been an increased interest in the study of social cognition (SC) (Varo et al., 2019a, 2020) which is defined as the ability to detect, process, and use social information to manage interpersonal functioning and social behavior. SC deficits may produce significant daily difficulties given the crucial importance of SC for social relations and well-being (Miskowiak & Varo, 2021). SC encompasses five distinct areas, namely (i) Emotional processing, (ii) Theory of Mind, (iii) Attributional bias, (iv) Social perception, (v) Social knowledge (Green, Horan, & Lee, 2019). In BD research, the study of SC has focused mainly on emotional processing, which has been also conceptualized as emotional intelligence (EI) (Samamé, Martino, & Strejilevich, 2015), and generally measured by means of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) (Mayer, Salovey, Caruso, & Sitarenios, 2003).

Deficits in EI have been detected in patients with chronic BD (Aparicio et al., 2017; Beatrice Frajo-Apor et al., 2020; McClure et al., 2005; Samamé et al., 2015; Varo et al., 2019a, 2020). However, the evolution of EI throughout the course of BD is unclear due to the paucity of studies that have examined the deficits in EI in patients experiencing a first episode mania (FEM) (Daros, Ruocco, Reilly, Harris, & Sweeney, 2014; Szmulewicz, Lomastro, Valerio, Igoa, & Martino, 2019) and the lack of longitudinal studies on EI of these patients. It remains to be solved whether the deficits are present since the beginning of the disease (i.e., as primary deficits) and remain stable from early stages to chronicity, or whether they emerge and worsen as a result of the burden of disease related with the chronicity of the illness (i.e., as secondary deficits). Moreover, to the best of our knowledge, no study so far has assessed EI in FEM patients in comparison with those in later stages of BD.

Previous evidence for the role of EI for patients suffering from a non-affective first episode psychosis (FEP) has been reported (Sanchez–Gistau et al., 2020). EI was found to be altered in non-affective FEP patients at onset and its impairment represents a stable pattern and a relevant feature of early schizophrenia (Green et al., 2012). Schizophrenia and BD share a chronic clinical course with impairments in neurocognitive and clinical features, although with different levels of severity (Lee et al., 2013). As a consequence, patients with a FEM might present a similar but subtler pattern of EI abnormalities than non-affective FEP patients. To date, no study has investigated the association between socio-demographic, clinical, neuropsychological variables and EI among patients with a FEM. A better comprehension of the relationship between these variables and EI performance would have implications in understanding the nature, trajectory and clinical relevance of the difficulties on this SC domain in the early stages of BD. Considering these gaps in the literature, the main aim of the present study was to explore EI using the full version of the MSCEIT in patients after a FEM in comparison with patients with chronic BD and HC. Also, the secondary aim was provided insight on the potential contribution of socio-demographic, clinical and neurocognitive variables on EI performance in patients after a FEM. We hypothesized that FEM patients would present intermediate EI performance between HC and chronic BD, and their performance would be influenced by neurocognitive performance, clinical and socio-demographic variables.

**Material and Methods**

*Participants*

Data was pooled from two projects developed by our research group. The first project recruited FEM patients as part of a two-year longitudinal multicentric study including the Bipolar and Depressive disorders Unit of IDIBAPS-Hospital Clinic in Barcelona, FIDMAG Research Foundation and the University Hospital Institut Pere Mata. The second project recruited cross-sectionally chronic BD patients both at the Hospital Clinic in Barcelona and at

mental health services in Oviedo. HC were recruited through advertisement at the Hospital Clinic in Barcelona. The four centers cooperate under the umbrella of the Spanish Research Network on Mental Health (CIBERSAM) (Salagre et al., 2019).

The inclusion criteria for FEM patients, evaluated at baseline, were: (i) aged between 18 and 45 years old at the time of first evaluation; (ii) having experienced their FEM (with or without psychotic symptoms) over the previous three years; (iii) being in full or partial remission (Hamilton Depression Rating Scale 17-item [HDRS-17] (HAMILTON, 1960; Ramos-Brieva & Cordero-Villafafila, 1988) ≤14 and Young Mania Rating Scale [YMRS] (Colom et al., 2002; Young, Biggs, Ziegler, & Meyer, 1978) ≤14). The inclusion criteria for patients with BD were: (i) aged over 18 years old; (ii) fulfilling DSM-IV-TR criteria for BD type I (BD-I) and (iii) being euthymic (HDRS-17≤8, YMRS≤6), at least in the 3 months before the inclusion. Patients could have experienced more than one affective episode over the previous three years, could then be considered within their early stage BD illness.

Exclusion criteria for both FEM and BD patients were the presence of (i) a mental intellectual disability (defined as intelligence quotient [IQ]<70); (ii) presence of any medical condition affecting neuropsychological performance; (iii) alcohol/substance dependence in the previous year to study inclusion; (iv) having received electroconvulsive therapy (ECT) in the 12 months before participation.

All patients were under stable treatment regimen.

HC without current or past psychiatric history, meeting the same exclusion criteria as patients, were recruited via advertisement. In addition, HC were asked if they had first-degree relatives with psychiatric disorders".

The study was carried out following the latest version of the Declaration of Helsinki, and it was reviewed by the ethical committee of the four institutions. Written informed consent was obtained from all participants.

*Clinical assessment*

In order to gather clinical data, all patients were assessed by means of the Structured Clinical Interview for DSM Disorders (SCID-I-II) (First, Gibbon, Spitzer, Williams, Benjamin, 1997a, 1997b). The YMRS and HDRS-17 scores were used to evaluate the severity of manic and depressive symptomatology, respectively. All the participants also completed the Functional Assessment Short Test (FAST) (Rosa et al., 2007), a scale designed to assess psychosocial functional impairment in psychiatric patients, with higher scores indicating poorer psychosocial functioning. The full description of other clinical variables is reported in the Supplementary Material.

*Emotional intelligence assessment*

EI was evaluated using the Spanish version of the MSCEIT, V2.0 (Mayer et al., 2003). This instrument consists of 141 items and provides eight task scores that measure the four branches of EI: (i) Perceiving Emotions: to recognize and to appraise emotions accurately; (ii) Using Emotions: to access or generate feelings when they facilitate thoughts; (iii) Understanding Emotions: to understand complex emotions and how emotions transition from one stage to another, to recognize the causes of emotions, and to understand relationships among emotions; (iv) Managing Emotions: to stay aware of one's emotions, and to solve emotion-laden problems. The Perceiving Emotions and Using Emotions branches are assigned to the Experiential Area, while the Understanding Emotions and Managing Emotions branches are assigned to the Strategic Area. The test provides an overall score, the EI quotient (EIQ), and also scores in the two areas, in the four branches and in each of the specific tasks. Lower scores indicate poorer performance in EI. The average range of EIQ is 100, with a standard deviation (SD) of 15.

*Neuropsychological assessment*

All participants were evaluated using a comprehensive neuropsychological battery exploring different cognitive domains: Processing Speed, Working Memory, Verbal Learning and Memory, Visual Memory, Executive Functions and Attention. The neuropsychological battery comprised the Digit-symbol Coding, Symbol Search, Arithmetic, Digits, and Letter-Number sequencing subtests from Wechsler Adult Intelligence Scale (WAIS-III) (Wechsler, 1997), Phonemic (F-A-S) and Categorical (Animal naming) components of the Controlled Oral Word Association Test (COWAT) (Patterson, 2018), the Trail Making Test-A (TMT-A) and Trail Making Test-B (TMT-B) (Reitan, 1958), the California Verbal Learning Test (CVLT) (Delis, Kramer, Kaplan, & Over, 1987), the Rey Osterrieth Complex Figure (ROCF) (Rey, 1958), the computerized version of the Wisconsin Card Sorting Test (WCST) (Heaton, Chelune, Talley, Kay, & Curtiss, 1993), the Stroop Color-Word Interference Test (Golden, 1994), and the Continuous Performance Test–II (CPT-II), version 5 (Conners, 2002). Finally, estimated IQ was assessed with the (WAIS-III) vocabulary subtest (Wechsler, 1997).

*Statistical analysis*

Comparison of socio-demographic and clinical characteristics among groups (FEM, BD, and HC) was carried out using Chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. The Tukey's test was carried out for post-hoc comparisons to identify pair-wise differences between groups. Effect sizes (Glass's d) were also calculated to estimate the magnitude of the differences between the groups. Neurocognitive tests raw scores were standardized to z-scores based on HCs' performance (for further information on the calculation of the composites of neurocognitive domains see Supplementary Material). Performance on MSCEIT and the neurocognitive domains was compared across the three groups using generalized linear models (GLM). All models were adjusted for those clinical and socio-demographic variables for which the three groups differed significantly. Then, a Bonferroni post-hoc correction was applied when significant main effects were present when

comparing the three groups, in order to identify pair-wise differences between groups. Estimated Marginal Means, adjusted for the other variables in the model, were reported for each variable of interest (i.e. EIQ), as well as the 95% Confidence Interval (CI), their Mean Difference (MD) and its Standard Error (SE).

Moreover, exploratory analyses were conducted to satisfy our secondary aim. In order to assess which socio-demographic, clinical and neuropsychological variables were associated with IEQ in the FEM and in the BD groups, we first performed Pearson bivariate correlations to identify those continuous variables significantly associated with EIQ. For categorical variables (i.e. sex), Student's t-test was run to evaluate the distribution of EIQ. Only those variables with a p value ≤0.05 were then entered into a hierarchical multiple regression model, aimed at evaluating the association between socio-demographic, clinical and neuropsychological variables and EIQ.

All statistical analyses were conducted using IBM SPSS Statistics version 23.0. Statistical significance was set at $p<0.05$.

**Results**

The total sample included 184 participants: 48 patients with a FEM in full or partial clinical remission, 75 euthymic BD patients and 61 HC. Socio-demographic variables among groups are reported in Table 1.

*Clinical features among the groups*

Regarding clinical variables, there were significant differences between patient groups (FEM and chronic BD) and HC in the total HDRS-17 ($p<0.001$) and YMRS scores ($p<0.001$), as well as in the overall psychosocial functioning ($p<0.001$). Both patient groups presented more subsyndromal depressive symptoms than HC (BD versus HC $p<0.001$, FEM versus HC $p<0.001$, respectively), whereas chronic BD patients exhibited more subsyndromal manic symptoms

than HC (p<0.001). No statistically significant differences were found in subsyndromal symptoms between patient groups. Significant group differences in the FAST total score were observed for both the patient groups, presenting significantly decreased functioning compared to HC (p<0.001). In addition, chronic BD patients showed poorer psychosocial function than patients in the FEM group (p<0.001).

Significant differences were observed in the comparison between chronic BD and FEM patients in age at first hospitalization (p=0.009), being lower in the case of the FEM group (p=0.009), but not regarding the polarity at onset (p=0.265) or the presence of family history for either BD (p=1.000) or major depressive disorder (p=0.986). Groups differed in terms of duration of illness (p<0.001) and total number of episodes (p<0.001). Patients after a FEM experienced an average of 1.19 episodes of mania whilst BD chronic patients an average of 3.62.

*Emotional intelligence performance*

Patients in the FEM group performed similarly to HC on MSCEIT Total score (Supplementary Table 1, Figure 1) an all measures of MSCEIT (Supplementary Table 1, Figure 2).

Significant differences were found for EIQ (p=0.005) and in the MSCEIT Understanding Emotions branch (p=0.007), even after controlling for age, subsyndromal manic and depressive symptoms. Bonferroni post-hoc testing revealed that BD patients presented significantly lower EIQ than HC (MD=10.09, SE=3.14, p=0.004) but no difference was found neither between HC and FEM patients (MD=2.69, SE=3.56, p=1.000) nor between FEM and chronic BD patients (MD=7.40, SE=3.61, p=0.121).

In addition, BD patients performed more poorly than HC on the Understanding Emotions branch (MD=7.46, SE=2.53, p=0.010). A trend-level difference was reported between patient groups, with BD patients showing lower scores than those in the FEM group (MD=-6.84, SE=2.93, p=0.056). No significant difference was reported between FEM patients and HC (MD=0.62, SE=2.87, p=1.000).

*Neurocognitive performance*

Concerning neurocognitive domains, there was a main effect of group in terms of processing speed ($p<0.001$), verbal memory ($p<0.001$), working memory ($p<0.001$), executive functions ($p<0.001$), visual memory ($p=0.033$) and attention ($p<0.001$), after controlling for age, subsyndromal depressive and manic symptoms (Supplementary Table 1, Figure 3).

Bonferroni post-hoc pair-wise comparisons between groups revealed that FEM patients performed worse than HC on processing speed (MD=0.96, SE=0.24, $p<0.001$), executive functions (MD=0.83, SE=0.30, $p=0.015$) and attention (MD=1.02, SE=0.26, $p<0.001$), but not on verbal, working and visual memory. On the contrary, FEM patients performed better than chronic BD patients on processing speed (MD=0.97, SE=0.25, $p<0.001$), executive functions (MD=1.02, SE=0.30, $p=0.002$) and attention (MD=1.79, SE=0.28, $p<0.001$), but not on verbal memory, working memory and visual memory. Chronic BD patients performed significantly worse than HC on all neurocognitive domains: processing speed (MD=1.93, SE=0.22, $p<0.001$), verbal memory (MD=1.00, SE=0.24, $p<0.001$), working memory (MD=0.72, SE=0.18, $p<0.001$), executive functions (MD=1.85, SE=0.26, $p<0.001$), visual memory (MD=0.51, SE=0.20, $p=0.035$) and attention (MD=2.81, SE=0.21, $p<0.001$).

*Socio-demographic, clinical and neurocognitive variables associated with EIQ in FEM patients*

In FEM patients, lower EIQ correlated with poorer performance in verbal memory ($r=0.371$, $p=0.011$). Also, male patients showed lower scores in EIQ than females ($t=2.054$, $p=0.046$) (see table 3). No other clinical variable correlated with EIQ.

After including the variables significant in bivariate analyses in a hierarchical regression model ($F(2,43)=6.202$, adjusted $R^2=0.188$, $p=0.004$), both male sex ($\beta=-0.293$, $p=0.034$) and the verbal memory domain ($\beta=0.374$, $p=0.008$) were significantly associated with EIQ, with a higher effect exerted by verbal memory performance.

Results for the chronic BD groups are reported in Supplementary Tables 3 and 4.

**Discussion**

To the best of our knowledge, this is the first study to comprehensively assess EI in patients after a FEM using the full MSCEIT version. The present study of EIQ in fully or partially remitted FEM (n=48) versus chronic BD-I (n=75) and HC (n=61) showed three main findings. While patients after a FEM presented intermediate EIQ scores between HC and chronic BD, with EIQ scores significantly lower in BD than HC, in the MSCEIT branches, FEM patients' performance was globally comparable to HC. In addition, lower performance in Understanding Emotions branch was found for chronic BD patients in comparison with HC. Whilst EI appeared to be preserved in FEM patients, neurocognition, and particularly processing speed, attention and executive functions performance was already impaired at the early stages of the illness. Lower EIQ in FEM was associated with male sex and lower performance in verbal memory.

Although EI has been widely studied in patients in later stages of BD (Aparicio et al., 2017; Beatrice Frajo-Apor et al., 2020; Samamé et al., 2015; Varo et al., 2019a), little is known about the EI performance of patients after a FEM and the course of EI impairment across the clinical stages of BD and the evidence is seldom conflicting. So far, only two studies assessed some level of EI patients after a FEM (Daros et al., 2014; Szmulewicz et al., 2019). Nonetheless, these studies were characterized by small sample size, which limited the generalizability of results, and only evaluated the lower levels of EI abilities such as labeling, discrimination, and appraising emotions. Daros and colleagues assessed 24 non-affective FEP and 16 FEM patients in comparison with 35 HC both during acute psychosis and after seven weeks of treatment (Daros et al., 2014). Both groups of patients presented difficulties recognizing facial expressions that did not resolve with treatment and clinical stabilization. In a small sample of 26 FEM patients, Szmulewicz and colleagues found that in comparison with HC, FEM patients presented a compromised cognitive theory of mind performance characterized by a reduced ability to infer intentions from others whilst the affective theory of mind performance was

preserved, indicating that FEM patients were capable to detect other's emotions and feelings (Szmulewicz et al., 2019). In the present study, FEM patients, in comparison with HC, did not present difficulties in EI, assessed through the full version of MSCEIT, which evaluates both lower and higher EI abilities.

Although EI appeared to be overall preserved among the patients after a FEM assessed in our study, their neurocognitive performance on processing speed, attention and executive functions was mildly impaired. These findings are in line with a recent study assessing cognitive groups of patients after recovery from a FEM (Chakrabarty et al., 2021). The authors identified that almost the 50% of FEM patients reported selective cognitive impairment after recovery, with pronounced deficits in processing speed and lower performance in verbal memory, working memory and executive functioning in comparison with HC. Furthermore, in line with our results, these deficits seemed to be stable over time in those patients that experienced a recurrence. Particularly, Kozicky and colleagues (2014) found that this impairment in cognitive performance was mostly evident in those who experienced longer manic or hypomanic episodes (Kozicky et al., 2014).

Patients suffering from chronic BD, included in this study, presented impairment in all the cognitive domains and lower EIQ and difficulties in the MSCEIT Understanding emotions branch. Our results are in line with previous studies, supporting the presence of less severe impairment in SC compared to neurocognitive domains in patients with BD (Bilderbeck et al., 2016). Deficits of EI were not observed in FEM patients. This might suggest that more severe SC deficits might be associated with other conditions, such as schizophrenia, instead of BD since in non-affective FEP patients EI impairment was found to start early in the course of illness and to remain stable (Green et al., 2012). Given that EI is more severely affected in psychosis than in mania, one may argue that patients reporting psychotic symptoms during the first episode of mania might show greater difficulties in EI than patients without psychotic symptoms. Despite this, we did not find any difference in terms of EIQ between FEM patients

who presented Psychotic Symptoms at Onset and those who did not. Our findings suggest that neurocognition seemed to be already altered at the first symptomatic manic presentation, whilst EI started out intact in the FEM patients and then slightly worsened with illness course. One recurring question is whether neurocognition and SC in BD are sufficiently distinct to be considered separately. Previous studies investigating the relationship between neurocognition and EI have yielded mixed and inconclusive results. While there are studies that reported that lower levels of EI may be mediated by neurocognitive abilities (Aparicio et al., 2017; Frajo-Apor et al., 2017), others have not found a relationship between the two constructs (Fanning, Bell, & Fiszdon, 2012). Our results highlight the connection between EI and neurocognition and the idea that they are two complementary but separated constructs (DeTore, Mueser, & McGurk, 2018), with partial overlap and with a different degree of impairment. Thus, our findings were in line with many other works supporting the idea that neurocognitive ability may represent a "necessary, but not sufficient" prerequisite for social cognitive abilities, especially in those that contain an emotional component (Bora, Veznedaroğlu, & Vahip, 2016; Lee et al., 2013; Varo et al., 2019). This view is consistent with studies from neuroimaging in social neuroscience (Mitchell, 2008). Nonetheless, the role of neurocognitive impairments on social cognition and EI in euthymic BD patients remains somewhat unclear. Therefore, the nature of this association should be the focus of further investigation.

Whilst in the present study the two groups of patients did not differ in terms of severity of symptoms at the time of evaluation, BD group performed worse than FEM group in measures of indicators assessing the burden of disease, such as longer duration of illness and higher total number of lifetime episodes, psychosocial functioning, and in the neurocognitive performance. Thus, our findings support the hypotheses that EI difficulties might be a result of the burden of disease and neurocognitive decline associated with the chronicity of the illness.

As for the socio-demographic, neurocognitive and clinical variables associated with EIQ in patients after a FEM, lower EIQ scores were found to be associated with male sex and lower

verbal memory performance. Regarding sex differences in EI, our findings are in line with previous studies in which men performed worse than women on EI in non-clinical samples (Pardeller, Frajo-Apor, Kemmler, & Hofer, 2017) and BD patients (Varo et al., 2019a). As for the role played by verbal memory in EI, our finding is in line with previous literature underlining how EI performance might be associated with cognitive abilities (Eack et al., 2010; Beatrice Frajo-Apor et al., 2020; Varo et al., 2019). In a previous study assessing BD patients, all neurocognitive domains were associated with EI (Varo et al., 2019). However, to date, it is difficult to ascertain which neuropsychological domain (among verbal memory, executive functions, psychomotor speed, working memory and attention) has a greater influence on social cognition, especially on EI. In the current study verbal memory resulted to be the central domain involved in EI ability. EI was assessed by MSCEIT which demands an accurate interpretation of the semantic meaning of the social situation. It involves exercises related to verbal memory skills, such as association, categorization and mental imagery. In another study assessing EI and cognitive abilities in healthy adults, verbal fluency was the only cognitive domain associated with EIQ (Pardeller, Frajo-Apor, Kemmler, & Hofer, 2017).

In the present study, being men with worse performance in verbal memory arose as risk factors for worse EI ability. In consequence, an exhaustive assessment of SC and EI in this population would be recommended in order to tailor specific early intervention strategies (Vieta et al., 2018).

The findings of the present study should be interpreted in light of the following limitations. First, since our study used data from two separate projects, the groups were not matched and there were uneven sample sizes. Moreover, some inclusion criteria differ between studies. In order to partially overcome this limitation, we decided to add age and both depressive and manic subsyndromal symptoms as covariates in the statistical models. Second, the cross-sectional design of this study did not enable us to determine causal inferences between EI, clinical symptomatology, and neurocognition, nor to examine the changes in EI ability

associated with neuroprogression in BD. Since the FEM sample size was derived from a longitudinal study, we will be able to provide insight on the course of EI in the early phases of BD, for the patients included in the present study, as soon as the follow-up will be ended. Similarly, the description of influence of treatment should be further detailed. Also, the ability of MSCEIT test to discriminate individuals at the mean and high level of EI has been questioned (Fiori et al., 2014).

Despite these limitations, the strength of the present study is to provide insight on EI in patients in the early stage of the illness, an almost unexplored aspect in this group of patients and is the first investigation aimed at understanding which socio-demographic, clinical, and neurocognitive factors may contribute to EI levels in the early stages of BD. Furthermore, the present study can rely on a quite big sample size for both FEM and BD patients, allowing for a cross-sectional comparison of the EI abilities in two different phases of BD using the four branches of MSCEIT. In particular, BD patients have difficulties in EI but not patients that experienced their FEM over last three years. Therefore, our findings suggest that EI is preserved in early stages, which represents an optimistic result. However, this might worsen in later stages of the disease. Difficulties in EI performance might be possibly associated with the increasing burden of disease, and neuroprogression in chronic BD, although this hypothesis will need to be confirmed in longitudinal studies. On the contrary, neurocognition and psychosocial functioning seemed to be impaired at an earlier stage than EI. These findings have important implications in terms of early interventions, which should address not only neurocognitive performance but also social cognitive functioning at the early stages in order to prevent or mitigate the cognitive decline often associated with BD in the long-term (Vieta et al., 2018). Both EI and neurocognitive performance should be assessed in the early stages of the disease. While neurocognitive performance could be already impaired in the early stages and thus represents a target of secondary preventive intervention, EI could be not impaired in

the early stages of the disease and should be addressed with primary preventive interventions aimed at possibly avoiding EI difficulties in these patients.

**Disclosures**

**Role of the Funding Source:** The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Conflicts of interest**

EV has received grants and served as consultant, advisor or CME speaker for the following entities (unrelated to the present work): AB-Biotics, Abbott, Allergan, Angelini, Dainippon Sumitomo Pharma, Ferrer, Gedeon Richter, Janssen, Lundbeck, Otsuka, Sage, Sanofi-Aventis, and Takeda. AMA has received funding for research projects and/or honoraria as a consultant or speaker for the following companies and institutions (work unrelated to the topic of this manuscript): Otsuka, Pfizer, AstraZeneca, Bristol-Myers Squibb, Lundbeck, the Spanish Ministry of Economy and Competitiveness and Instituto de Salud Carlos III. AB has received grants and served as consultant, advisor or CME speaker for the following entities in the last five years (unrelated to the present work): Janssen, Lundbeck, Otsuka and Pfizer. PAS has been a consultant to and/or has received honoraria or grants from Adamed, CIBERSAM, European Comission, Government of the Principality of Asturias, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, Plan Nacional sobre Drogas and Servier. MPGP has been a consultant to and/or has received honoraria/grants from Angelini, Alianza Otsuka-Lundbeck, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, and SAGE Therapeutics.
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**Data Availability Statement**

The data that support the findings of this study are available on request from the corresponding authors.

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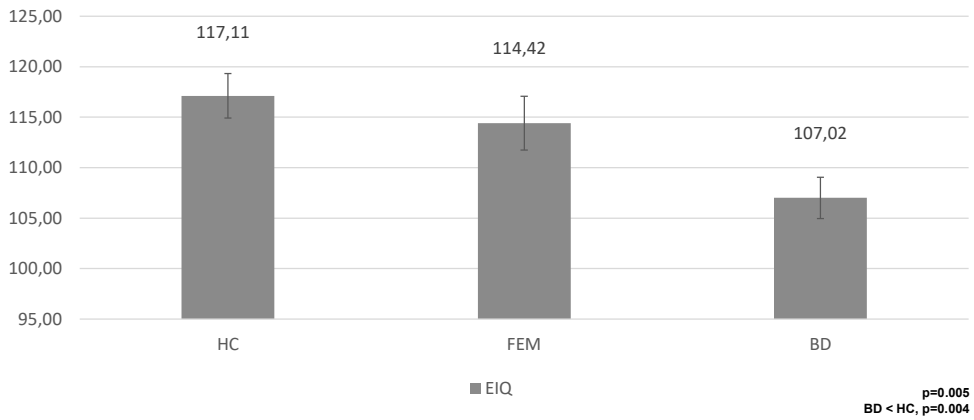
**Figure legends**

**Figure 1: Emotional Intelligence Quotient with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

**Figure 2: Mean MSCEIT scores with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

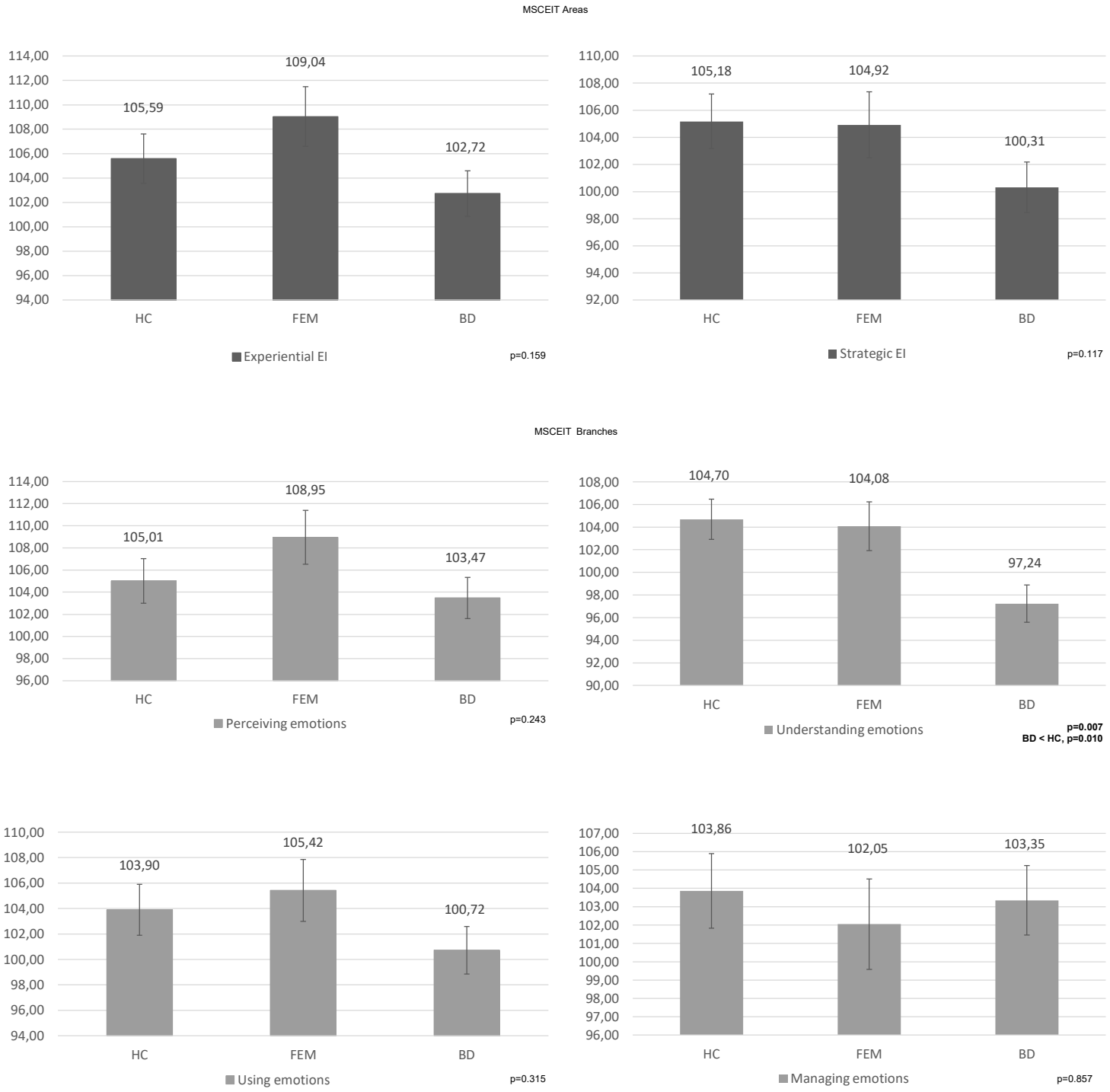
**Figure 3. Neuropsychological composite mean scores with error bars in the three groups**
Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; PS=Processing Speed Composite; VM=Verbal Memory Composite; WM=Working Memory Composite; EF=Executive Functions Composite; VisM=Visual Memory Composite; AT= Attention composite

**Figure 1. Emotional Intelligence Quotient with error bars in the three groups**




Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

**Figure 2. Mean MSCEIT scores with error bars in the three groups**




Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

Figure 3 bw

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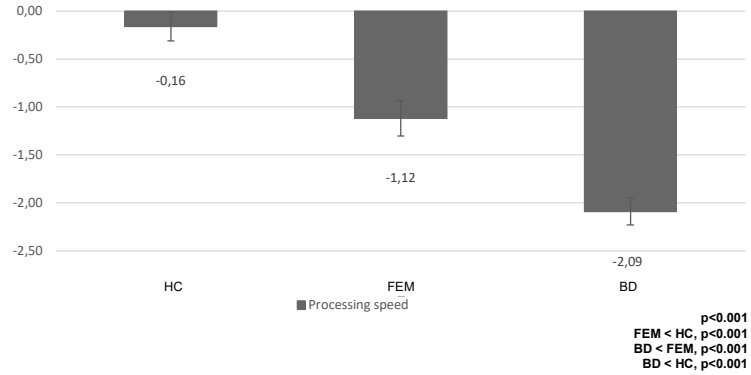
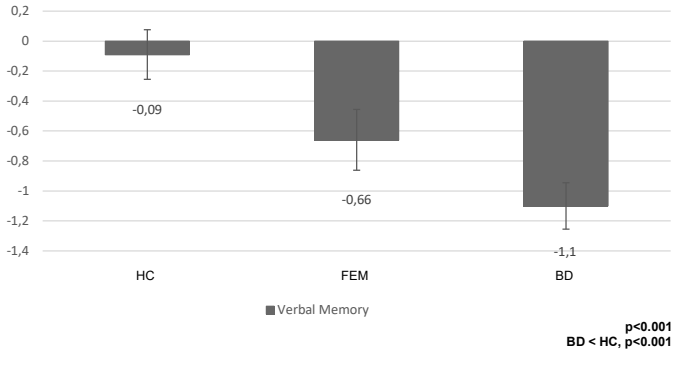
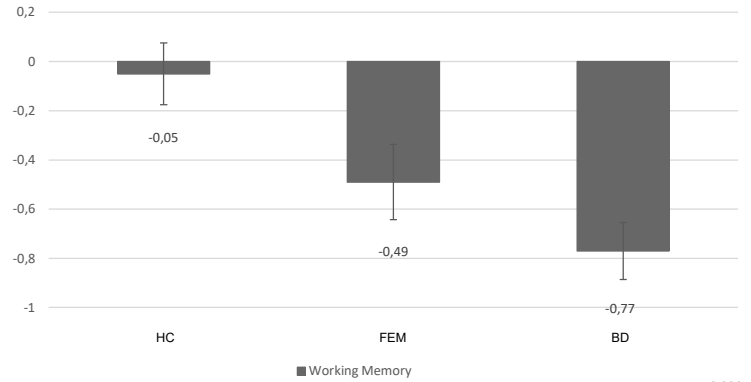
**Figure 3. Neuropsychological composite mean scores with error bars in the three groups**



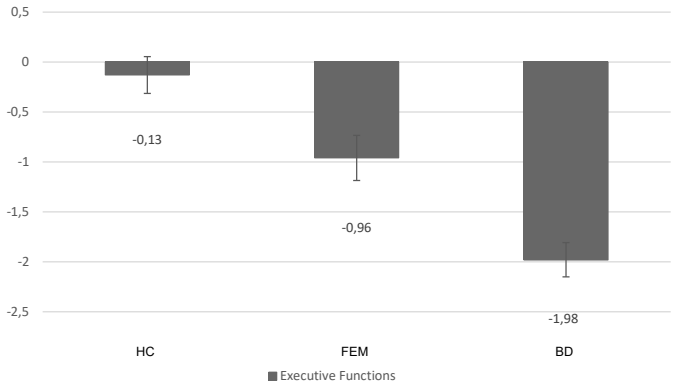

**p<0.001**
**FEM < HC, p<0.001**
**BD < FEM, p<0.001**
**BD < HC, p<0.001**



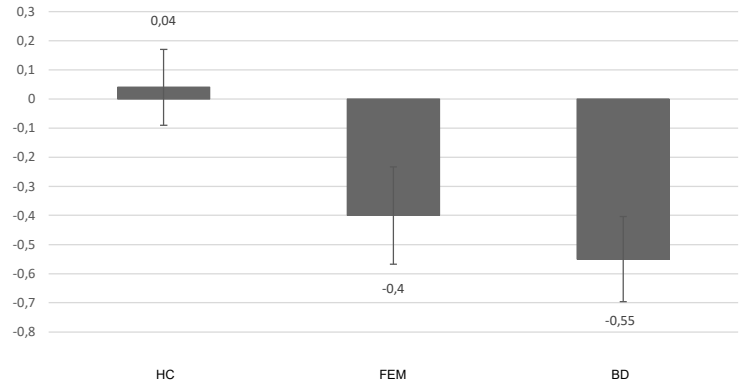

**p<0.001**
**BD < HC, p<0.001**



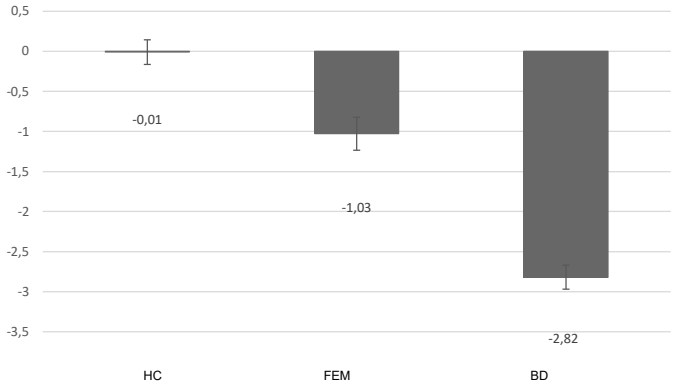

**p<0.001**
**BD < HC, p<0.001**




**p<0.001**
**FEM < HC, p=0.015**
**BD < FEM, p=0.002**
**BD < HC, p<0.001**




**p=0.003**
**BD < HC, p=0.035**




**p<0.001**
**FEM < HC, p<0.001**
**BD < FEM, p<0.001**
**BD < HC, p<0.001**

Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls.

Figure 1 colour

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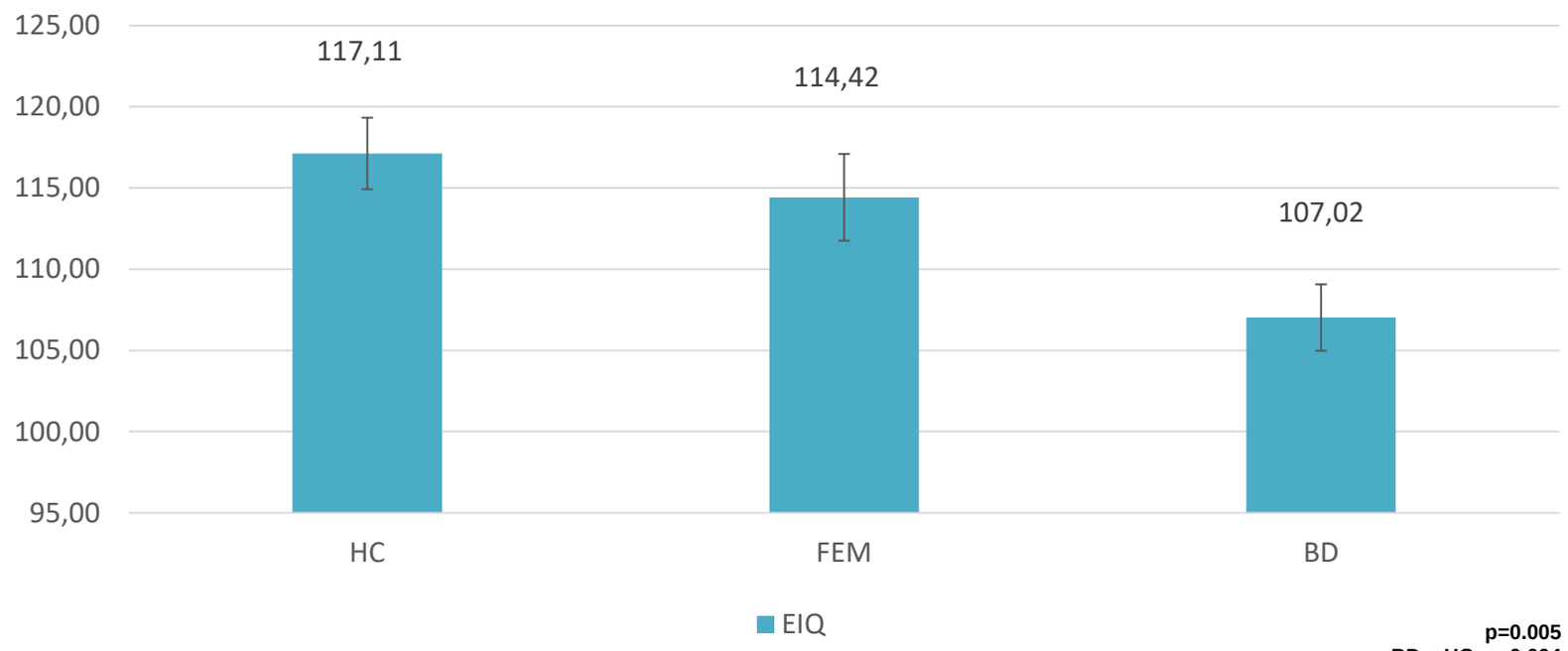
**Figure 1. Emotional Intelligence Quotient with error bars in the three groups**




Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

Figure 2 colour

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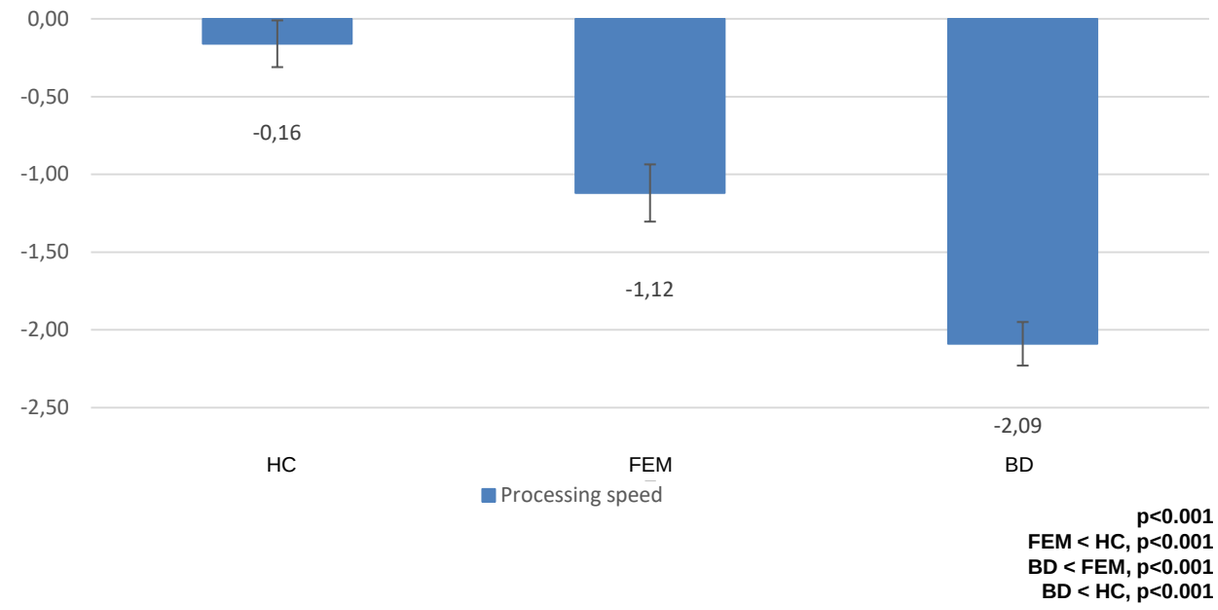
**Figure 2. Mean MSCEIT scores with error bars in the three groups**


Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls; MSCEIT=Mayer-Salovey-Caruso Intelligence Test.

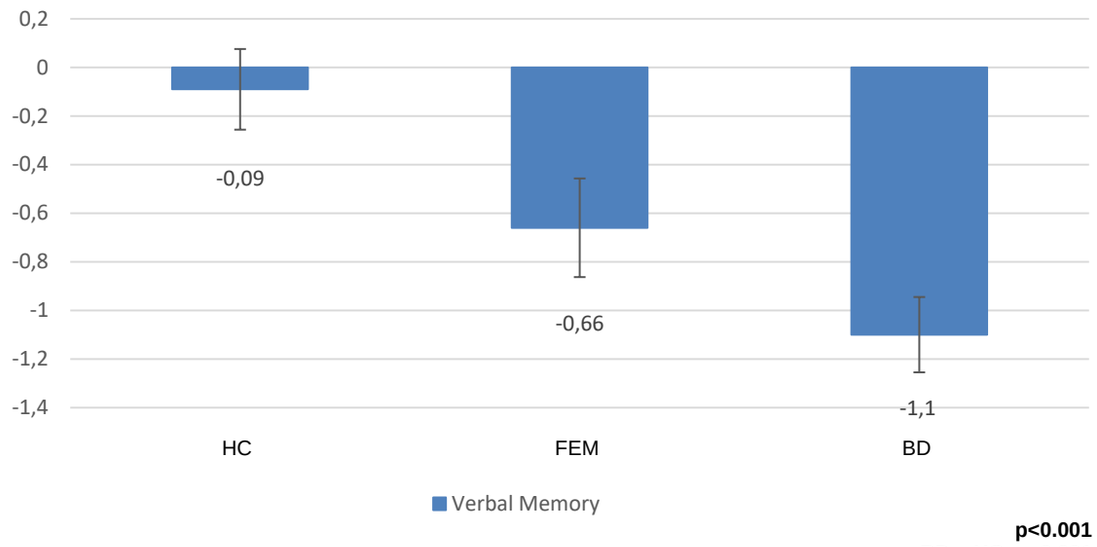
Figure 3 colour



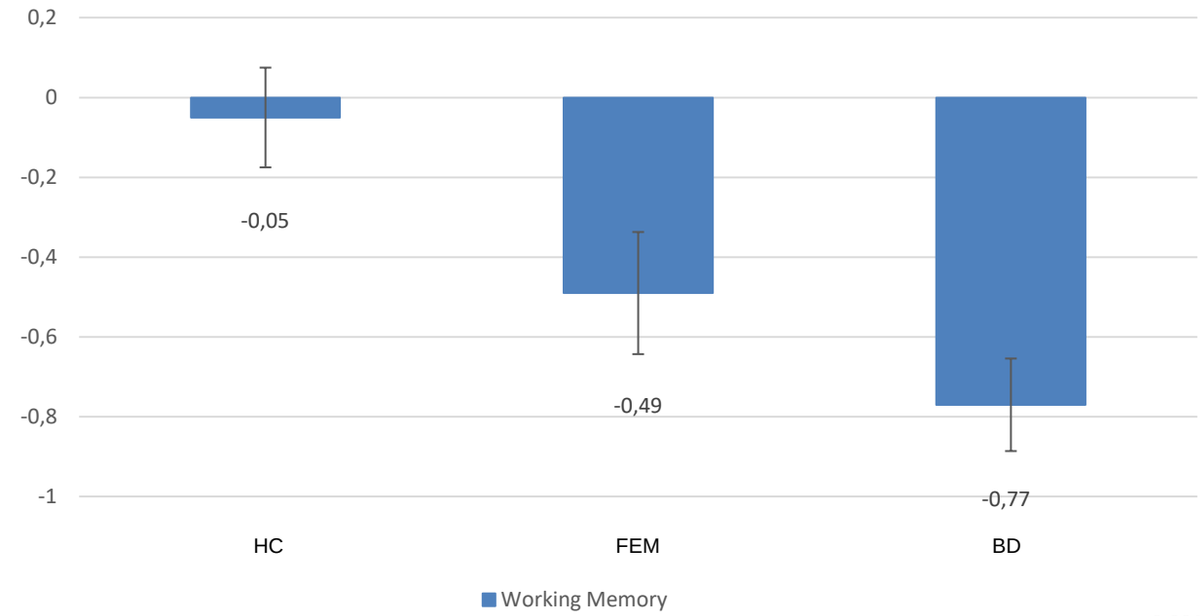
**Figure 3. Neuropsychological composite mean scores with error bars in the three groups**



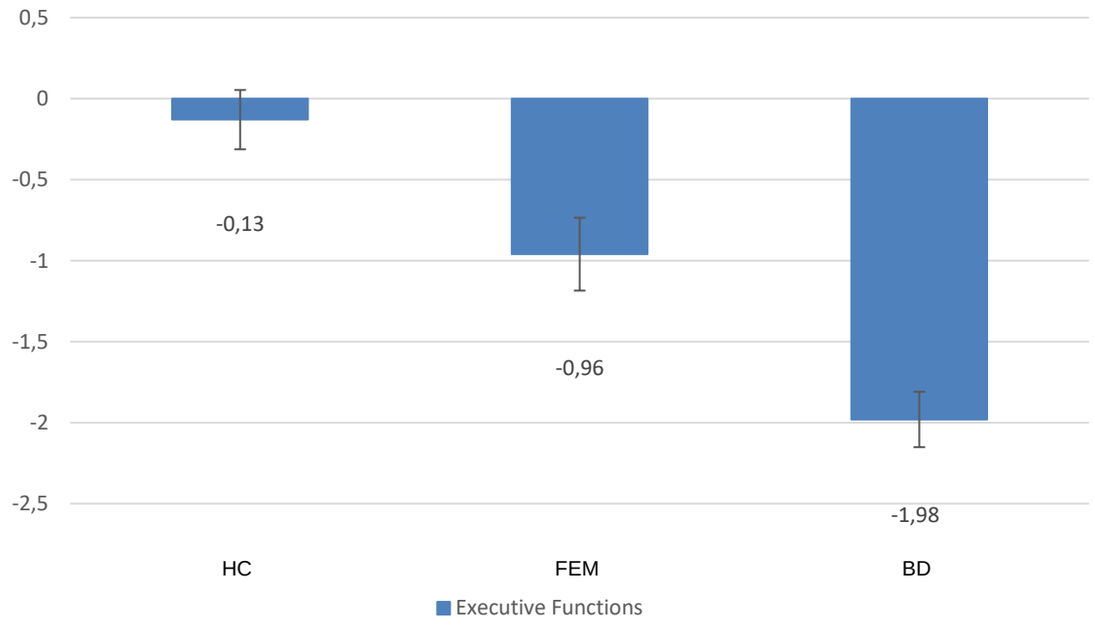

**p<0.001**
**FEM < HC, p<0.001**
**BD < FEM, p<0.001**
**BD < HC, p<0.001**



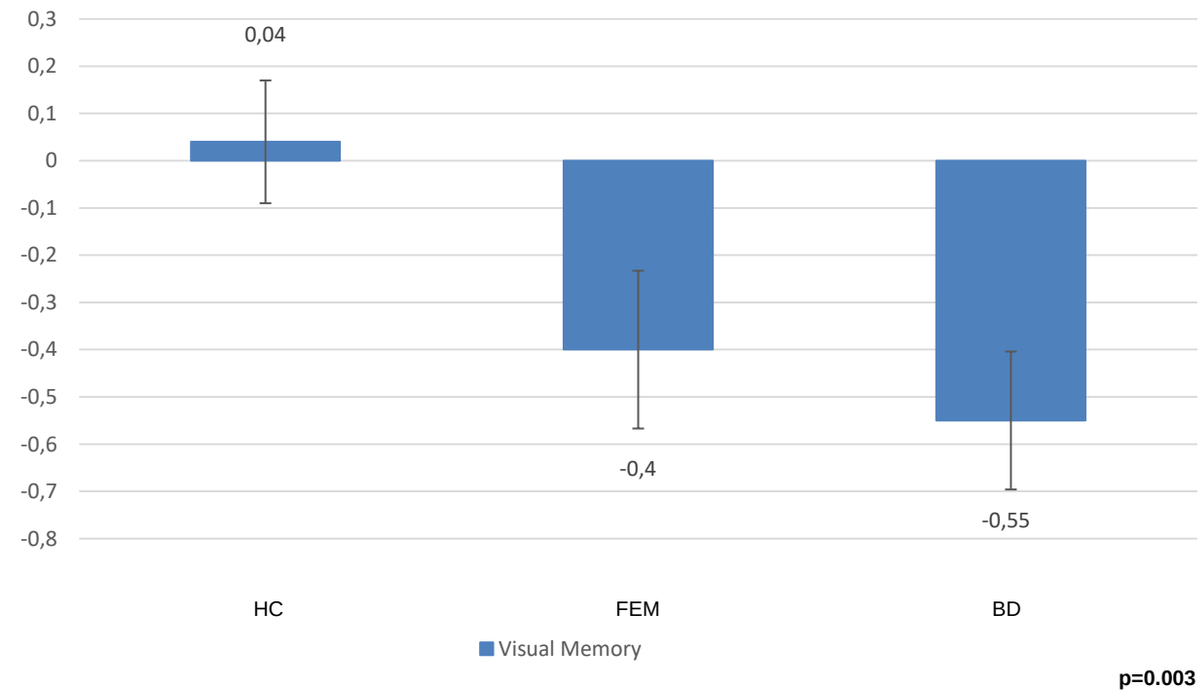

**p<0.001**
**BD < HC, p<0.001**



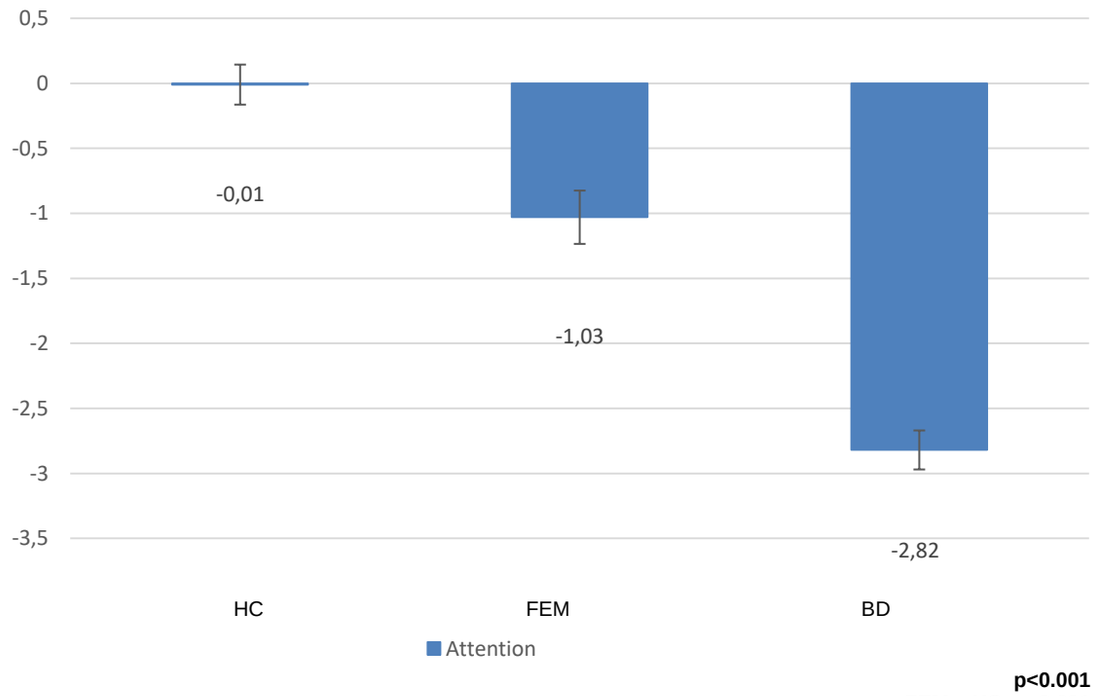

**p<0.001**
**BD < HC, p<0.001**




**p<0.001**
**FEM < HC, p=0.015**
**BD < FEM, p=0.002**
**BD < HC, p<0.001**




**p=0.003**
**BD < HC, p=0.035**




**p<0.001**
**FEM < HC, p<0.001**
**BD < FEM, p<0.001**
**BD < HC, p<0.001**

Abbreviations: BD=Bipolar Disorder; FEM=First Episode Mania; HC=Healthy Controls.

**Table 1. Socio-demographic and clinical variables of First Episode Mania (FEM) or Bipolar Disorder (BD) patients and Healthy Controls (HC)**

| Variables | | FEM (A) (n=48, 26.09%) | BD (B) (n=75, 40.76%) | HC (C) (n=61, 33.15%) | Statistics $\chi^2$ or F | p | Pairwise Comparison Tukey HSD or Chi-square* | p | Effect Size (Glass's delta) |
|---|---|---|---|---|---|---|---|---|---|
| **Socio-demographic Variables** | | | | | | | | | |
| **Age** | Mean (SD) | 28.31 (7.40) | 45.87 (10.53) | 38.72 (11.09) | 44.970 | **<0.001** | B<A<C | **<0.001**<br>**<0.001**<br>**<0.001** | 1.40<br>0.68<br>2.37 |
| **Sex** (Women yes) | n (%) | 25 (52.1) | 45 (60.0) | 37 (60.7) | 0.989 | 0.637 | | | |
| **Civil Status** (Married yes) | n (%) | 12 (25.0) | 28 (37.3) | 28 (46.7) | 5.483 | 0.068 | A<C | **0.027** | |
| **Education Level** | n (%) | | | | 8.990 | **0.011** | | | |
| Secondary School | | 26 (54.2) | 43 (57.3) | 20 (32.8) | | | A>C<br>B>C | **0.041**<br>**0.006** | |
| University | | 22 (45.8) | 32 (42.7) | 41 (67.2) | | | A<C<br>B<C | **0.041**<br>**0.006** | |
| **Employment** | n (%) | | | | 62.335 | **<0.001** | | | |
| Studying | | 16 (33.3) | 4 (5.3) | 6 (9.8) | | | B<A<br>C<A | **<0.001**<br>**0.005** | |
| Working | | 15 (31.3) | 24 (32.0) | 49 (80.3) | | | A<C<br>B<C | **<0.001**<br>**<0.001** | |
| Not studying /Not working | | 17 (35.4) | 47 (62.7) | 6 (9.8) | | | A<B<br>C<A<br>C<B | **0.003**<br>**0.006**<br>**<0.001** | |
| **Estimated IQ** | Mean (SD) | 105.13 (11.96) | 106.12 (15.70) | 109.75 (9.89) | 2.008 | 0.137 | | | |
| **Clinical Variables** | | | | | | | | | |
| **Family History of BD** | n (%) | 12 (25.0) | 17 (23.3) | - | <0.001 | 1.000 | | | |
| **Family History of MDE** | n (%) | 18 (37.5) | 26 (35.6) | - | <0.001 | 0.986 | | | |
| **Age at Onset** | Mean (SD) | 24.15 (8.40) | 25.21 (8.94) | - | 0.049 | 0.825 | | | |
| **Onset Polarity** | n (%) | | | | 2.562 | 0.265 | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Mania | | 25 (52.1) | 30 (40.0) | - | | | | | |
| Depression | | 20 (41.7) | 42 (56.0) | - | | | | | |
| Hypomania | | 3 (6.3) | 3 (4.0) | - | | | | | |
| **Age at First Hospitalization**[¥] | Mean (SD) | 27.57 (7.58) | 31.20 (11.20) | - | 7.184 | **0.009** | | | **0.48** |
| **Duration of Illness** | Mean (SD) | 4.17 (5.01) | 20.65 (8.98) | - | 13.058 | **<0.001** | | | **3.29** |
| **Number of Episodes** | Mean (SD) | | | | | | | | |
| Total | | 2.35 (1.28) | 10.41 (8.55) | - | 19.480 | **<0.001** | | | **6.29** |
| Mania | | **1.19 (0.53)** | **3.62 (4.00)** | | **19.969** | **<0.001** | | | **4.62** |
| Hipomania | | **0.23 (0.59)** | **1.86 (3.23)** | | **19.435** | **<0.001** | | | **2.76** |
| Depression | | **0.88 (0.98)** | **4.45 (4.31)** | | **21.127** | **<0.001** | | | **3.64** |
| Mixed episodes | | **0.06 (0.24)** | **0.46 (1.4)** | | **13.351** | **<0.001** | | | **1.67** |
| **Psychiatric Comorbidities** | n (%) | | | | | | | | |
| Axis I | | 4 (8.3) | 17 (23.0) | - | 3.412 | 0.065 | | | |
| Axis II | | 4 (8.3) | 15 (20.3) | - | 2.313 | 0.128 | | | |
| Axis III | | 11 (22.9) | 19 (26.0) | - | 0.030 | 0.863 | | | |
| **FAST Total Score**[†] | Mean (SD) [Range] | 16.79 (13.16) [1-64] | 25.53 (14.45) [0-61] | 5.27 (4.48) [0-20] | 49.449 | **<0.001** | B<A<C | **<0.001**<br>**<0.001**<br>**<0.001** | 0.87<br>4.45<br>0.64 |
| **YMRS Total Score**[†] | Mean (SD) [Range] | 1.10 (0.63) [0-7] | 1.68 (1.63) [0-6] | 0.63 (1.01) [0-3] | 8.556 | **<0.001** | C<B | **<0.001** | 1.01<br>0.87 |
| **HAM-D Total Score**[†] | Mean (SD) [Range] | 4.15 (2.94) [0-10] | 4.07 (2.52) [0-8] | 1.67 (1.78) [0-6] | 20.173 | **<0.001** | C<A<br>C<B | **<0.001**<br>**<0.001** | 0.84<br>0.91 |
| **Psychotropic Medication**[†] | n (%) | | | | | | | | |
| Lithium | | 38 (79.2) | 50 (66.7)) | - | 1.674 | 0.196 | | | |
| Antiepileptic | | 8 (16.7) | 38 (50.7) | - | 15.404 | **<0.001** | | | |
| Antipsychotic | | 25 (52.1) | 59 (78.7) | - | 8.364 | **0.004** | | | |
| Antidepressant | | 4 (8.3) | 28 (37.3) | - | 11.326 | **0.001** | | | |

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines | 7 (14.6) | 13 (17.3) | - | 0.023 | 0.879 |

Abbreviations: **BD**=Bipolar Disorder; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

*Only statistically significant or almost significant comparisons are reported. **Bold** for statistically significant values

†At Time of Evaluation **ˇ Missing information for 7 FEM. 4 FEM and 14 BD patients had not history of hospitalization**

Table 2. MSCEIT and Neuropsychological Scores of First Episode Mania (FEM) or Bipolar Disorder (BD) patients and Healthy Controls (HC)

| Variables | | FEM (A) (n=48, 26.09%) | BD (B) (n=75, 40.76%) | HC (C) (n=61, 33.15%) | Statistics $\chi^2$ | p | Pairwise Comparison* | p‡ |
|---|---|---|---|---|---|---|---|---|
| **Emotional Intelligence** | | | | | | | | |
| MSCEIT EIQ | Mean (IC 95%) | 114.42 (109.19 – 119.66) | 107.02 (103.01 – 111.03) | 117.11 (112.80 – 121.43) | 10.748 | 0.005 | B<C | 0.004 |
| MSCEIT Experiential EI | | 109.04 (104.25 – 113.82) | 102.72 (99.06 – 106.39) | 105.59 (101.65 – 109.54) | 3.681 | 0.159 | | |
| MSCEIT Strategic EI | | 104.92 (100.68 – 109.17) | 100.31 (97.05 – 103.56) | 105.18 (101.68 – 108.68) | 4.293 | 0.117 | | |
| MSCEIT Perceiving emotions | | 108.95 (104.18 – 113.72) | 103.47 (99.81 – 107.13) | 105.01 (101.07 – 108.95) | 2.830 | 0.243 | | |
| MSCEIT Using emotions | | 105.42 (100.65 – 110.19) | 100.72 (97.07 – 104.38) | 103.90 (99.97 – 107.84) | 2.308 | 0.315 | | |
| MSCEIT Understanding emotions | | 104.08 (99.86 – 108.31) | 97.24 (94.01 – 100.48) | 104.70 (101.22 – 108.19) | 9.955 | 0.007 | B<C<br>B<A | 0.010<br>0.056 |
| MSCEIT Managing emotions | | 102.05 (97.22 – 106.89) | 103.35 (99.65 – 107.05) | 103.86 (99.87 – 107.85) | 0.308 | 0.857 | | |
| **Neurocognition** | | | | | | | | |
| Processing Speed Composite | | -1.12 (-1.48 – -0.76) | -2.09 (-2.37 – -1.82) | -0.16 (-0.45 – 0.13) | 80.454 | <0.001 | A<C<br>B<C<br>B<A | <0.001<br><0.001<br><0.001 |
| Verbal Memory Composite | | -0.66 (-1.06 – -0.26) | -1.10 (-1.40 – -0.79) | -0.09 (-0.42 – 0.23) | 17.828 | <0.001 | B<C | <0.001 |
| Working Memory Composite | | -0.49 (-0.79 – -0.19) | -0.77 (-1.00 – -0.55) | -0.05 (-0.29 – 0.20) | 16.675 | <0.001 | B<C | <0.001 |
| Executive Functions Composite | | -0.96 (-1.40 – -0.52) | -1.98 (-2.31 – -1.64) | -0.13 (-0.49 – 0.23) | 49.356 | <0.001 | A<C<br>B<C<br>B<A | 0.015<br><0.001<br>0.002 |
| Visual Memory Composite | | -0.40 (-0.73 – -0.07) | -0.55 (-0.84 – -0.26) | 0.04 (-0.29 – 0.22) | 6.852 | 0.033 | B<C | 0.035 |
| Attention Composite | | -1.03 (-1.43 – -0.63) | -2.82 (-3.11 – -2.52) | -0.01 (-0.31 – 0.29) | 168.426 | <0.001 | A<C<br>B<C<br>B<A | <0.001<br><0.001<br><0.001 |

Abbreviations: EI=Emotional Intelligence; EIQ=Emotional Intelligence Quotient; IC 95%=Lower–Upper values within Wald Confidence Interval of 95%; MSCEIT=Mayer-Salovey-Caruso Emotional Intelligence Test;
*Only statistically significant or almost significant comparisons are reported. Bold for statistically significant values
†Bonferroni post-hoc significance

**Table 3. Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in First Episode Mania (FEM) patients**

| | | MSCEIT EIQ | | |
|---|---|---|---|---|
| | | | Statistics | |
| Variables | | Mean (SD) | Pearson correlation or Student t | p |
| **Socio-demographic variables** | | | | |
| Age | | | 0.181 | 0.219 |
| Sex | M | 107.78 (17.68) | 2.054 | **0.046** |
| | F | 117.64 (15.56) | | |
| Estimated IQ | | | 0.181 | 0.222 |
| **Clinical variables** | | | | |
| PAS | | | 0.070 | 0.638 |
| Family History of BD | Y | 112.75 (16.91) | 0.038 | 0.970 |
| | N | 112.97 (17.49) | | |
| Family History of MDE | Y | 113.61 (19.68) | 0.215 | 0.831 |
| | N | 112.50 (15.81) | | |
| Duration of Illness | | | 0.172 | 0.242 |
| Total Number of Episodes | | | 0.138 | 0.349 |
| Number of Psychiatric Hospitalizations | | | 0.096 | 0.520 |
| Age at first hospitalization | | | 0.300 | 0.071 |
| Psychotic Symptoms at Onset | Y | 113.00 (17.12) | 0.110 | 0.913 |
| | N | 112.00 (20.42) | | |
| Cannabis use in the prodromal phase | Y | 116.96 (14.34) | 1.195 | 0.238 |
| | N | 111.55 (16.31) | | |
| Alcohol use in the prodromal phase | Y | 111.03 (17.39) | 1.611 | 0.114 |
| | N | 119.50 (14.03) | | |
| HAM-D Total Score[‡] | | | 0.061 | 0.686 |

| | | | | |
|---|---|---|---|---|
| YMRS Total Score[‡] | | | 0.262 | 0.072 |
| FAST Total Score[‡] | | | 0.038 | 0.796 |
| **Psychotropic Medication** | | | | |
| Lithium | Y | 112.24 (18.55) | 0.720 | 0.478 |
| | N | 115.50 (10.71) | | |
| Antiepileptics | Y | 114.25 (9.97) | 0.350 | 0.730 |
| | N | 112.65 (18.35) | | |
| Antipsychotics | Y | 114.25 (15.16) | 0.534 | 0.596 |
| | N | 111.58 (19.20) | | |
| Antidepressants | Y | 114.50 (27.04) | 0.191 | 0.850 |
| | N | 112.77 (16.46) | | |
| Benzodiazepines | Y | 116.43 (24.54) | 0.581 | 0.564 |
| | N | 112.32 (15.92) | | |
| **Neurocognitive domains** | | | | |
| Processing Speed Composite | | | 0.111 | 0.457 |
| Verbal Memory Composite | | | 0.371 | **0.011** |
| Working Memory Composite | | | 0.055 | 0.713 |
| Executive Functions Composite | | | 0.136 | 0.367 |
| Visual Memory Composite | | | 0.008 | 0.961 |
| Attention Composite | | | 0.059 | 0.705 |

Abbreviations: **BD**=Bipolar Disorder; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **PAS**=Premorbid Adjustment Scale; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale
**Bold** for statistically significant values
[†]At Time of Evaluation

**Table ~~3~~ 2. Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in First Episode Mania (FEM) patients**

| | | MSCEIT EIQ | | |
|---|---|---|---|---|
| | | Mean (SD) | Statistics | |
| **Categorical variables** | | | **Student t** | **p** |
| Sex | M | 107.78 (17.68) | 2.054 | **0.046** |
| | F | 117.64 (15.56) | | |
| Family History of BD | Y | 112.75 (16.91) | 0.038 | 0.970 |
| | N | 112.97 (17.49) | | |
| Family History of MDE | Y | 113.61 (19.68) | -0.215 | 0.831 |
| | N | 112.50 (15.81) | | |
| Psychotic Symptoms at Onset | Y | 113.00 (17.12) | -0.110 | 0.913 |
| | N | 112.00 (20.42) | | |
| Cannabis use in the prodromal phase | Y | 116.96 (14.34) | -1.195 | 0.238 |
| | N | 111.55 (16.31) | | |
| Alcohol use in the prodromal phase | Y | 111.03 (17.39) | 1.611 | 0.114 |
| | N | 119.50 (14.03) | | |
| Lithium | Y | 112.24 (18.55) | 0.720 | 0.478 |
| | N | 115.50 (10.71) | | |
| Antiepileptics | Y | 114.25 (9.97) | -0.350 | 0.730 |
| | N | 112.65 (18.35) | | |
| Antipsychotics | Y | 114.25 (15.16) | -0.534 | 0.596 |
| | N | 111.58 (19.20) | | |
| Antidepressants | Y | 114.50 (27.04) | -0.191 | 0.850 |
| | N | 112.77 (16.46) | | |
| Benzodiazepines | Y | 116.43 (24.54) | -0.581 | 0.564 |
| | N | 112.32 (15.92) | | |
| **Continuous variables** | | | **Pearson correlation** | **p** |
| Age | | | 0.181 | 0.219 |
| Estimated IQ | | | 0.181 | 0.222 |
| PAS | | | 0.070 | 0.638 |

| | | |
|---|---|---|
| Duration of Illness | 0.172 | 0.242 |
| Total Number of Episodes | -0.138 | 0.349 |
| Number of Psychiatric Hospitalizations | -0.096 | 0.520 |
| Age at first hospitalization | 0.300 | 0.071 |
| HAM-D Total Score† | -0.061 | 0.686 |
| YMRS Total Score† | -0.262 | 0.072 |
| FAST Total Score† | -0.038 | 0.796 |
| Processing Speed Composite | 0.111 | 0.457 |
| Verbal Memory Composite | 0.371 | **0.011** |
| Working Memory Composite | -0.055 | 0.713 |
| Executive Functions Composite | 0.136 | 0.367 |
| Visual Memory Composite | -0.008 | 0.961 |
| Attention Composite | 0.059 | 0.705 |

Abbreviations: **BD**=Bipolar Disorder; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **PAS**=Premorbid Adjustment Scale; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale
**Bold** for statistically significant values
†At Time of Evaluation

**Table 1. Socio-demographic and clinical variables of First Episode Mania (FEM) or Bipolar Disorder (BD) patients and Healthy Controls (HC)**

| Variables | | FEM (A) (n=48, 26.09%) | BD (B) (n=75, 40.76%) | HC (C) (n=61, 33.15%) | Statistics $\chi^2$ or F | p | Pairwise Comparison Tukey HSD or Chi-square* | p | Effect Size (Glass's delta) |
|---|---|---|---|---|---|---|---|---|---|
| **Socio-demographic Variables** | | | | | | | | | |
| **Age** | Mean (SD) | 28.31 (7.40) | 45.87 (10.53) | 38.72 (11.09) | 44.970 | **<0.001** | B<A<C | **<0.001**<br>**<0.001**<br>**<0.001** | 1.40<br>0.68<br>2.37 |
| **Sex** (Women yes) | n (%) | 25 (52.1) | 45 (60.0) | 37 (60.7) | 0.989 | 0.637 | | | |
| **Civil Status** (Married yes) | n (%) | 12 (25.0) | 28 (37.3) | 28 (46.7) | 5.483 | 0.068 | A<C | **0.027** | |
| **Education Level** | n (%) | | | | 8.990 | **0.011** | | | |
| Secondary School | | 26 (54.2) | 43 (57.3) | 20 (32.8) | | | A>C<br>B>C | **0.041**<br>**0.006** | |
| University | | 22 (45.8) | 32 (42.7) | 41 (67.2) | | | A<C<br>B<C | **0.041**<br>**0.006** | |
| **Employment** | n (%) | | | | 62.335 | **<0.001** | | | |
| Studying | | 16 (33.3) | 4 (5.3) | 6 (9.8) | | | B<A<br>C<A | **<0.001**<br>**0.005** | |
| Working | | 15 (31.3) | 24 (32.0) | 49 (80.3) | | | A<C<br>B<C | **<0.001**<br>**<0.001** | |
| Not studying /Not working | | 17 (35.4) | 47 (62.7) | 6 (9.8) | | | A<B<br>C<A<br>C<B | **0.003**<br>**0.006**<br>**<0.001** | |
| **Estimated IQ** | Mean (SD) | 105.13 (11.96) | 106.12 (15.70) | 109.75 (9.89) | 2.008 | 0.137 | | | |
| **Clinical Variables** | | | | | | | | | |
| **Family History of BD** | n (%) | 12 (25.0) | 17 (23.3) | - | <0.001 | 1.000 | | | |
| **Family History of MDE** | n (%) | 18 (37.5) | 26 (35.6) | - | <0.001 | 0.986 | | | |
| **Age at Onset** | Mean (SD) | 24.15 (8.40) | 25.21 (8.94) | - | 0.049 | 0.825 | | | |
| **Onset Polarity** | n (%) | | | | 2.562 | 0.265 | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Mania | | 25 (52.1) | 30 (40.0) | - | | | | | |
| Depression | | 20 (41.7) | 42 (56.0) | - | | | | | |
| Hypomania | | 3 (6.3) | 3 (4.0) | - | | | | | |
| **Age at First Hospitalization**[¥] | Mean (SD) | 27.57 (7.58) | 31.20 (11.20) | - | 7.184 | **0.009** | | | **0.48** |
| **Duration of Illness** | Mean (SD) | 4.17 (5.01) | 20.65 (8.98) | - | 13.058 | **<0.001** | | | **3.29** |
| **Number of Episodes** | Mean (SD) | | | | | | | | |
| Total | | 2.35 (1.28) | 10.41 (8.55) | - | 19.480 | **<0.001** | | | **6.29** |
| Mania | | 1.19 (0.53) | 3.62 (4.00) | | 19.969 | **<0.001** | | | **4.62** |
| Hipomania | | 0.23 (0.59) | 1.86 (3.23) | | 19.435 | **<0.001** | | | **2.76** |
| Depression | | 0.88 (0.98) | 4.45 (4.31) | | 21.127 | **<0.001** | | | **3.64** |
| Mixed episodes | | 0.06 (0.24) | 0.46 (1.4) | | 13.351 | **<0.001** | | | **1.67** |
| **Psychiatric Comorbidities** | n (%) | | | | | | | | |
| Axis I | | 4 (8.3) | 17 (23.0) | - | 3.412 | 0.065 | | | |
| Axis II | | 4 (8.3) | 15 (20.3) | - | 2.313 | 0.128 | | | |
| Axis III | | 11 (22.9) | 19 (26.0) | - | 0.030 | 0.863 | | | |
| **FAST Total Score**[†] | Mean (SD) [Range] | 16.79 (13.16) [1-64] | 25.53 (14.45) [0-61] | 5.27 (4.48) [0-20] | 49.449 | **<0.001** | B<A<C | **<0.001**<br>**<0.001**<br>**<0.001** | 0.87<br>4.45<br>0.64 |
| **YMRS Total Score**[†] | Mean (SD) [Range] | 1.10 (0.63) [0-7] | 1.68 (1.63) [0-6] | 0.63 (1.01) [0-3] | 8.556 | **<0.001** | C<B | **<0.001** | 1.01<br>0.87 |
| **HAM-D Total Score**[†] | Mean (SD) [Range] | 4.15 (2.94) [0-10] | 4.07 (2.52) [0-8] | 1.67 (1.78) [0-6] | 20.173 | **<0.001** | C<A<br>C<B | **<0.001**<br>**<0.001** | 0.84<br>0.91 |
| **Psychotropic Medication**[†] | n (%) | | | | | | | | |
| Lithium | | 38 (79.2) | 50 (66.7)) | - | 1.674 | 0.196 | | | |
| Antiepileptic | | 8 (16.7) | 38 (50.7) | - | 15.404 | **<0.001** | | | |
| Antipsychotic | | 25 (52.1) | 59 (78.7) | - | 8.364 | **0.004** | | | |
| Antidepressant | | 4 (8.3) | 28 (37.3) | - | 11.326 | **0.001** | | | |

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines | 7 (14.6) | 13 (17.3) | - | 0.023 | 0.879 |

Abbreviations: **BD**=Bipolar Disorder; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

*Only statistically significant or almost significant comparisons are reported. **Bold** for statistically significant values

†At Time of Evaluation ᵛMissing information for 7 FEM. 4 FEM and 14 BD patients had not history of hospitalization

**Table 2. Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in First Episode Mania (FEM) patients**

| | MSCEIT EIQ | | | |
|---|---|---|---|---|
| | | Mean (SD) | Statistics | |
| **Categorical variables** | | | **Student t** | **p** |
| Sex | M | 107.78 (17.68) | 2.054 | **0.046** |
| | F | 117.64 (15.56) | | |
| Family History of BD | Y | 112.75 (16.91) | 0.038 | 0.970 |
| | N | 112.97 (17.49) | | |
| Family History of MDE | Y | 113.61 (19.68) | -0.215 | 0.831 |
| | N | 112.50 (15.81) | | |
| Psychotic Symptoms at Onset | Y | 113.00 (17.12) | -0.110 | 0.913 |
| | N | 112.00 (20.42) | | |
| Cannabis use in the prodromal phase | Y | 116.96 (14.34) | -1.195 | 0.238 |
| | N | 111.55 (16.31) | | |
| Alcohol use in the prodromal phase | Y | 111.03 (17.39) | 1.611 | 0.114 |
| | N | 119.50 (14.03) | | |
| Lithium | Y | 112.24 (18.55) | 0.720 | 0.478 |
| | N | 115.50 (10.71) | | |
| Antiepileptics | Y | 114.25 (9.97) | -0.350 | 0.730 |
| | N | 112.65 (18.35) | | |
| Antipsychotics | Y | 114.25 (15.16) | -0.534 | 0.596 |
| | N | 111.58 (19.20) | | |
| Antidepressants | Y | 114.50 (27.04) | -0.191 | 0.850 |
| | N | 112.77 (16.46) | | |
| Benzodiazepines | Y | 116.43 (24.54) | -0.581 | 0.564 |
| | N | 112.32 (15.92) | | |
| **Continuous variables** | | | **Pearson correlation** | **p** |
| Age | | | 0.181 | 0.219 |
| Estimated IQ | | | 0.181 | 0.222 |
| PAS | | | 0.070 | 0.638 |

| | | |
|---|---|---|
| Duration of Illness | 0.172 | 0.242 |
| Total Number of Episodes | -0.138 | 0.349 |
| Number of Psychiatric Hospitalizations | -0.096 | 0.520 |
| Age at first hospitalization | 0.300 | 0.071 |
| HAM-D Total Score† | -0.061 | 0.686 |
| YMRS Total Score† | -0.262 | 0.072 |
| FAST Total Score† | -0.038 | 0.796 |
| Processing Speed Composite | 0.111 | 0.457 |
| Verbal Memory Composite | 0.371 | **0.011** |
| Working Memory Composite | -0.055 | 0.713 |
| Executive Functions Composite | 0.136 | 0.367 |
| Visual Memory Composite | -0.008 | 0.961 |
| Attention Composite | 0.059 | 0.705 |

Abbreviations: **BD**=Bipolar Disorder; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **PAS**=Premorbid Adjustment Scale; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale
**Bold** for statistically significant values
†At Time of Evaluation

# Supplemental Data

## Methods

*Participants*

Subjects with a first episode mania (FEM) were drawn from the "Prodromes and Predictors in First Episode Mania and Psychosis" – ProPreF project. a two-year longitudinal. multicentric study investigating prodromes and predictors of clinical and longitudinal outcomes in patients presenting a FEM or a first episode psychosis (FEP).

*Procedures*

Socio-demographic data, among others age, educational level, working status, were collected and stored in an electronic data repository. Medical records were assessed for completeness of information.

To verify the diagnosis and to determine the presence of a first full psychotic or manic episode, the summaries of the patients' files, the life charts of psychotic and mood episodes and the assessment of the clinical presentation at first inpatient hospitalization or first mental health service presentation, were reviewed by at least two psychiatrists and an agreement was reached on the diagnosis. If the patient met the DSM-5 A-D criteria for a manic episode a diagnosis of FEM was posed. If the patient presented at least two of the five symptoms of the criterion A for a DSM-5 psychotic disorder and no mood episode co-occurred a diagnosis of FEP was posed. After full or partial clinical remission (i.e. after discharge from the hospital) the patients were clinically assessed by a trained psychiatrist by means **of** ~~**a semi-structured interview based on**~~ the Structured Clinical Interview for DSM Disorders (SCID-I-II) )~~(Fairbairn & Rowan, 1975; Mohammadkhani et al., 2011)~~ **(First, M., Gibbon, M., Spitzer, R., Williams, J., &**

**Benjamin, 1997a, 1997b)** and diagnoses were determined according to DSM-5 criteria. Patients with schizophrenia or a schizophreniform disorder diagnosis were excluded and patients who met bipolar disorder (BD) diagnostic criteria were classified as FEM.

Also HC underwent a semi-structured interview based on the Structured Clinical Interview for DSM Disorders (SCID-I-II) ~~(Fairbairn & Rowan, 1975; Mohammadkhani et al., 2011)~~ **(First, M., Gibbon, M., Spitzer, R., Williams, J., & Benjamin, 1997a, 1997b)** to exclude current or past psychiatric history~~. In addition, HC were asked if they had first degree relatives with psychiatric disorders.~~

*Clinical assessment*

Clinical information was collected for the subgroups of patients, assessing onset features (i.e. age at onset. age at first hospitalization) , characteristics of the longitudinal course (i.e. total number of episodes, **number of manic, hippomaniac, depressive and missed episodes**, total number of hospitalizations. duration of illness) or the presence of a positive family history for Depressive and Bipolar Disorders and **pharmacological treatment (all patients were under stable treatment regimen).**

In order to explore the variables associated with the EI performance in patients with a FEM, other specific clinical variables were collected. Particularly, the Premorbid adjustment, namely levels of functioning before the onset of illness, was assessed with The Premorbid Adjustment Scale (PAS)(Cannon-Spoor, Potkin, & Jed Wyatt, 1982). Only childhood and early adolescence life periods have been taken into account since they are the two periods answered by all the participants. Higher scores indicate worse premorbid adjustment. In addition, information on the presence of psychotic symptoms at onset, the use of alcohol or cannabis before the onset. was also assessed.

*Neurocognitive domains*

Patients' raw scores on neuropsychological tests were standardized to z-scores (i.e.. M=0. SD=1) based on HCs' scores using the formula: (test score – HC test M)/HC test SD. Furthermore, several *z*-scores of different tests were summed and averaged to create six cognitive composites. Following this procedure, cognitive composites were standardized against the composite scores obtained for the HC subgroup. The variables included in each cognitive domain were adjusted to cognitive domains proposed by the ISBD-BANC (Yatham et al., 2010) as follows: Processing Speed (WAIS-III Digit-symbol Coding, the Category fluency (Animal naming) , and the TMT-A); (ii) the Working Memory (WAIS-III (Letter-number sequencing and the Digit-span subtests)); (iii) Verbal Memory (CVLT (total trials 1–5 list A,short free recall, short cued recall, delayed free recall. and delayed cued recall) (iv) Visual Memory (ROCF immediate recall); (v) Executive Functions (WCST (number of categories and perseverative errors). the Stroop Test (Interference) , and the TMT-B); and (vi) Attention (CPT-II (omission, reaction time and reaction time standard error). Outlying z-scores of > 4 SDs below HC mean were then truncated at z = -4.0. The z-scores for CPT-II, WCST perseverative errors, and TMT (A and B) were inverted so that higher scores represented poorer performance.

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**Supplementary tables**

**Supplementary Table 1. MSCEIT and Neuropsychological Scores of First Episode Mania (FEM) or Bipolar Disorder (BD) patients and Healthy Controls (HC)**

| Variables | FEM (A) (n=48, 26.09%) Mean (IC 95%) | BD (B) (n=75, 40.76%) Mean (IC 95%) | HC (C) (n=61, 33.15%) Mean (IC 95%) | Statistics $\chi^2$ | p | Pairwise Comparison* | p† | Effect Size (Glass's delta) |
|---|---|---|---|---|---|---|---|---|
| **Emotional Intelligence** | | | | | | | | |
| EIQ | 114.42 (109.19 – 119.66) | 107.02 (103.01 – 111.03) | 117.11 (112.80 – 121.43) | 10.748 | **0.005** | B<C | **0.004** | **0.91** |
| Experiential EI | 109.04 (104.25 – 113.82) | 102.72 (99.06 – 106.39) | 105.59 (101.65 – 109.54) | 3.681 | 0.159 | | | |
| Strategic EI | 104.92 (100.68 – 109.17) | 100.31 (97.05 – 103.56) | 105.18 (101.68 – 108.68) | 4.293 | 0.117 | | | |
| Perceiving emotions | 108.95 (104.18 – 113.72) | 103.47 (99.81 – 107.13) | 105.01 (101.07 – 108.95) | 2.830 | 0.243 | | | |
| Using emotions | 105.42 (100.65 – 110.19) | 100.72 (97.07 – 104.38) | 103.90 (99.97 – 107.84) | 2.308 | 0.315 | | | |
| Understanding emotions | 104.08 (99.86 – 108.31) | 97.24 (94.01 – 100.48) | 104.70 (101.22 – 108.19) | 9.955 | **0.007** | B<C<br>B<A | **0.010**<br>0.056 | **0.73**<br>0.44 |
| Managing emotions | 102.05 (97.22 – 106.89) | 103.35 (99.65 – 107.05) | 103.86 (99.87 – 107.85) | 0.308 | 0.857 | | | |

**Neurocognition**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Processing Speed | -1.12 (-1.48 – -0.76) | -2.09 (-2.37 – -1.82) | -0.16 (-0.45 – 0.13) | 80.454 | **<0.001** | A<C | **<0.001** | **0.92** |
| | | | | | | B<C | **<0.001** | **2.52** |
| | | | | | | B<A | **<0.001** | **1.30** |
| Verbal Memory | -0.66 (-1.06 – -0.26) | -1.10 (-1.40 – -0.79) | -0.09 (-0.42 – -0.23) | 17.828 | **<0.001** | B<C | **<0.001** | **1.27** |
| Working Memory | -0.49 (-0.79 – -0.19) | -0.77 (-1.00 – -0.55) | -0.05 (-0.29 – 0.20) | 16.675 | **<0.001** | B<C | **<0.001** | **0.85** |
| Executive Functions | -0.96 (-1.40 – -0.52) | -1.98 (-2.31 – -1.64) | -0.13 (-0.49 – 0.23) | 49.356 | **<0.001** | A<C | **0.015** | **0.71** |
| | | | | | | B<C | **<0.001** | **2.21** |
| | | | | | | B<A | **0.002** | **1.08** |
| Visual Memory | -0.40 (-0.73 – -0.07) | -0.55 (-0.84 – -0.26) | 0.04 (-0.29 – 0.22) | 6.852 | **0.033** | B<C | **0.035** | **0.81** |
| Attention | -1.03 (-1.43 – -0.63) | -2.82 (-3.11 – -2.52) | -0.01 (-0.31 – 0.29) | 168.426 | **<0.001** | A<C | **<0.001** | **0.95** |
| | | | | | | B<C | **<0.001** | **2.87** |
| | | | | | | B<A | **<0.001** | **1.25** |

Abbreviations: **EI**=Emotional Intelligence; **EIQ**=Emotional Intelligence Quotient; **IC 95%=**Lower–Upper values within Wald Confidence Interval of 95%; **MSCEIT**=Mayer-Salovey-Caruso Emotional Intelligence Test;

*Only statistically significant or almost significant comparisons are reported. **Bold** for statistically significant values

†Bonferroni post-hoc significance

**Supplementary Table 2. Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in chronic Bipolar Disorder (BD) patients**

| | | MSCEIT EIQ | | |
|---|---|---|---|---|
| | | | Statistics | |
| **Variables** | | **Mean (SD)** | **Pearson correlation or Student t** | **p** |
| **Socio-demographic variables** | | | | |
| Age | | | -0.034 | 0.769 |
| Sex | M | 103.50 (16.71) | 0.996 | 0.322 |
| | F | 107.27 (15.59) | | |
| Estimated IQ | | | 0.170 | 0.148 |
| **Clinical variables** | | | | |
| Family History of BD | Y | 105.65 (19.27) | -0.025 | 0.980 |
| | N | 105.54 (15.36) | | |
| Family History of MDE | Y | 105.08 (17.97) | 0.189 | 0.851 |
| | N | 105.83 (15.34) | | |
| Duration of Illness | | | -0.055 | 0.642 |
| Total Number of Episodes | | | -0.155 | 0.185 |
| Number of Psychiatric Hospitalizations | | | **-0.288** | **0.012** |
| Age at first hospitalization | | | 0.241 | 0.061 |
| Psychotic Symptoms at Onset | Y | 101.81 (13.79) | -1.898 | 0.062 |
| | N | 108.78 (17.46) | | |
| HAM-D Total Score[†] | | | **-0.268** | **0.021** |
| YMRS Total Score[†] | | | 0.117 | 0.320 |
| FAST Total Score[†] | | | **-0.298** | **0.010** |
| **Psychotropic Medication** | | | | |
| Lithium | Y | 104.70 (15.28) | 0.807 | 0.422 |
| | N | 107.88 (17.59) | | |
| Antiepileptics | Y | 106.76 (16.76) | -0.546 | 0.587 |

| | | | | |
|---|---|---|---|---|
| | N | 104.73 (15.43) | | |
| Antipsychotics | Y | 104.44 (15.80) | 1.376 | 0.173 |
| | N | 110.63 (16.51) | | |
| Antidepressants | Y | 100.61 (15.04) | **2.202** | **0.031** |
| | N | 108.83 (15.98) | | |
| Benzodiazepines | Y | 106.15 (18.61) | -0.197 | 0.923 |
| | N | 105.68 (15.62) | | |
| **Neurocognitive domains** | | | | |
| Processing Speed Composite | | | **0.407** | **<0.001** |
| Verbal Memory Composite | | | **0.386** | **0.001** |
| Working Memory Composite | | | 0.160 | 0.171 |
| Executive Functions Composite | | | **0.353** | **0.002** |
| Visual Memory Composite | | | -0.006 | 0.966 |
| Attention Composite | | | **0.274** | **0.017** |

Abbreviations: **BD**=Bipolar Disorder; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

**Bold** for statistically significant values

†At Time of Evaluation

**Supplementary Table 3. Hierarchical multiple linear regression of the socio-demographic, clinical and neuropsychological variables associated with MSCEIT Emotional Intelligence Quotient (EIQ) in chronic Bipolar Disorder (BD) patients**

| | MSCEIT EIQ | | | |
|---|---|---|---|---|
| **Model** | | **ßeta** | **t** | **p** |
| **1** | F=6.917, df (1.71), p=0.010 | | | |
| FAST Total Score† | | **-0.298** | -2.630 | **0.010** |
| Constant | | | 31.004 | <0.001 |
| **2** | F=3.907, df (2.70), p=0.025 | | 29.723 | <0.001 |
| FAST Total Score† | | -0.214 | -1.491 | 0.140 |
| HAM-D Total Score† | | -0.137 | -0.952 | 0.344 |
| Constant | | | | |
| **3** | F=3.169, df (3.69), p=0.03 | | | |
| FAST Total Score† | | -0.190 | -1.317 | 0.192 |
| HAM-D Total Score† | | -0.096 | -0.656 | 0.514 |
| Antidepressants | | -0.155 | -1.274 | 0.207 |
| Constant | | | 29.881 | <0.001 |
| 4 | F=3.761, df (4.68), p=0.008 | | | |
| FAST Total Score† | | -0.129 | -0.907 | 0.368 |
| HAM-D Total Score† | | -0.104 | -0.730 | 0.468 |
| Antidepressants | | -0.170 | -1.432 | 0.157 |
| Number of Psychiatric Hospitalizations | | **-0.251** | -2.233 | **0.029** |
| Constant | | | 29.650 | <0.001 |
| **5** | F=4.629, df (5.67), p=0.001 | | | |
| FAST Total Score† | | -0.108 | -0.784 | .436 |
| HAM-D Total Score† | | -0.021 | -.150 | 0.881 |
| Antidepressants | | -0.139 | -1.212 | 0.230 |

| | | | |
|---|---|---|---|
| Number of Psychiatric Hospitalizations | **-0.214** | -1.968 | **0.053** |
| Processing Speed Composite* | **0.301** | 2.610 | **0.011** |
| Constant | | 28.637 | <0.001 |

Abbreviations: **BD**=Bipolar Disorder; **df**=degrees of freedom; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

**Bold** for statistically significant values

†At Time of Evaluation

* Among the neurocognitive composites, only the Processing Speed Composite was entered in the regression to avoid multicollinearity and because it was the most correlated with the MSCEIT EIQ.

# Supplemental Data

## Methods

*Participants*

Subjects with a first episode mania (FEM) were drawn from the "Prodromes and Predictors in First Episode Mania and Psychosis" – ProPreF project. a two-year longitudinal. multicentric study investigating prodromes and predictors of clinical and longitudinal outcomes in patients presenting a FEM or a first episode psychosis (FEP).

*Procedures*

Socio-demographic data, among others age, educational level, working status, were collected and stored in an electronic data repository. Medical records were assessed for completeness of information.

To verify the diagnosis and to determine the presence of a first full psychotic or manic episode, the summaries of the patients' files, the life charts of psychotic and mood episodes and the assessment of the clinical presentation at first inpatient hospitalization or first mental health service presentation, were reviewed by at least two psychiatrists and an agreement was reached on the diagnosis. If the patient met the DSM-5 A-D criteria for a manic episode a diagnosis of FEM was posed. If the patient presented at least two of the five symptoms of the criterion A for a DSM-5 psychotic disorder and no mood episode co-occurred a diagnosis of FEP was posed. After full or partial clinical remission (i.e. after discharge from the hospital) the patients were clinically assessed by a trained psychiatrist by means of the Structured Clinical Interview for DSM Disorders (SCID-I-II) (First, M., Gibbon, M., Spitzer, R., Williams, J., & Benjamin, 1997a, 1997b) and diagnoses were determined according to DSM-5 criteria. Patients

with schizophrenia or a schizophreniform disorder diagnosis were excluded and patients who met bipolar disorder (BD) diagnostic criteria were classified as FEM.

Also HC underwent a semi-structured interview based on the Structured Clinical Interview for DSM Disorders (SCID-I-II) (First, M., Gibbon, M., Spitzer, R., Williams, J., & Benjamin, 1997a, 1997b) to exclude current or past psychiatric history.

*Clinical assessment*

Clinical information was collected for the subgroups of patients, assessing onset features (i.e. age at onset. age at first hospitalization) , characteristics of the longitudinal course (i.e. total number of episodes, number of manic, hippomaniac, depressive and missed episodes, total number of hospitalizations. duration of illness) or the presence of a positive family history for Depressive and Bipolar Disorders and pharmacological treatment (all patients were under stable treatment regimen).

In order to explore the variables associated with the EI performance in patients with a FEM, other specific clinical variables were collected. Particularly, the Premorbid adjustment, namely levels of functioning before the onset of illness,. was assessed with The Premorbid Adjustment Scale (PAS)(Cannon-Spoor, Potkin, & Jed Wyatt, 1982). Only childhood and early adolescence life periods have been taken into account since they are the two periods answered by all the participants. Higher scores indicate worse premorbid adjustment. In addition, information on the presence of psychotic symptoms at onset, the use of alcohol or cannabis before the onset. was also assessed.

*Neurocognitive domains*

Patients' raw scores on neuropsychological tests were standardized to z-scores (i.e.. M=0. SD=1) based on HCs' scores using the formula: (test score – HC test M)/HC test SD.

Furthermore, several *z*-scores of different tests were summed and averaged to create six cognitive composites. Following this procedure, cognitive composites were standardized against the composite scores obtained for the HC subgroup. The variables included in each cognitive domain were adjusted to cognitive domains proposed by the ISBD-BANC (Yatham et al., 2010) as follows: Processing Speed (WAIS-III Digit-symbol Coding, the Category fluency (Animal naming) ,. and the TMT-A); (ii) the Working Memory (WAIS-III (Letter-number sequencing and the Digit-span subtests)); (iii) Verbal Memory (CVLT (total trials 1–5 list A,short free recall, short cued recall, delayed free recall. and delayed cued recall) (iv) Visual Memory (ROCF immediate recall); (v) Executive Functions (WCST (number of categories and perseverative errors). the Stroop Test (Interference) , and the TMT-B); and (vi) Attention (CPT-II (omission, reaction time and reaction time standard error). Outlying z-scores of > 4 SDs below HC mean were then truncated at z = -4.0. The z-scores for CPT-II, WCST perseverative errors, and TMT (A and B) were inverted so that higher scores represented poorer performance.

**Online references**

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**Supplementary tables**

**Supplementary Table 1. MSCEIT and Neuropsychological Scores of First Episode Mania (FEM) or Bipolar Disorder (BD) patients and Healthy Controls (HC)**

| Variables | FEM (A) (n=48, 26.09%) Mean (IC 95%) | BD (B) (n=75, 40.76%) Mean (IC 95%) | HC (C) (n=61, 33.15%) Mean (IC 95%) | Statistics $\chi^2$ | p | Pairwise Comparison* | p† | Effect Size (Glass's delta) |
|---|---|---|---|---|---|---|---|---|
| **Emotional Intelligence** | | | | | | | | |
| EIQ | 114.42 (109.19 – 119.66) | 107.02 (103.01 – 111.03) | 117.11 (112.80 – 121.43) | 10.748 | **0.005** | B<C | **0.004** | **0.91** |
| Experiential EI | 109.04 (104.25 – 113.82) | 102.72 (99.06 – 106.39) | 105.59 (101.65 – 109.54) | 3.681 | 0.159 | | | |
| Strategic EI | 104.92 (100.68 – 109.17) | 100.31 (97.05 – 103.56) | 105.18 (101.68 – 108.68) | 4.293 | 0.117 | | | |
| Perceiving emotions | 108.95 (104.18 – 113.72) | 103.47 (99.81 – 107.13) | 105.01 (101.07 – 108.95) | 2.830 | 0.243 | | | |
| Using emotions | 105.42 (100.65 – 110.19) | 100.72 (97.07 – 104.38) | 103.90 (99.97 – 107.84) | 2.308 | 0.315 | | | |
| Understanding emotions | 104.08 (99.86 – 108.31) | 97.24 (94.01 – 100.48) | 104.70 (101.22 – 108.19) | 9.955 | **0.007** | B<C<br>B<A | **0.010**<br>0.056 | **0.73**<br>0.44 |
| Managing emotions | 102.05 (97.22 – 106.89) | 103.35 (99.65 – 107.05) | 103.86 (99.87 – 107.85) | 0.308 | 0.857 | | | |

**Neurocognition**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Processing Speed | -1.12 (-1.48 – -0.76) | -2.09 (-2.37 – -1.82) | -0.16 (-0.45 – 0.13) | 80.454 | **<0.001** | A<C | **<0.001** | **0.92** |
| | | | | | | B<C | **<0.001** | **2.52** |
| | | | | | | B<A | **<0.001** | **1.30** |
| Verbal Memory | -0.66 (-1.06 – -0.26) | -1.10 (-1.40 – -0.79) | -0.09 (-0.42 – -0.23) | 17.828 | **<0.001** | B<C | **<0.001** | **1.27** |
| Working Memory | -0.49 (-0.79 – -0.19) | -0.77 (-1.00 – -0.55) | -0.05 (-0.29 – 0.20) | 16.675 | **<0.001** | B<C | **<0.001** | **0.85** |
| Executive Functions | -0.96 (-1.40 – -0.52) | -1.98 (-2.31 – -1.64) | -0.13 (-0.49 – 0.23) | 49.356 | **<0.001** | A<C | **0.015** | **0.71** |
| | | | | | | B<C | **<0.001** | **2.21** |
| | | | | | | B<A | **0.002** | **1.08** |
| Visual Memory | -0.40 (-0.73 – -0.07) | -0.55 (-0.84 – -0.26) | 0.04 (-0.29 – 0.22) | 6.852 | **0.033** | B<C | **0.035** | **0.81** |
| Attention | -1.03 (-1.43 – -0.63) | -2.82 (-3.11 – -2.52) | -0.01 (-0.31 – 0.29) | 168.426 | **<0.001** | A<C | **<0.001** | **0.95** |
| | | | | | | B<C | **<0.001** | **2.87** |
| | | | | | | B<A | **<0.001** | **1.25** |

Abbreviations: **EI**=Emotional Intelligence; **EIQ**=Emotional Intelligence Quotient; **IC 95%=**Lower–Upper values within Wald Confidence Interval of 95%; **MSCEIT**=Mayer-Salovey-Caruso Emotional Intelligence Test;

*Only statistically significant or almost significant comparisons are reported. **Bold** for statistically significant values

†Bonferroni post-hoc significance

**Supplementary Table 2. Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in chronic Bipolar Disorder (BD) patients**

| | | MSCEIT EIQ | | |
|---|---|---|---|---|
| | | | Statistics | |
| **Variables** | | **Mean (SD)** | **Pearson correlation or Student t** | **p** |
| **Socio-demographic variables** | | | | |
| Age | | | -0.034 | 0.769 |
| Sex | M | 103.50 (16.71) | 0.996 | 0.322 |
| | F | 107.27 (15.59) | | |
| Estimated IQ | | | 0.170 | 0.148 |
| **Clinical variables** | | | | |
| Family History of BD | Y | 105.65 (19.27) | -0.025 | 0.980 |
| | N | 105.54 (15.36) | | |
| Family History of MDE | Y | 105.08 (17.97) | 0.189 | 0.851 |
| | N | 105.83 (15.34) | | |
| Duration of Illness | | | -0.055 | 0.642 |
| Total Number of Episodes | | | -0.155 | 0.185 |
| Number of Psychiatric Hospitalizations | | | **-0.288** | **0.012** |
| Age at first hospitalization | | | 0.241 | 0.061 |
| Psychotic Symptoms at Onset | Y | 101.81 (13.79) | -1.898 | 0.062 |
| | N | 108.78 (17.46) | | |
| HAM-D Total Score[†] | | | **-0.268** | **0.021** |
| YMRS Total Score[†] | | | 0.117 | 0.320 |
| FAST Total Score[†] | | | **-0.298** | **0.010** |
| **Psychotropic Medication** | | | | |
| Lithium | Y | 104.70 (15.28) | 0.807 | 0.422 |
| | N | 107.88 (17.59) | | |
| Antiepileptics | Y | 106.76 (16.76) | -0.546 | 0.587 |

| | | | | |
|---|---|---|---|---|
| | N | 104.73 (15.43) | | |
| Antipsychotics | Y | 104.44 (15.80) | 1.376 | 0.173 |
| | N | 110.63 (16.51) | | |
| Antidepressants | Y | 100.61 (15.04) | **2.202** | **0.031** |
| | N | 108.83 (15.98) | | |
| Benzodiazepines | Y | 106.15 (18.61) | -0.197 | 0.923 |
| | N | 105.68 (15.62) | | |
| **Neurocognitive domains** | | | | |
| Processing Speed Composite | | | **0.407** | **<0.001** |
| Verbal Memory Composite | | | **0.386** | **0.001** |
| Working Memory Composite | | | 0.160 | 0.171 |
| Executive Functions Composite | | | **0.353** | **0.002** |
| Visual Memory Composite | | | -0.006 | 0.966 |
| Attention Composite | | | **0.274** | **0.017** |

Abbreviations: **BD**=Bipolar Disorder; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

**Bold** for statistically significant values

†At Time of Evaluation

**Supplementary Table 3. Hierarchical multiple linear regression of the socio-demographic, clinical and neuropsychological variables associated with MSCEIT Emotional Intelligence Quotient (EIQ) in chronic Bipolar Disorder (BD) patients**

| | MSCEIT EIQ | | | |
|---|---|---|---|---|
| **Model** | | **ßeta** | **t** | **p** |
| **1** | F=6.917, df (1.71), p=0.010 | | | |
| FAST Total Score† | | **-0.298** | -2.630 | **0.010** |
| Constant | | | 31.004 | <0.001 |
| **2** | F=3.907, df (2.70), p=0.025 | | 29.723 | <0.001 |
| FAST Total Score† | | -0.214 | -1.491 | 0.140 |
| HAM-D Total Score† | | -0.137 | -0.952 | 0.344 |
| Constant | | | | |
| **3** | F=3.169, df (3.69), p=0.03 | | | |
| FAST Total Score† | | -0.190 | -1.317 | 0.192 |
| HAM-D Total Score† | | -0.096 | -0.656 | 0.514 |
| Antidepressants | | -0.155 | -1.274 | 0.207 |
| Constant | | | 29.881 | <0.001 |
| 4 | F=3.761, df (4.68), p=0.008 | | | |
| FAST Total Score† | | -0.129 | -0.907 | 0.368 |
| HAM-D Total Score† | | -0.104 | -0.730 | 0.468 |
| Antidepressants | | -0.170 | -1.432 | 0.157 |
| Number of Psychiatric Hospitalizations | | **-0.251** | -2.233 | **0.029** |
| Constant | | | 29.650 | <0.001 |
| **5** | F=4.629, df (5.67), p=0.001 | | | |
| FAST Total Score† | | -0.108 | -0.784 | .436 |
| HAM-D Total Score† | | -0.021 | -.150 | 0.881 |
| Antidepressants | | -0.139 | -1.212 | 0.230 |

| | | | |
|---|---|---|---|
| Number of Psychiatric Hospitalizations | **-0.214** | -1.968 | **0.053** |
| Processing Speed Composite* | **0.301** | 2.610 | **0.011** |
| Constant | | 28.637 | <0.001 |

Abbreviations: **BD**=Bipolar Disorder; **df**=degrees of freedom; **EIQ**=Emotional Intelligence Quotient; **FAST**=Functioning Assessment Short Test; **HAM-D**=Hamilton Depression Rating Scale; **IQ**=Intelligence Quotient; **MDE**=Major Depressive Episode; **SD**=Standard deviation; **YMRS**=Young Mania Rating Scale

**Bold** for statistically significant values

†At Time of Evaluation

* Among the neurocognitive composites, only the Processing Speed Composite was entered in the regression to avoid multicollinearity and because it was the most correlated with the MSCEIT EIQ.

Nov 10th 2021

Prof. Eduard Vieta

Director Bipolar and Depressive Disorders Unit

Clinical Institute of Neuroscience

Hospital Clinic, University of Barcelona,

Villarroel 170, 08036 Barcelona, Spain

Ref.: Ms. No. PSM-D-21-01217

Emotional Intelligence: A comparison between patients with First Episode Mania and those suffering from chronic Bipolar Disorder type I

Dear Editor and Reviewers,

Thank you for giving us the opportunity to resubmit our manuscript. We feel that the present version has largely benefited from the comments of the reviewers. We thank you for the detailed and constructive review of our manuscript. In the manuscript showing our revisions, you will find newly inserted text marked with **yellow,** and deleted text marked with ~~**red**~~. Below we have included our replies to each of the points that the Reviewers raised.

*Reviewers' and editor's comments:*

*Reviewer #1: This is an interesting manuscript on a rarely studied topic in an even less-studied patient population (early stage bipolar disorder). It reads fluently and is easy to understand. I have only a few suggestions:*

*1) In my opinion, the title is a bit misleading. I would suggest to rephrase it to: "Emotional Intelligence: A comparison between patients after (instead of with) First Episode Mania and those suffering from chronic Bipolar Disorder type I". With the current wording, the reader is misguided to think patients in an acute manic episode were investigated*.

**Reply:** We thank the reviewer for this suggestion. We have changed the wording of "~~**with**~~ First Episode Mania" to "**after** First Episode Mania" in the title and throughout the manuscript.

- **Abstract**

**Introduction:** Deficits in emotional intelligence (EI) were detected in patients with Bipolar Disorder (BD), but little is known about whether these deficits are already present in patients

**after** presenting a first episode mania (FEM). We sought (i) to compare EI in patients **after a** FEM, chronic BD and healthy controls (HC); (…)

**Method:** (...) In patients **after** a FEM, the influence of socio-demographic, clinical and neurocognitive variables on the EIQ was examined using a linear regression model.

**Results:** (…) In patients **after a** FEM, EIQ was positively associated with female sex (β=-0.293, p=0.034) and verbal memory performance (β=0.374, p=0.008). FEM patients performed worse than HC but better than BD on few neurocognitive domains.

**Conclusions:** Patients ~~**with**~~ **after** a FEM showed preserved EI, while patients in later stages of BD presented lower EIQ, suggesting that impairments in EI might result from the burden of disease and neurocognitive decline, associated with the chronicity of the illness.

*2) According to table 1 patients in the FEM group had experienced a mean number of episodes of 2.35. For those having more than one episode: were these episodes of depression? Or did the FEM sample include patients with more than one episode of mania? If this is the case, it would eventually be more fitting to speak of patients "in the early stage of bipolar disorder" than "first episode mania".*

**Reply:** We thank the reviewer for bringing this to our attention. FEM group had experienced a mean number of 1.19 manic episodes. Patients in the present study could have experienced more than one affective episode over previous three years, thus they could be considered within their early stage of disease. In order to clarify this point and to avoid any confusion to the reader, we have added this information in the methods in the results sections and in table 1 we included the mean number of different type of episodes. As a result, throughout the manuscript, we have specified that FEM patients were those patients recruited after a FEM (instead of with a FEM) and we referred to them as they are in the early stage of illness or FEM over the last three years.

- Method, p.6: The inclusion criteria for FEM patients, evaluated at baseline, were (…). **Patients could have experienced more than one affective episode over the previous three years, could then be considered within their early stage BD illness.**
- Result, p.10: **Patients after a FEM experienced an average of 1.19 episodes of mania whilst BD chronic patients an average of 3.62.**

*3) The medication of patients is listed in table 1. But were patients at time of study inclusion in a stable treatment regimen? Information on treatment should be added in the methods*

*section.*

**Reply:** We thank the reviewer for this suggestion. We have mentioned that we have collected the pharmacological treatment among clinical information.

- Method, p.6: **All patients were under stable treatment regimen.**
- Supplementary material, Clinical assessment, p.2: Clinical information was collected for the subgroups of patients, assessing onset features (...), characteristics of the longitudinal course (...) and Bipolar Disorders and **pharmacological treatment (all patients were under stable treatment regimen).**

4) *I would recommend to add a better description of how "current or past psychiatric history" was assessed in healthy controls. The authors have mentioned it in the supplement, but it should be included in the paper for clarification. The authors state "patients as well as healthy controls underwent a semi-structured interview "based on" the Structured Clinical Interview for DSM Disorders (SCID-I/II)". What does "based on" mean? Were the whole SCID I+II inverviews conducted?*

**Reply:** Following the reviewer's recommendation, a better description of how "current or past psychiatric history" was assessed in healthy controls has been moved from supplement to the main document. We have added this to the method section:

- Method, p. 6: "´(…)~~**None of the HC had first-degree relatives with psychiatric disorders.**~~ **In addition, HC were asked if they had first-degree relatives with psychiatric disorders".**

To avoid potentially misleading the reader we have deleted the wording "based on", now it is stated:

- Method, p. 7: all patients were assessed by means of ~~**a semi-structured interview based on**~~ the Structured Clinical Interview for DSM Disorders (SCID-I-II)
- Supplementary material, p. 1: After full or partial clinical remission (i.e. after discharge from the hospital) the patients were clinically assessed by a trained psychiatrist by means of ~~**a semi-structured interview based on**~~ the Structured Clinical Interview for DSM Disorders (SCID-I-II).

*5) Lastly, the supplemental material section shows many incorrect punctuation marks. For example: "Socio-demographic data. among others age. educational level. working status. were collected and stored in an electronic data repository."*

**Reply:** We thank the reviewer for pointing this out. We have amended the sentence replacing "." with ",".

*Reviewer #2: Review of "Emotional Intelligence: A comparison between patients with First Episode Mania and those suffering from chronic Bipolar Disorder type I"*

*Article Summary: The authors pooled data from two samples of patients with bipolar disorder (BD) and healthy controls (HC), separating out BD patients who had recently experienced a first episode of mania (FEM) vs those who had a longer illness course (chronic BD). After assessing demographics, clinical status, and psychosocial functioning, they tested chronic BD patients, FEM BD patients, and HC on emotional intelligence (EI) and neurocognitive functioning using standardized tests for both. The authors found that chronic BD patients showed reduced overall EI scores relative to HC, but FEM BD patients did not. This pattern was also true for one out of four subscales of the EI measure. Despite their similar EI performance compared to HC, FEM BD patients showed reductions in some neurocognitive abilities relative to HC, whereas chronic BD patients showed widespread reductions in neurocognitive abilities relative to both HC and FEM BD patients. There was a sex difference in EI abilities (women > men), mirroring what is found in the general population, and a correlation between EI and verbal working memory. Overall, the authors propose that reductions in EI are a symptom of BD that may occur later in the course of the disorder and suggest that EI may be a target for preventative intervention techniques early in the disorder.*

*Strengths:*

* *Good sample size*

* *Well characterized sample using standard clinical, EI, and neurocognitive measures*

* *Appropriate analysis techniques with apparent correction for multiple comparisons (but see below)*

* *Timely and interesting focus (EI) in an understudied population (FEM BD patients)*

*Suggestions for Improvement:*

1. *The title should be changed. We typically do not emphasize the "suffering" aspect of mental disorders, so that word should be removed. Perhaps "Differences in emotional intelligence between patients with first episode mania and patients with chronic bipolar disorder" would work better. Both groups are type-I (by definition) so this distinction is not needed.*

**Reply:** The authors thank the reviewer for this request. To avoid potentially misleading the reader and following the Reviewer #1 point 1 as well, we have now provided a new title.

Title: **Differences in emotional intelligence between patients after ~~with~~ first episode mania and patients with chronic bipolar disorder**

2. *In the Methods section, the inclusion criteria for FEM BD patients had only one cutoff for HDRS-17 and YMRS (≤14), even though the word "respectively" is used.*

**Reply:** We thank the reviewer for this suggestion. We have added the cutoff for HDRS-17 for clarification purposes. The following has been added to the method section:

Methods, Participants, p. 6: (iii) being in full or partial remission (Hamilton Depression Rating Scale 17-item [HDRS-17] **(≤14)** (…) and Young Mania Rating Scale [YMRS] (…) (≤14)**~~, respectively~~**).

3. *It would be helpful to know more about the chronic BD patients. Some of the FEM BD patients were several years removed from their FEM and according to the authors' table, they had an average of over 2 episodes. How exactly did the authors distinguish between FEM BD patients and chronic BD patients? Was it simply 1 episode of mania (FEM) vs. 2 or more episodes of mania (chronic BD)? Regardless, within the BD group as a whole, does number of manic episodes correlate with anything?*

**Reply:** We thank the reviewer for bringing this to our attention. We only considered in the FEM BD patients group those patients that had experienced their first manic episode over the last three years. On the contrary, chronic BD patients had a long-lasting course of illness as stated by their longer duration of illness. Indeed, BD patients presented an average duration of illness of 20.65 years, while FEM patients presented duration of illness of 4.17 years. Of note,

in the calculation of duration of illness we considered not only the FEM, but also previous affective episodes, even though the FEM should be over the last 3 years to be included in the present study.

Considering that EI is our main variable of interest, we assessed the correlation between number of manic episodes and EI both in FEM patients and BD group and found no correlation.

- Pearson correlation between number of mania episodes and EI in FEM r=-0.087; p=0.558

**Correlations**

| | | MSCEIT EIQ | Number of manic episodes |
|---|---|---|---|
| MSCEIT EIQ | Pearson Correlation | 1 | -,087 |
| | Sig. (2-tailed) | | ,558 |
| | N | 48 | 48 |
| Number of manic episodes | Pearson Correlation | -,087 | 1 |
| | Sig. (2-tailed) | ,558 | |
| | N | 48 | 48 |

- Pearson correlation between number of mania episodes and EI in BD r=-0.216; p=0.06

**Correlations**

| | | MSCEIT EIQ | Number of manic episodes |
|---|---|---|---|
| MSCEIT EIQ | Pearson Correlation | 1 | -,216 |
| | Sig. (2-tailed) | | ,060 |
| | N | 75 | 75 |
| Number of manic episodes | Pearson Correlation | -,216 | 1 |
| | Sig. (2-tailed) | ,060 | |
| | N | 75 | 75 |

4. *I am a little confused about the finding that EI correlates with verbal memory impairment in the FEM BD subgroup. A correlation of .371 with N=48 FEM BD patients should yield a p-value of .0094 (https://eu-central-1.protection.sophos.com?d=socscistatistics.com&u=aHR0cHM6Ly93d3cuc29jc2Npc3RhdGlzdGljcy5jb20vcHZhbHVlcy9wZWFyc29uZGlzdHJpYnV0aW9uLmFzcHg=&i=NWZkYjRiODc3M2ZiN2EwZGZmZjAzYWJl&t=SjkzN2hzVWRscStoSXp2WHh5RW9JQjVZQkFOTm1NNnRveTNUM09SVXhvMD0=&h=85d397b815834ac69fe1c51e5379b089), not p = .011. However, this .0094 finding would still not be significant by a Bonferroni correction (corrected p is .05 / 6 neurocognitive domains = .0083). Can the authors please clarify how they conducted their multiple comparisons correction?*

**Reply:** We thank the reviewer for raising this important point. We have re-run the correlations analysis between MSCEIT total score and verbal memory in the FEM BD subgroup. This analysis was conducted using IBM SPSS Statistics version 23.0.

**Correlations**

| | | Verbal Memory | MSCEIT EIQ |
|---|---|---|---|
| Verbal Memory | Pearson Correlation | 1 | ,371* |
| | Sig. (2-tailed) | | ,011 |
| | N | 46 | 46 |
| MSCEIT EIQ | Pearson Correlation | ,371* | 1 |
| | Sig. (2-tailed) | ,011 | |
| | N | 46 | 48 |

*. The correlation is significant at the 0.05 level (bilateral).

These analyses were not corrected for multiple comparisons as they were exploratory analyses.

Anyway, we would like to underline that Bonferroni post-hoc correction was applied (i.e., not correcting for multiple comparisons) when significant main effects were present when comparing the three groups in the GLM models, in order to identify pair-wise differences between groups. See Reviewer #3 point 3 below for further information on multiple comparisons.

5. *Did this verbal memory-EI correlation hold up in the chronic BD sample (or the HC sample, for that matter)? Why were similar correlations between EI and the other variables not also run in the chronic BD sample? Finding these correlations in the other sample would support the idea that they are real and not a statistical fluke. There is not much theoretical justification for why EI would necessarily relate to verbal memory, rather than other neurocognitive domains, so this needs to be addressed.*

**Reply:** We thank the reviewer for this comment. As for the association between verbal memory and EI not only in FEM patients but also BD patients, in the Supplementary Table 2 we reported the results of the "Correlations between MSCEIT Emotional Intelligence Quotient (EIQ) and socio-demographic and clinical variables in chronic Bipolar Disorder (BD) patients". In BD patients, EI impairment was associated with verbal memory, as in FEM patients. Moreover, there was an association between EI with other cognitive domains in BD patients, such as processing speed, executive functions and attention. To date, it is difficult to ascertain which neuropsychological domain (among verbal memory, executive functions, processing speed, working memory, etc.) has a greater influence on social cognition, especially on EI. For this reason, those neuropsychological variables with a p value ≤0.05 in Pearson correlation analyses were entered into a hierarchical multiple regression model, aimed at evaluating the association between neuropsychological performance and EIQ. In the present study, we found an effect of verbal memory, which encompasses different skills such as association, categorization and mental imagery, which recalled to complete the MSCEIT successfully. We agree reviewer's suggestion, that this point needs further investigation. We have therefore added the following sentence in the manuscript:

- Discussion, p. 15: As for the role played by verbal memory in EI, our finding is in line with previous literature underlining how EI performance might be associated with cognitive abilities (Eack et al., 2010; Beatrice Frajo-Apor et al., 2020; Varo et al., 2019). In a previous study assessing BD patients, all neurocognitive domains were associated with EI (Varo et al., 2019). **However, to date, it is difficult to ascertain which neuropsychological domain (among verbal memory, executive functions, psychomotor speed, working memory and attention) has a greater influence on social cognition, especially on EI. In the current study verbal memory resulted to be the central domain involved in EI ability. EI was assessed by MSCEIT which demands an accurate interpretation of the semantic meaning of the social situation. It involves exercises related to verbal memory skills, such as association, categorization and mental imagery.** In another study assessing EI and cognitive abilities in healthy adults,

verbal fluency was the only cognitive domain associated with EIQ (Pardeller, Frajo-Apor, Kemmler, & Hofer, 2017).

6. *In the Discussion, the authors seem to be trying to have it both ways by stating that neurocognitive domains are completely separate from EI abilities but then later stating that verbal memory performance is associated with EI. Could the authors please clarify this inconsistency?*

**Reply**: We apology if this was not clear enough. Even though neurocognitive domains and EI are two different constructs, neurocognitive domains are not completely separated from EI abilities. Indeed, they are related and share certain overlap. As a consequence, these are two different but complementary constructs. We have added the following to the manuscript for clarification purposes:

- Discussion, p. 13-14: One recurring question is whether neurocognition and SC in BD are sufficiently distinct to be considered separately. **Previous studies investigating the relationship between neurocognition and EI have yielded mixed and inconclusive results. While there are studies that reported that lower levels of EI may be mediated by neurocognitive abilities (Aparicio et al., 2017; Frajo-Apor et al., 2017), others have not found a relationship between the two constructs** (Fanning, Bell, & Fiszdon, 2012)**.** Our results highlight the connection between EI and neurocognition and the idea that they are two complementary but separated constructs (DeTore, Mueser, & McGurk, 2018), **with partial overlap and** with a different degree of impairment. Thus, **our findings were in line with many other works supporting the idea that neurocognitive ability may represent a "necessary, but not sufficient" prerequisite for social cognitive abilities, especially in those that contain an emotional component (Bora, Veznedaroğlu, & Vahip, 2016; Lee et al., 2013; Varo et al., 2019).** This view is consistent with studies from neuroimaging in social neuroscience (Mitchell, 2008). **Nonetheless, the role of neurocognitive impairments on social cognition and EI in euthymic BD patients remains somewhat unclear. Therefore, the nature of this association should be the focus of further investigation.**

7. *Table 3 should be organized by the type of tests being run (t-tests vs. correlations) to make it more readable.*

**Reply:** We thank the reviewer for this comment. As suggested, we have organized the table 3 by the type of tests being run.

8. *For both Figures, line graphs are less appropriate here because line graphs imply a time course, whereas these graphs are depicting intergroup comparisons. I recommend changing these graphs to bar graphs. You could most likely put the EIQ in one graph and then many of the subscales in another graph or another part of the graph, rather than having a bunch of separate figures. You could also do something similar with the neurocognitive data, as they are all Z-scored values.*

**Reply:** We thank the reviewer for pointing this out. We changed Figures 1 and 2 on the basis of these recommendations and we replaced the line graphs to bar graphs. Moreover, we have made one graph for EIQ (Figure 1) and another graph for the subscales (Figure 2). Now Figure 3 refers to neurocognitive data.

9. *Table 2 seems redundant with the Figures and should probably be included in the Supplementary Material.*

**Reply:** We thank the reviewer for raising this important point. The Table 2 has been moved from results section to the Supplemental Material.

10. *In the References, the Fairbairn & Rowan (1975) citation is unclear. Why is a cannabis article being cited as a reference for the SCID?*

**Reply:** We have checked again this issue. It seems it is a reference manager malfunction. We thank the reviewer for this note. The reference has been revised and amended.

- References:

**First, M., Gibbon, M., Spitzer, R., Williams, J., & Benjamin, L. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II); American Psychiatric Press: Washington, DC, USA, 1997.**

**First, M., Spitzer, R., Gibbon, M., & Williams, J. Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician (SCID-I); American Psychiatric Press: Washington, DC, USA, 1997.**

*Overall Impression:*

*Thank you for the opportunity to review this paper. Despite my critiques, the overall paper is solid, and the findings are interesting and timely. I recommend that the paper be published pending some minor revisions, as outlined above.*

**Reply:** We would like to thank reviewer #2 for his/her enriching suggestions and positive comments.

Reviewer #3:

*With 48 individuals with first-episode mania, 75 individuals with a diagnosis of bipolar disorder type 1 and 61 healthy controls, this study aims to improve the understanding of emotional intelligence differences between first episode mania and chronic bipolar disorder as well as what variables may pose as potential risk factors in worse performance on MSCEIT. This study has several strengths including the inclusion of two patient groups (i.e., first-episode mania and chronic bipolar disorder), the use of a standardized measure to assess emotional intelligence and the inclusion of neurocognitive assessments. The research question that this study addressed is important and could provide valuable knowledge on the trajectory of emotional processing difficulties in bipolar disorder. However, I also have several concerns, which are listed below.*

*First, this study aims to understand the trajectory of emotional processing difficulties in bipolar disorder and potential factors that might affect these difficulties. Given this goal, it is unclear why the authors did not examine the effect of socio-demographic and neurocognitive variables in both patient groups and compare whether any of these variables affect the performance of first episode patients versus chronic patients in a different way. This is especially puzzling when the authors presented the results from the chronic patients in the Supplemental. It would have been nice if the authors conducted a series of regression analyses to examine whether any of these variables affect emotional intelligence in first episode patients versus chronic patients in a different way (e.g., any interaction involving group).*

**Reply**: We thank the reviewer for this comment. The reviewer 3 suggest "to examine the effect of socio-demographic and neurocognitive variables in both patient groups and compare whether any of these variables affect the performance of first episode patients versus chronic patients in a different way." … "It would have been nice if the authors conducted a series of regression analyses to examine whether any of these variables affect emotional intelligence in

first episode patients versus chronic patients in a different way (e.g., any interaction involving group)." This is actually the statistical analysis that we developed, reflected in the method section in which we stated that:

- Material and Methods, p.9: "In order to assess which socio-demographic, clinical and neuropsychological variables were associated with IEQ in the FEM and in the BD groups, we first performed Pearson bivariate correlations to identify those continuous variables significantly associated with EIQ. For categorical variables (i.e. sex), Student's t-test was run to evaluate the distribution of EIQ. Only those variables with a p value ≤0.05 were then entered into a hierarchical multiple regression model, aimed at evaluating the association between socio-demographic, clinical and neuropsychological variables and EIQ".

As for the interaction involving group, in the methods, we stated that:

- Material and Methods, p.9: "Performance on MSCEIT and the neurocognitive domains was compared across the three groups using generalized linear models (GLM). All models were adjusted for those clinical and socio-demographic variables for which the three groups differed significantly. Then, a Bonferroni post-hoc correction was applied when significant main effects were present when comparing the three groups, in order to identify pair-wise differences between groups. Estimated Marginal Means, adjusted for the other variables in the model, were reported for each variable of interest (i.e. EIQ), as well as the 95% Confidence Interval (CI), their Mean Difference (MD) and its Standard Error (SE)."

*Second, it does not appear that the authors included neurocognitive performance as a covariate when comparing MSCEIT performance. As neurocognitive performance is thought to be related to emotional intelligence and three groups do differ on performance on neurocognitive tasks, it will be important to include neurocognitive performance as covariates to show that any difference in MSCEIT performance between first episode mania and chronic patients is not due to differential neurocognitive performance.*

**Reply:** We agree with the reviewer on the fact that the EI performance might be influenced by neurocognitive performance. We have not included neurocognitive domains as covariates since our secondary aim was actually to examine the potential contribution of neurocognitive variables on EI performance in patients with a FEM. To be clearer for the reader, we have clarified this issue in the introduction section-

- Introduction, p. 5: the main aim of the present study was to explore EI using the full version of the MSCEIT in patients ~~with~~ **after** a FEM in comparison with patients with chronic BD and HC. Also, **the secondary aim was** to provide insight on the potential contribution of socio-demographic, clinical and neurocognitive variables on EI performance in patients ~~with~~ **after** a FEM.

According to our findings, lower EIQ correlated with poorer performance in verbal memory among patients after a FEM and with poorer performance in processing speed, verbal memory, executive function and attention domains in BD patients. Thus, our results suggest that EI and neurocognition are two different but complementary constructs. We have discussed this point in the discussion section. We are actually working on another article of the same project whose main aim is to assess the role of neuropsychological domains as moderators of EI in both BD patients or patients after a FEM.

*Third, I have several comments on the method and result section. In the Supplemental, the authors stated that age at onset and age at first hospitalization were collected for the subgroups of patients. Please indicate how many patients provided information in Table 1.*

**Reply:** We thank the reviewer for this suggestion. We updated Table 1 with this information. We added a note in the table only for the age at first hospitalization (**Missing information for 7 FEM. 4 FEM and 14 BD patients had not history of hospitalization**) since for age at onset we did not have any missing data.

*It will be helpful to provide effect sizes for Tables 1 and 2*

**Reply:** We thank the reviewer for this suggestion. We reported the effect sizes in Table 1 and provide effect sizes in Supplementary Table 1 (that was Table 2 in the previous version since Table 2 has been moved to supplementary materials as suggested by Reviewer #2)

*It appears that correlations between MSCEIT performance and several variables (presented in Table 3) are not corrected for multiple comparisons. Given that none of significant correlations would remain significant after correcting for multiple comparisons, it will be helpful for the authors provide a clear rationale of not correcting for multiple comparisons.*

**Reply:** We thank the reviewer for this comment. As far as we know, this is the first study to analyse the contribution of socio-demographic, clinical and neurocognitive variables to emotional intelligence, measured by means of the MSCEIT in a sample of patients after a first episode mania. For this reason, our secondary aim was to conduct an exploratory analysis aimed at comparing EI in patients with a fully or partially remitted FEM, chronic BD and healthy controls. In accordance with this exploratory purpose, we considered not conducting any statistic procedure in the univariate analyses to control for multiple comparisons, since it would have increased the risk of running type II error. In order to underline the exploratory nature of these analyses, we added a statement in the methods:

- Material and Methods, p.9: **Moreover, exploratory analyses were conducted to satisfy our secondary aim.**

*The authors indicate that some of patients had psychotic symptoms during their manic episode. Given that emotional processing is more severely affected in psychosis than in mania, would it be possible that patients with psychotic symptoms in the first episode mania group shows greater difficulties in emotional intelligence than patients without psychotic symptoms?*

**Reply:** We thank the reviewer for pointing this out. We already checked for this aspect before conducting the analysis since we are aware of the fact that psychotic symptoms could represent a bias. We report here this analysis. There were no differences in terms of MSCEIT total score (EIQ) between FEM patients who presented Psychotic Symptoms at Onset and those who did not (t=-0.110; p=0.913). Also, we have run analysis assessing the difference between those with or without hallucinations (t=0.508; p=0.614) and with or without delusions (t=0.224; p=0.824) and we didn't find any significant difference. This result might suggest that patients with psychotic symptoms in the first episode mania group did not show greater difficulties in emotional intelligence than patients without psychotic symptoms. We have therefore added the following to the manuscript:

- Discussion, p. 13-14: "This might suggest that more severe SC deficits might be associated with other conditions, such as schizophrenia, instead of BD since in non-affective FEP patients EI impairment was found to start early in the course of illness and to remain stable (Green et al., 2012). **Given that EI is more severely affected in psychosis than in mania, one may argue that patients reporting psychotic symptoms during the first episode of mania might show greater difficulties in EI than patients without psychotic symptoms. Despite this, we did not find any difference in terms of**

**EIQ between FEM patients who presented Psychotic Symptoms at Onset and those who did not.**

We really hope that all the above described changes are going to fulfil your expectations and turn the paper into suitable for publication in your very prestigious journal. We thank the reviewers for the very useful suggestions and important remarks that helped us to improve our manuscript.

Yours sincerely,

Eduard Vieta and Anabel Martinez-Aran