The impact of affective temperaments on clinical and functional outcome of Bipolar I patients that initiated or changed pharmacological treatment for mania


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ABSTRACT

Background: Affective temperaments have been shown to impact on the clinical manifestations and the course of bipolar disorder. We investigated their influence on clinical features and functional outcome of manic episode.

Method: In a naturalistic, multicenter, national study, a sample of 194 BD I patients that initiated or changed pharmacological treatment for DSM-IV-TR manic episode underwent a comprehensive evaluation including briefTEMPS-M, CTQ, YMRS, MADRS, FAST, and CGI-BP. Factorial, correlation and comparative analyses were conducted on different temperamental subtypes.

Results: Depressive, cyclothymic, irritable and anxious temperaments resulted significantly correlated with each other. On the contrary, hyperthymic temperament scores were not correlated with the other temperamental dimensions. The factorial analysis of the briefTEMPS-M sub-scales total scores allowed the extraction of two factors: the Cyclothymic-Depressive-Anxious (Cyclo-Dep-Anx) and the Hyperthymic. At final evaluation Dominant Cyclo-Dep-Anx patients reported higher scores in MADRS and in CTQ emotional neglect and abuse subscale scores than Dominant Hyperthymic patients. The latter showed a greater functional outcome than Cyclo-Dep-Anx patients.

Conclusions: Affective temperaments seem to influence the course of mania. Childhood emotional abuse and neglect were related to the cyclothymic disposition. Cyclothymic subjects showed more residual depressive symptoms and Hyperthymic temperament is associated with a better short-term functional outcome.

1. Introduction

In clinical setting, the course of bipolar disorder (BD) (El-Mallakh et al., 2008) is characterized by a high number of relapses with frequent chronicity and consequent impairment in psychosocial functioning and health-related quality of life (Rosa et al., 2008; Sylvia et al., 2014; Tohen et al., 2009). As a consequence, the definition of remission in BD comprises both symptomatic and functional recovery. Symptomatic remission means the resolution of the symptoms of the disorder, which disappear or at least decrease to a minimal level. Functional recovery means the ability to return to an adequate level of functioning, including occupational status, familial and social adjustment and personal well-being (Harvey, 2006; Martinez-Aran et al., 2007; Tohen et al., 2003).

Acute mania seems to present a favorable prognosis, although incomplete symptomatic remission and persisting impairment of psychosocial functioning are not uncommon. In fact, most patients achieve symptomatic remission but less than half reach a functional recovery within 24 months after a manic/mixed episode (Haro et al., 2011; Strejilevich et al., 2013; Swann et al., 2002; Tohen et al., 2003; van der Voort et al., 2015). For this reason, there is a growing interest in the factors related to outcome and remission of BD episodes (Haro et al., 2011; Kora et al., 2008; Treuer and Tohen, 2010).

Several studies explored the role of socio-demographic and clinical features in predicting remission of mania (Haro et al., 2011; Kora et al., 2008; Sylvia et al., 2014; Treuer and Tohen, 2010). Affective temperaments seem to impact on the clinical features and the course of BD (Akiskal, 2000; Hantouche et al., 1998; Iasevoli et al., 2013; Perugi...
et al., 2012; Pompili et al., 2014). In particular, temperaments might play a predisposing or pathoplastic role in the state symptomatology and in several co-morbid syndromes (Perugi and Akiskal, 2002). An Italian study on a national sample of BD I patients in different phase of the illness prospectively explored the influence of affective temperaments and psychopathological traits, such as separation anxiety and interpersonal sensitivity, on the clinical features of BD (Perugi et al., 2012). Interestingly, the cyclothymic-sensitive patients reported a higher number of suicide attempts and a prevalently depressive course of the illness, while hyperthymic patients showed higher number of severe manic episodes requiring hospitalization. Finally, the two temperamental subtypes showed a different profile in term of lifetime comorbidity. Cyclothymic patients presented more frequently Panic Disorder/Agoraphobia, Social Anxiety Disorder and Borderline Personality Disorder in comparison with hyperthymics. On the contrary, Antisocial Personality Disorder was more represented among hyperthymic than cyclothymic patients (Perugi et al., 2012).

More recently, a relationship between temperamental subtype and neurocognition has been reported. In particular, high ratings of cyclothymia and irritability in BD patients have been associated with better processing speed, working memory, reasoning and problem-solving (Russo et al., 2014). On the other hand, BD patients with hyperthymic temperament showed greater cognitive deficits in set shifting and verbal working memory than BD patients with non-predominant temperaments (Xu et al., 2014). The role of affective temperaments in the prediction of the illness severity and global functioning has been prospectively explored in inpatients with major depressive disorder and BD (Pompili et al., 2013), suggesting a long-term predictive power of the hyperthymic temperament with respect to better health and social functioning.

Previous studies on the influence of affective temperaments on the clinical features and the course of BD have been conducted mainly in patients evaluated during depression. The aim of the present study is to investigate the influence of affective temperaments on the clinical and functional outcome of manic episodes.

2. Materials and methods

2.1. Study design and sample

This was a multicentric, prospective, longitudinal, non-interventional study conducted in 34 recruiting Italian sites representative of the entire national territory. The study population included in- or outpatient aged $\geq 18$ years with manic episode in the context of a BD I, diagnosed according to DSM-IV-TR criteria (American Psychiatric Association, 2000), and requiring the initiation or a change (but not a dose change) of treatment for mania with an oral antipsychotic and/or mood stabilizer. The assignment of the patients to a particular therapeutic strategy was independent of the decision to include the patient in the study. Therapeutic choices were made, in a naturalistic setting, by the treating psychiatrist according to his/her clinical experience and guidelines. Patients not able to read or understand the informed consent, pregnant or breast-feeding women, subjects participating in a separate study that had an interventional design and the members of the site personnel or their immediate family members were not eligible for participation.

The study duration was 3 months for each patient (5 visits): screening for inclusion in the study and baseline assessment were concomitants; follow-up visits at week 1, 3, 8 and 12 (± 1 week). Participating psychiatrists recorded observational data on a regular basis. However, these observations had to occur only during visits that where part of the standard course of care. Although patient consent had to be achieved as required by local laws and regulations, data collection did not require any patient intervention beyond usual practice and did not alter the care provided.

Patients meeting all inclusion criteria were assessed by the Young Mania Rating Scale (YMRS) and the Montgomery and Asberg Depression Rating Scale (MADRS) for the evaluation of the severity of affective symptomatology (Montgomery and Asberg, 1979; Young et al., 1978). The global severity of manic episode was evaluated by the Clinical Global Impression Scale-Bipolar Illness (CGI-BP), which allowed determining the degree of change from the immediately preceding phase and from the worst phase of illness (Spearling et al., 1997). The Functioning Assessment Short Test (FAST) scale was used to assess the social, occupational, psychological and cognitive functioning (Rosa et al., 2007). At each visit after baseline (week 1, 3, 8 and 12, ± 1 week), psychiatrist used the same psychopathological tools to assess symptoms evolution over time. At week 12, patients were administered the Childhood Trauma Questionnaire (CTQ) to assess the occurrence of childhood trauma (Bernstein et al., 2003). The Temperament Evaluation of Memphis, Pisa, Paris and San Diego brief-version (briefTEPS-M) was also administered at week 12 to investigate temperamental characteristics (depressive, cyclothymic, hyperthymic, irritable, anxious) (Erfurth et al., 2005a).

2.2. Ethics

All patients gave their written informed consent prior to any study-related procedure was started. The study protocol was approved by the reference Ethic Committee of each study site.

2.3. Diagnostic assessment

The diagnosis of manic episode in BD I patients was made by the treating psychiatrist according to the DSM-IV-TR criteria (American Psychiatric Association, 2000). Manic symptoms were quantitatively and qualitatively assessed through the YMRS (Young et al., 1978), an 11-items scale that carefully investigates the key symptoms of mania, i.e. those that are generally present during all the course of mania. The investigated areas pertained to mood, motor activity, thought disorders, judgment ability, aggressiveness, libido, sleep and general behaviour. The YMRS was specifically created for the evaluation of manic symptoms and their evolution during treatment.

Depressive symptomatology was investigated by the MADRS (Montgomery and Asberg, 1979), which was expressly created to be sensitive to the evolution of depressive symptoms over time. The assessment of depressive symptoms is thought to be relevant also during manic phases, since the possible occurrence of dysphoria and switching towards a mixed state. Its 10 items explore depressed mood, inner tension, sleep and appetite disturbances, concentration difficulties, asthenia, inability to feel, pessimistic and suicidal thoughts.

The global psychopathology was evaluated by the CGI-BP (Spearling et al., 1997), a version of CGI that preserves the fundamental assets of the original global rating instrument focusing on the specific components of BD. It allows determining a global evaluation in three areas: the severity of the illness, the global improvement and the efficacy index (comparison of the patient’s baseline condition to a ratio of current therapeutic benefit and severity of side effects).

Impairment in different areas of functioning (e.g. cognitive and social functioning) could be present in BD patients (Depp et al., 2010; Iverson et al., 2011). In addition to symptoms, the evaluation of various areas of psychosocial functioning is relevant for understanding the clinical outcome and the recovery process. The psychosocial functioning was investigated through the administration of the FAST (Rosa et al., 2007). The FAST is organized in 6 clusters (autonomy, occupational functioning, cognitive functioning, financial management, social functioning and leisure time) whose items are evaluated from absence of difficulty to high difficulty. The FAST shows strong psychometric properties and it is sensitive to different mood states.

The assessment of temperamental characteristics was performed by the briefTEPS-M version (Erfurth et al., 2005a). The briefTEPS-M allows investigating 5 temperamental sub-scales: depressive,
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