Distinctive Sociodemographic, Clinical and Temperament Characteristics of Bipolar-I, Bipolar-II and Major Depressive Disorders

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SUMMARY

Introduction: Mood disorders are one of the significant mental disorders that decrease the quality of human life and disrupt the psychosocial functionality and interpersonal relationships. Recently, studies have suggested that affective temperaments are factors that determine the emergence and characteristics of mood disorders.

Methods: 150 patients total were enrolled in the study, which aimed to compare the temperament, clinical and sociodemographic characteristics of 50 BD-I, 46 BD-II and 54 MDD patients. In order to determine clinical and sociodemographic features, we administered the SKIP-TURK structured follow-up questionnaire, the Hamilton Depression Rating Scale (HDRS), the Young Mania Rating Scale (YMRS) and the TEMPS-A temperament rating scale for all patients.

Results: The following clinical, sociodemographic and temperament characteristics were evaluated: such as history of psychiatric disorder of first and second degree relatives, comorbid hypothyroidism, age of onset of the mood disorder symptoms, the nature of the first episode of the mood disorder, seasonal course, mean duration of the episode, total number of episodes, severity of the mood episodes, and total number of hospitalizations.

Conclusion: Our results demonstrated that some sociodemographic, clinical and affective temperament characteristics may be good predictors for early diagnoses and treatment of BD and MDD.

Key Words: bipolar disorder, major depressive disorder, clinical characteristics, sociodemographic characteristics, temperament

INTRODUCTION

Mood disorders are one of the significant mental disorder groups that decrease the quality of human life and disrupt the psychosocial functionality and interpersonal relationships. The mood disorders are very common. This are increased to importance of mood disorders (Abood et al., 2002). The mood disorders are very common. This increases to importance.

The text revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) classifies mood disorders (MD) into major depressive disorder (MDD) (also known as unipolar depression), bipolar

disorder (BD) and mood disorders caused by general medical condition and/or substance abuse (American Psychiatric Association, 2000). The prevalence of MD ranges from 10% to 25% in women and from 5% to 15% in men. Estimates of the prevalence of BD range from 5% in the general populations and from 50% in all episodes of depression (Goodwin & Jamison, 1990; Öztürk, 2002). Recently, studies reported that 69% of bipolar disorder patients are not diagnosed during the first interview and that the correct diagnosis was not made for an average of 10 years after the first diagnosis (Angst & Marneos, 2001; Ghaemi, 2006). The repetitive and chronic nature and difficulties in the diagnosis of MD also impo-

se significant burdens on families, caregivers, and employers (Öztürk, 2002).

It is generally accepted since ancient times that the affective temperament is the precursor of some psychiatric disorders (Hirschfield et al., 1986; Von Zerssen & Akiskal, 1998).

Some studies have investigated whether depressive, hyperthymic, cyclothymic, irritable and anxious temperaments, as identified by temperament rating scales, are related to features of MDD or BD and if affective temperament influences the emergence and features of MD (Angst and Marneos, 2001; Ghaemi, 2006).

The aim of this study was to investigate whether bipolar disorder type I (BD-I), bipolar disorder type II (BD-II) and MDD patients had sociodemographic, clinical and affective temperament characteristics, and their influence on the early diagnosis of disease.

MATERIALS

Participants

This study involved a total of 150 randomized patients who agreed to participate in the study and who were admitted to the psychiatry outpatient clinic of the Ankara Atatürk Training and Research Hospital, between August 2009- February 2010 and who were followed regularly for least one year. They were diagnosed with BD-I, BD-II and MDD according to the Structured Clinical Interview (SCID-I) found in the DSM-IV-TR (First et al., 1996, 1997).

Inclusion and Exclusion Criteria

Inclusion criteria for the present study included fulfilling the DSM-IV criteria for BD-I, BD-II and MDD (including cases accompanied by psychotic symptoms), being between the ages of 18-60, understanding the required reading, giving consent to participate in the study and the remission period had to be 8 weeks (total Hamilton depression scale score ≤ 7 and Young mania rating scale score ≤ 5). Exclusion criteria for the present study included fulfilling DSM-IV criteria for mental retardation, having a disorder related to alchol substance abuse, the spectrum of anxiety disorders, schizophrenia and other psychotic disorders, dementia/other cognitive disorders, personality traits due to neurological diseases such as epilepsy, migraines, multiple sclerosis and Parkinson's disease, having a systemic disease that causes cognitive impairment or the presence of physical illness affecting vision, auditory and/or motor capabilities.

Procedure

The patients falling within the inclusion criteria and who had a remission period were interviewed using the Diagnostic and Monitoring Form for Mood Disorders (SCIP-TURK) (Ozerdem

et al., 2004; Tirpan et al., 2004). Subsequently, information obtained from hospital files was integrated. Thus, the clinical course of the disease features were recorded (such as the type of the first episode, the total number of episodes and the other episodes, the number and duration of hospitalizations, suicide attempts and methods, social support and stories of childhood trauma or abuse, and the treatments obtained). Subsequently, the HDRS (Hamilton, 1960; Akdemir, 1996), YMRS (Young, 1978; Karadag, 2002) and TEMPS-A (Temperament Evaluation of Memphis, Pisa, Paris, San Diego Autoquestionaire) were performed (Akiskal, 1996; Vahip, 2005).

Materials

Structured Clinical Interview for DSM-Axis I Disorders (SCID-I), is a structured interview developed by First and colleagues (1997) used to make the major DSM-IV Axis I diagnoses (First et al., 1997). The validity and reliability studies have been conducted for Turkey (Corapcioglu et al., 1999).

Diagnostic and Monitoring Form for Mood Disorders (SCIP-TURK), the SCIP-TURK has semi-structured scales and consists of 4 modules and was developed by Ozerdem and Yazici (2004).

The Hamilton Rating Scale for Depression (HDRS), was developed by Hamilton, and the original scale had 17 questions which were used to measure the severity of depression (Hamilton, 1960). The reliability and validity of the Turkish form has been examined (Akdemir, 1996).

The Young Mania Rating Scale (YMRS): Young *et al.* (1978) developed a mania rating scale, which has eleven items and five grades of severity specific to each item. The reliability and validity have been examined in Turkey (Karadag et al., 2002).

The Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Auto questionnaire (TEMPS-A), is a Likert-type scale which was developed by Akiskal (1997) and is used to identify the five temperament sub-types which include depressive, hyperthymic, irritable, cyclothymic and anxious temperaments. In this study, the Turkish version was used (Vahip 2005).

Statistical analysis

We used the Statistical Package for Social Sciences, version 11.0 (SPSS 11.0) for all analyses. All data was analyzed using normal distribution statistics. The categorical variables were compatible with normally distributed, but the continuous variables were not compatible. The Mann–Whitney U test was used to analyze variables that were not normally distributed. For categorical data, the chi-square test was used to analyze differences between groups. A p-value of <0.05 was considered statistically significant (SPSS, Inc, Chicago, IL).

Parameters		BD-I	BD-II	MDD	X^2	p value
		N =50 (%)	N =46 (%)	N =54 (%)		•
Gender	Female	33 (66.0)	34(73.9)	44 (81.5)		
	Male	17 (34.0)	12(26.1)	10 (18.5)	0.368	0.198
Age groups	19-24	4 (8.0)	1 (2.2)	3(5.6)		
	25-34	13(26.0)	18(39.1)	19(35.2)		
	35-44	18(36.0)	14(30.4)	11(20.4)	6.701	0.569
	45-54	11(22.0)	11(23.9)	17(31.5)		
	55-60	4 (8.0)	2 (4.3)	4(7.4)		
Education level	Primary education	17(34.0)	14(30.4)	23(42.6)	0.311	
	High education	17(34.0)	12(26.1)	13(24.1)	0.607	0.527
	Higher education	16(32.0)	20(43.5)	18(33.4)	0.782	
Marital status	Single	17(34.0)	10(21.7)	13(24.5)	0.397	
	Married	30(60.0)	30(65.2)	34(64.2)	0.843	0.311
	Widowed	1(2.0)	5(10.9)	6(11.3)	0.174	
	Divorced	2(4.0)	1(2.2)	0(0.0)	0.564	
Socioeconomic level	Lower	0 (0)	0 (0)	1(1.9)	0.025	
	Medium-lower	21(42.0)	14(30.4)	32(59.3)	0.418	
	Medium-higher	23(46.0)	28(60.9)	19(35.2)		0.045
	Higher	6(12.0)	4(8.7)	2(3.7)	0.368	
Location	Urban	41(82.0)	41(89.1)	25(45.5)	1.000	
	Skirt	4(8.0)	1(2.2)	20(45.1)	0.058	
	Town	5(10.0)	3(6.5)	4(7.4)	0.779	0.033
	Village	0(0.0)	1(2.2)	1(1.9)	1.000	
Habits	Alchol	15(30.0)	10(21.7)	12(22.2)		
	Cigarette	24(48.0)	25(54.3)	27 (50.0)		0.839

RESULTS

1. Sociodemographic characteristics

The sample of 150 participants consisted of 50 BD-I, 46 BD-II and 54 MDD. Approximately 26% of the participants were men and 74% were women. The median age at interview for BD-I was 39.5 \pm 10.9 years, for BD-II was 37.9 \pm 8.5 years and for MDD was 39.6 \pm 11.6 years. The sociodemographic characteristics of our patients are presented in Table 1.

2. Clinical characteristics

2.1. Onset characteristics of MD

We compared the clinical characteristics of the BD-I, BD-II and MDD groups. The mean age of the first symptoms for mood disorder were 24.8 ± 4.3 years, for BD-I, 25.4 ± 3.6 years for BD-II and 27.7 ± 5.7 years for MDD. There was a statistically significant difference in the age at onset of the symptoms when comparing the three groups ($\chi^2 = 8.328$, p = 0.007). BD symptoms were diagnosed earlier than MDD.

The mean time until diagnosis for BD-I was 5.5 \pm 2.9 years and for BD-II was 5.7 \pm 2.8 years and there was no significant differences between the groups (χ^2 = 1.009, p= 0.789). The mean age of first treatment for BD-1 was 30.2 \pm 6.0 years and for BD-II was 31.3 \pm 4.8 years (χ^2 = 3.620, p= 0.291).

The percentage who had a first episode with depressive characteristics was 54% for BD-I and 72% for BD-II (p= 0.000, χ^2 = 33.724). The prevalence rates of the melancholic characteristics were significantly higher in the BD-II group than in the BD-I and MDD group (p= 0.000, χ^2 = 32.743), and atypical characteristics were significantly higher in the MDD than in the BD groups (p= 0.000, χ^2 = 14.743). The mood of the depressive episodes compatible with psychotic tendencies were 42% for BD-I, 21.7% for BD-II, and 24.1 % for MDD (p= 0.015, χ^2 = 11.829).

The mood episodes were associated with stressful life events (p= 0.501, χ^2 = 0.188) and type and severity of the first depressive episode (p= 0.329, χ^2 = 0.382 and p= 0.779, χ^2 = 0.494) were not significantly different between the three groups.

2.2. Clinical characteristics of the course of mood disorders

In this study, the mean severity of the depressive episodes after the first mood episode was not significantly different between the three groups. The mean time of the depressive episode with MD was 25.2 \pm 6.0 days for BD-I, 27.9 \pm 5.8 days for BD-II and 31.2 \pm 8.9 days for MDD. The mean time of the depressive episode with MDD was significantly higher than the other groups (p= 0.000, χ ²= 33.207).

In our study, the frequency of poor social support for patients with BD-I, BD-II and MDD was 20.0 %, 37.0 % and 24.1 %, respectively and for childhood trauma or abuse history was 28.0 %, 37.0 % and 18.5 %, respectively. The frequency of the number of lifetime depressive episodes, poor social support (p= 0.104, χ^2 = 7.684), childhood trauma or abuse history (χ^2 = 4.268, p= 0.118), suicide attempt (p= 0.965, χ^2 = 0.072) and method (p= 0.845, χ^2 = 0.134) were not significantly different between the BD-I, BD-II and MDD patients.

2.3. History of Psychiatric and medical disorders

The history of medical disorders, excepted hypothyroidism (p= 0.010, χ^2 = 9.270), were not significantly different between the BD-I, BD-II and MDD patients (p= 0.283, χ^2 = 2.525). The mean frequency of hypothyroidism was higher in the BD-I group than the other groups (p= 0.005, χ^2 = 17.829).

In our study, the percentage of non-mood disorder previous psychiatric diagnoses was 53% panic disorder, 17.3% social phobia, and 6.7% personality disorder and obsessive compulsive disorder. In terms of the previous history of psychiatric disorders and the age of onset of treatment, there were no significantly differences between the three groups (p= 0.157, χ ²= 2.829).

2.4. History of psychiatric disorder of first and second degree relatives

In our study, a statistically difference was observed among the first and second degree relatives of patients with BD and MDD. The incidence of first and second degree relatives having a MD was higher in BD-I (p= 0.028, χ^2 = 21.429; p= 0.027, χ^2 = 22.467) than in BD-II and MDD and that BD-II was also higher than MDD (p= 0.047, χ^2 = 16.829; p= 0.040, χ^2 = 23.628).

3. Temperament

In our study, a significant difference was observed between the three groups with regards to the prevalance of anxious, hyperthymic, cyclothymic and depressive temperaments (*p*= 0.000, p= 0.000, p= 0.002, p= 0.007) however, the prevalence of the irritable temperament was not significantly different (p= 0.613). There was a frequency of 22.2% for MDD with depressive temperament, 26.0 % and 23.9% for BD-I and BD-II with cyclothymic temperament, 14.0% and 13.0% for BD-I and BD-II with hyperthymic temperament and 14.8% for MDD with anxious temperament. The comparison of the mean TEMPS-A scores for BD-I, BD-II and MDD are presented in Table 2.

DISCUSSION

The bipolar patients described fewer symptoms with hypomania and mania. There are potential problems when correlating bipolar depression to psychopathology due to overlap of other psychiatric disorder symptoms, especially BD and MDD (Mitchell and Malhi, 2004; Bowden, 2005; Sadock and Sadock, 2007).

The data in this paper provides evidence for the value of prompt diagnosis and treatment of MD. We have shown that a statistically difference was observed between some of the socio-demographic, clinical, and temperamental characteristics of mood disorders. The age of onset of symptoms of BD-I and BD-II were significantly lower than MDD.

There are other studies that suggest that the initial age of diagnosis of BD-I and BD-II are close to each other but significantly lower than that of MDD (Özerdem et al., 2001; Akiskal, 2002). It is widely known that at least half of all BD has an onset before the age of 20 (Mitchell et al., 2001; Kupfer and Shatzberg, 2005). Additionally, the presence of a family history of both unipolar and bipolar diagnoses changed significantly depending upon the age of the youth (Benazzi, 1999; Thase, 2000; Maj et al., 2002).

In this study, it was found that patients with BD-I and BD-II and a family history of mood disorders had a 77.3% increased risk of early-age onset compared to patients without a family

TEMPS-A scores	BD-I N=50	BD-II N=46	MDD N=54	X^2	p value
Depressive temperament	7.2 ± 2.5	7.1 ± 2.5	10.5 ± 3.7	22.164	BD-I/MDD=0.000
Anxious temperament	(4-9) 9.0 ± 3.3	(4-14) 8.4 ± 2.4	4-18) 19.0 ± 11.4	10.027	BD-II/MDD=0.000 BD-I/MDD=0.001
	(5-23)	(3-17)	(5-19)		BD-II/MDD=0.007
Cyclothymic temperament	13.3 ± 5.1 (4-23)	11.8 ± 5.0 (4-23)	10.7 ± 3.6 (4-19)	3.728	BD-I/MDD=0.020
Hyperthymic temperament	12.4 ± 5.4 (5-24)	11.5 ± 6.0 (4-27)	9.4 ± 2.8 (5-16)	5.46	BD-I/MDD=0.004
Irritable temperament	9.2 ± 3.1 (4-19)	8.6 ± 2.4 (4-14)	9.0 ± 2.7 (4-13)	0.491	0.613

history of MD, and that these patients were recurrence of the disorder associated with the less stressors.

In accordance with the data from this study, previous research has found that BD patients tend to have a higher socioeconomic class and MDD patients tend to have a lower socioeconomic class (Akiskal, 2002; Agosti and Stewart, 2001; Angst et al., 2003). The MD may be caused by unemployment, divorce, and low socioeconomic levels and these factors are contributing to socio-economic decline seen in these patients.

In our study, it was found that more patients who were living in the city were diagnosed with BD compared to those living in the village. Some studies suggest that people who live in a city or heavily populated environment have a higher risk of being diagnosed with BD (Agosti and Stewart, 2001; Sadock and Sadock, 2007). This may be an explanation for the data seen in this study.

In our study, a statistically significant difference was observed between the first episodes of BD-I and BD-II. The frequency of BD with a first episode having depressive characteristics was 54.0%. Some of the previous studies have shown that depressive episodes are more common than other episodes in patients with BD (Öztürk, 2002; Sadock and Sadock, 2007), however, there was also a study that showed that there was not a significant different in terms of the type of episodes experienced by patients with BD-I and BD-II (Ghaemi et al., 1999). Additionally, it was found that more depressive episodes were experienced by patients with BD-I and BD-II than patients with MDD in this study. The past literature is consistent with this finding (Mitchell et al., 2001; Kupfer et al., 2002).

In our study, the total number of hospitalizations were higher in the BD-I group compared to the BD-II and MDD groups and this finding is consistent with the previous literature (Mitchell et al., 2001; Kupfer et al., 2002), however there are also some studies that suggest that the total number of episodes and hospitalizations are higher in MDD (Dell'Osso et al., 1991; Bowden et al., 2005). Although no significant difference was found between the groups in terms of the severity of the depressive episodes, some authors have noted that depressive episodes are more moderate in MDD (Yazıcı, 2007; Sadock and Sadock, 2007), while other studies report that the severity is similar in the BD and MDD groups (Goodwin and Jamison, 1990; Ghaemi et al., 1999) or that more severe depressive episodes are seen in MDD patients (Mitchell and Malhi, 2004).

In our study, the number of cases experiencing at least one atypical and melancholic depressive episode was higher in the BD group compared to the MDD group. In some studies, depressive episodes with psychotic, melancholic or atypical features are suggested to be possible risk factors for mania or hypomania induced by antidepressants (Dell'Osso et al., 1991; Piccinni et al., 2007). Also there are some studies suggesting

that depressive episodes with atypical and psychotic features, particularly seen in the young, might predict the development of BD (Klein et al., 1985; Agosti and Stewart, 2001).

In this study, the incidence of hypothyroidism was higher in the BD-I group (16%) compared to the others (with an incidence of 7.4% in the MDD group). Some previous studies suggest that hypothyroidism is more frequent in BD, with a rate of 25-35%, compared to MDD (Öztürk, 2002; Sadock and Sadock, 2007; Yazıcı, 2007), whereas other studies found that there was no difference in the rate of hypothyroidism between the mood disorders (Thase, 2000; Kupfer and Shatzberg, 2005). However, the possible increased incidence of hypothyroidism in the BD-I group suggests that the rate of lithium use in this group should be considered as an underlying factor (Öztürk, 2002). The most common effect of lithium on the thyroid gland is hypothyroidism and it is reported to occur with various rates in different studies (Schou, 1999; Livingstone and Rampes, 2006). However, there are some studies emphasizing that the incidence of lithium-induced clinical hypothyroidism does not differ in frequency among normal and MD individuals (Bocchetta, 2001).

The most common psychiatric disorder among first and second degree relatives of our patients was MDD. Compared with other groups, the MDD rates were higher in the first and second degree relatives of MDD cases, and BD rates were higher in the first and second degree relatives of BD-I cases. Some studies report that the frequency of mood disorders are 8-18 times higher among first degree relatives of the patients compared to normal population (Rice et al., 1987; Blackwood et al., 2001). In a previous study, there was no significant difference detected between BD and MDD cases with regards to a family history of MDD (Mitchell et al., 2001). Also, it is important to note that a family history of BD is much more common in bipolar patients (Kupfer et al., 2002; Chiaroni et al., 2004). In the literature, it is emphasized that the risk of MDD is 2-3 times higher in first degree relatives of MDD cases compared to the normal population (Thase, 2000; Öztürk, 2002) and it is 2-10 times higher in individuals having a first degree relative diagnosed with BD (Kupfer and Shatzberg, 2005). The risk for having BD in the general population is 0.4-1.6% and this risk increases to 3-8% when a first degree relative is diagnosed with the disorder (Sadock and Sadock, 2007; Yazici, 2007).

Our findings showed that there were no significant differences between the three groups in terms of marital status, educational level and gender. In the literature, there are publications stating that there is a significant difference between the groups in terms of gender (Öztürk, 2002; Kessing, 2004; Sadock and Sadock, 2007) but others noted that gender did not have an effect on experiencing manic or depressive periods (Angst and Marneos, 2001; Kessing, 2004). Such a difference might be explained by differing methodologies between

the studies or the gender may be not efficient on the number of episodes and hospitalizations. Also, another significant reason for the differences in these findings might be inaccurate recall of the number and types of periods (Öztürk, 2002).

The present study observed that within the randomized study population, the female patients were admitted to the outpatient clinic more frequently than male patients. As in other studies, the present study show that in terms of the gender may be not significant differences efficient on MD (Mitchell et al., 2001; Akiskal, 2002).

Living alone is accepted as a risk factor for all types of mood disorders (Sadock and Sadock, 2007), and particularly, the being single/widower for male and the being married for women are accepted as a risk factor. Also a divorced family is associated with an increased risk for BD (Öztürk, 2002; Kupfer and Shatzberg, 2005). In contrast with our study, in the National Comorbidity Survey-2001 it was notified that low educational level increased the risk for any MD.

No differences were found in this study between the period of time until diagnosis in the BD-I and BD-II groups. However, some authors have noted that the mean time from the first referral to the diagnosis of BD is approximately 7.5- 12 years (Goodwin and Jamison, 1990; Ghaemi et al., 1999) and it could be misdiagnosed as MDD (Öztürk, 2002; Akiskal, 2002; Eroglu and Özpoyraz, 2010).

We found no differences between groups in terms of a history of previous psychiatric disorder. Among these, the most common disorder was panic disorder and the least was alcohol-substance abuse, interestingly. Some studies claim that the most common previous disorders in BD cases are alcohol-substance abuse and anxiety disorders (Sadock and Sadock, 2007; Eroglu and Özpoyraz, 2010). The low rates of alcohol-substance abuse, in our findings, might be attributed to the lower use in our country (Öztürk, 2002) and the higher number of women in our sample.

Although we didn't find any differences between the groups in terms of suicide attempts and methods in the literature, it has been emphasized that among BD cases suicide is a significant problem during depressive periods (Mitchell and Malhi, 2004) and 15- 19% of these cases lose their lives this way (Sadock and Sadock, 2007; Öztürk 2002).

The present study shows that MDD is predominantly associated with anxious and depressive temperaments and that BD is often associated with cyclothymic and hyperthymic temperaments. Consistent with our findings, some other studies reported that cylothymic and especially hyperthymic tem-

peraments are associated with BD and depressive temperament with MDD (Akiskal et al., 1998; Kupfer et al., 2002). Additionally, as some studies stated, cyclothymic, hyperthymic and neurotic temperaments are at the forefront in BD and these have an impact on clinical manifestations (Angst and Marneos, 2001; Kesebir et al., 2005). On the contrary, other studies noted that BD cases had the highest depressive temperament scores. Then the higher depressive temperament scores are seen in groups that experiencing recurrent depressive and single depressive episode, respectively (Mendlowicz, 2005b).

Some authors emphasized that cyclothymic temperament scores are much higher in BD-II with depressive episodes than MDD (Akiskal et al. 1998; Henry et al. 1999) and moreover, a hyperthymic temperament is associated with good prognosis (Akiskal and Hantouche, 2003; Chiaroni et al., 2004; Mendlowicz et al., 2005a). Also, consistent with our findings, some publications suggest that an anxious temperament is more frequent in depressive patients than BD cases and that depressive and anxious temperaments coexist commonly (Akiskal, 1996; Thase, 2000).

CONCLUSION

It has become important to determine the characteristics of mood disorders, to follow these patients regularly and continuously and also to plan management of the disorder appropriately in order to have a positive impact on psychosocial functionality. Simply differentiating between BD-I and BD-II may not be enough and other factors such as sociodemographics, clinical and temperament features could be predictive factors for early diagnosis and accordingly a better follow- up and treatment.

Limitations of the study

This study was conducted in an education and research hospital and the patients had a particular sociocultural level, thus it is impossible to generalize our findings to all BD and MDD cases.

Another limitation is that the individuals in this study may not all of their life into consideration when filling out the questionnaire, despite being instructed to do so. Even though all participants were between episodes, it is impossible to exclude the effects of the disease or subsyndromal symptoms on temperament. Owing to these limitations, it is an obligation for us to state that further prospective and randomized controlled studies with a larger sample size are needed to illuminate this issue.

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