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Research report

Cyclothymic and hyperthymic temperaments may predict bipolarity in major depressive disorder: A supportive evidence for bipolar II1/2 and IV

Shinjiro Goto, Takeshi Terao *, Nobuhiko Hoaki, Yumei Wang

Department of Neuropsychiatry, Oita University Faculty of Medicine, Idaigaoka 1-1, Hasama machi, Yufu city, Oita, 879-5593, Japan

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ABSTRACT

Background: The concept of soft bipolar spectrum has not been fully confirmed. The aim of the present study is to investigate the validity of bipolar II1/2 and IV concept.
Methods: The subjects were 46 consecutive outpatients. The individual temperament of each patient was recorded using the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Autoquestionnaire (TEMPS-A). The operational definition of bipolar II1/2 was those who had depression with cyclothymic temperament and that of bipolar IV was those who had depression with hyperthymic temperament. Finally, drug responses were investigated.
Results: DSM-IV-TR diagnoses were bipolar I (N = 1), bipolar II (N = 9), major depressive disorder (N = 34) and depressive disorder not otherwise specified (N = 2). Excluding one bipolar I patient, who had both cyclothymic and hyperthymic temperaments, patients with bipolar II1/2 (N = 32) and IV (N = 13) as well as bipolar II (N = 9) were classified into the soft bipolar spectrum, although there was considerable overlap. The categorization of soft bipolar spectrum and unipolar depression significantly predicted depressive, cyclothymic, irritable, and anxious temperaments. Moreover, soft bipolar spectrum patients with lithium treatment were significantly more in remission than those without lithium treatment. In addition, more of those with selective serotonin reuptake inhibitors (SSRIs) had a significant tendency to lower remission than those without SSRIs.
Limitations: This is a cross-sectional study with a relatively small number of subjects.
Conclusions: The present findings suggest that cyclothymic and hyperthymic temperaments may predict bipolarity, and the validity of bipolar II1/2 and IV concept is supported.

1. Introduction

Most bipolar disorder patients are 'hidden'; not diagnosed at all or falsely diagnosed as suffering from unipolar disorder (De Fruyt and Demyttenaere, 2007). For example, Ghaemi et al. (1999) investigated 48 consecutively admitted bipolar patients and found that 40% (19/48) had been previously diagnosed with unipolar major depressive disorder. A mean period of 7.5 years elapsed before a bipolar diagnosis was made in this group; antidepressant use was high on admission (38%) and was reduced with acceptable treatment response rates (Ghaemi et al., 1999). Moreover, Judd et al. (2002, 2003) showed that patients with bipolar I and II disorder suffered from depressive symptoms majority of the time — more than with manic or hypomanic symptoms; 31.9 versus 9.3% for bipolar I disorder, and 50.3 versus 1.3% for bipolar II disorder, respectively. Therefore, one is more likely to come into contact with a bipolar patient during a depressive episode than during a manic or hypomanic episode.

Katzow et al. (2003) showed that the relative misdiagnosis and underdiagnosis of bipolar disorder is due in part to the 'soft' symptoms of bipolarity that characterize patients with non-classical bipolar disorder. For such patients, the most common classification used is the "(soft) bipolar spectrum" and clinicians should focus on careful evaluation of patients with mixed anxiety/depressive symptoms or impulsivity conditions (substance abuse, borderline personality, bulimia,

* Corresponding author. Tel.: +81 97 586 5823; fax: +81 97 549 3583.
E-mail address: terao@med.oita-u.ac.jp (T. Terao).

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and attention deficit disorder). Utsumi et al. (2006) suggested that the identification of a hypomanic episode tends to be made more difficult because hypomania has not been experienced as a morbid event but rather as a favorable ego-syntonic episode. De Fruyt and Demyttenaere (2007) stated that the following features of the course and symptoms in depressed patients are indicative of bipolar origins: an admixture of psychomotor-retarded melancholic and atypical features, atypical features themselves, early age of onset, brief major depressive episode, antidepressant-induced mania, and post-partum depression. Additionally, Rihmer et al. (2010) stated that specific affective temperament types (depressive, cyclothymic, hyperthymic, irritable and anxious) are the subsyndromal (trait-related) manifestations and commonly the antecedents of minor and major mood disorders. According to Akiskal and Pinto (1999), there are 2 subtypes of bipolar spectrum which are not associated with manic or hypomanic state. These are bipolar II1/2 (depression in those who have cyclothymic temperament) and bipolar IV (depression in those who have hyperthymic temperament).

In the present study, we focused on these two temperaments and investigated depressive patients in those who have cyclothymic temperament (bipolar II1/2) and depressive patients in those who have hyperthymic temperament (bipolar IV) as well as bipolar II. This is a cross-sectional study and a single blind manner is used to perform the study as objectively as possible.

2. Methods

2.1. Subjects

Our sample consisted of 46 (17 male and 29 female) consecutive depressive outpatients with minimum treatment duration of 3 months, who consulted one of the authors (T.T.) at our university hospital during 1-month entry period. Their DSM-IV-TR diagnoses were bipolar I (N = 1), bipolar II (N = 9), major depressive disorder (N = 34) and depressive disorder not otherwise specified (N = 2). At the first visit to our department, as a routine assessment performed by T.T., patients showed mean scores on the 17-item Hamilton Rating Scale for Depression (HAM-D) of 14.8 ± 5.5 and for the Clinical Global Impression Severity Score (CGI-S) the score was 3.6 ± 1.0. At the study entry, all the patients gave a written informed consent. At that time, mean age was 45.8 ± 15.3 years old and their mean treatment duration at our outpatient department was 28.6 ± 18.8 months.

2.2. Assessment and questionnaire

At the study entry, the patients were asked to fill out the Japanese version of Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Autoquestionnaire (TEMPS-A) which is designed to identify depressive, hyperthymic, cyclothymic, anxious, and irritable temperament (Matsumoto et al., 2005). Whilst blind to the results of TEMPS-A, T.T. performed the assessment of their depressive state by using HAM-D and CGI-S. If their HAM-D score was equal to or less than 7, they were considered to be in remission. At that time, none of the patients were in a hypomanic or manic state and most patients were in or close to remission except in a few cases.

2.3. Procedures

2.3.1. Comparison of demographic data for bipolar disorder versus major depressive disorder

Apart from T.T. who assessed the patients' depressive state, another author (S.G.) dealt with all the data and analyzed them independently. The 46 patients were divided into two groups (10 with bipolar disorder and 36 with major depressive disorder and depressive disorder not otherwise specified) using DSM-IV-TR diagnoses, and compared from the viewpoints of age, gender, comorbidity, HAM-D and CGI-S scores at the first visit, treatment duration at our department, HAM-D and CGI-S scores at the study entry, and number in or out of remission.

2.3.2. Identification of temperaments and soft bipolar spectrum

Secondly, he (S.G.) recorded the temperaments of individual patients by using the TEMPS-A with its cut-off point. Although there were patients with overlapping temperaments, the operational definition of bipolar II1/2 was those who had depression with cyclothymic temperament and bipolar IV was those who had depression with hyperthymic temperament. Following this, patients with bipolar II, II1/2 and IV were classified into the soft bipolar spectrum. In this study, a patient with bipolar I was excluded at this time because the "soft" bipolar spectrum does not contain bipolar I. Thereafter, patients suffering from soft bipolar spectrum were compared with the remaining patients with unipolar depression from the viewpoints of age, gender, duration of treatment, HAM-D scores at the first visit and at the study entry, rate of remission at the study entry, and CGI-S at the study entry.

2.3.3. Assessment of drug effectiveness in soft bipolar disorder

Since the treatment duration from the first visit to the study entry assessment was variable in patients with soft bipolar spectrum, their drug effectiveness was estimated by using rate of remission (i.e., HAM-D score is equal to or less than 7). Patient medications consisted of mood stabilizers such as lithium, valproic acid and carbamazepine, and antidepressants including selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenalin reuptake inhibitors (SNRIs).

2.4. Statistical analysis

For continuous variables such as age, treatment duration, HAM-D score and CGI-S score, Mann–Whitney *U* test was used. For categorical variables such as gender, temperament and remission, Fisher's exact probability test was used. A p-value of $<.05$ was judged as statistically significant.

3. Results

3.1. Comparison of demographic data for bipolar disorder versus major depressive disorder

As shown in Table 1, patients with bipolar disorder had a significant tendency for lower HAM-D score and CGI-S score at the first visit, and a significantly lower HAM-D score at the study entry. Although bipolar patients had no comorbidity, 3 patients with MDD had obsessive compulsive disorder, panic