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Research report

# Differences between bipolar I and bipolar II disorders in clinical features, comorbidity, and family history

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ABSTRACT

*Background:* The present study was designed to investigate whether bipolar II disorder (BP-II) has different characteristics from bipolar I disorder (BP-I), not only in manic severity but also in clinical features, prior course, comorbidity, and family history, sufficiently enough to provide its nosological separation from BP-I.
*Methods:* Comprehensive clinical evaluation was performed based on information available from ordinary clinical settings. Seventy-one BP-I and 34 BP-II patients were assessed using the Diagnostic Interview for Genetic Studies, Korean version. Psychiatric assessment for first-degree relatives ($n=374$) of the probands was performed using the modified version of the Family History-Research Diagnostic Criteria.
*Results:* The frequency of depressive episodes was higher in BP-II ($p=0.009$) compared to BP-I. Further, seasonality ($p=0.035$) and rapid-cycling course ($p=0.062$) were more common in BP-II. Regarding manic expression, 'elated mood' was predominant in BP-II whereas 'elated mood' and 'irritable mood' were equally prevalent in BP-I. With regard to depressive symptoms, psychomotor agitation, guilty feeling, and suicidal ideation were more frequently observed in BP-II. BP-II patients exhibited a higher trend of lifetime co-occurrence of an axis I diagnosis ($p=0.09$), and a significantly higher incidence of phobia and eating disorder. The overall occurrence rate of psychiatric illness in first-degree relatives was 15.4% in BP-I and 26.5% in BP-II ($p=0.01$). Major depression ($p=0.005$) and substance-related disorder ($p=0.051$) were more prevalent in relatives of BP-II probands.
*Conclusion:* Distinctive characteristics of BP-II were identified in the current study and could be adopted to facilitate the differential diagnosis of BP-I and BP-II in ordinary clinical settings.


## 1. Introduction

Bipolar disorder (BPD) is a polymorphous condition, with diverse clinical features and courses. In order to determine a more homogeneous subgroup, various clinical sub-diagnoses have been proposed (Akiskal and Pinto, 1999). Among them, bipolar I disorder (BP-I) and bipolar II disorder (BP-II) are the most well-established disorders to have been adopted as separate diagnoses in the DSM-IV classification (American Psychiatric Association, 1994). According to the DSM-IV, BP-I and BP-II are distinguished only by the presence of a manic or hypomanic episode. Criteria for mania and hypomania have the same symptom profile (apart from psychotic symptoms, that can occur in mania alone) and differ only in the degree of severity. For these reasons, nosological issues regarding the

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separation of BP-II from BP-I has been raised (Ghaemi et al., 2008). However, whether BP-I and BP-II differ only in the severity of manic-side episodes or in other clinically and biologically meaningful ways remains controversial (Brugue et al., 2008).

Based on family study, Gershon et al. (1982) proposed that all forms of BPD were best conceptualized as a spectrum of illness representing thresholds on a continuum of underlying vulnerability, i.e., schizoaffective>BP-I>BP-II>unipolar disorder. However, in other genetic epidemiologic studies, morbid risk of BP-II was shown to be much higher in relatives of BP-II probands than in those of BP-I probands, suggesting a somewhat different genetic liability between them (Coryell et al., 1984; Endicott et al., 1985; Andreasen et al., 1987; Heun and Maier, 1993). Further controversial results relate to clinical features and comorbidity. According to comparative studies, BP-II appears to develop less severe symptoms, but exhibits more of a chronic course with more frequent episodes (Vieta et al., 1997; Judd et al., 2003a). Moreover, unstable interpersonal relationships and social adjustment (Akiskal et al., 2006b), and comorbidity of psychiatric illness were more frequently observed in BP-II than in BP-I (Vieta et al., 2000; Mantere et al., 2006). A higher risk of suicide has also been reported in patients with BP-II as compared to those with BP-I (Arato et al., 1988; Rihmer and Pestality, 1999; Valtonen et al., 2008). In the evaluation of long-term diagnostic stability, only a small portion of BP-II was converted to BP-I, i.e., 5% in 5 years (Joyce et al., 2004) and 7.5% in 10 years (Coryell et al., 1995). However, some other study findings have been opposed to the distinction between BP-I and BP-II reporting similar rates of suicidal attempt, rapid cycling, seasonality, and comorbid psychiatric illness in both (Vieta et al., 1997; Valtonen et al., 2005).

The present study was designed to provide a comparison of BP-I and BP-II with respect to comprehensive clinical aspects based on information available in ordinary clinical settings, i.e., the clinical characteristics, prior course, patterns of axis I comorbidity, and family history. Cumulative data on the relationship between BP-I and BP-II could provide important clues for validation of the classification system of mood disorders. Furthermore, given that the criteria for subdividing manic and hypomanic episodes have been quite arbitrary and ambiguous, identification of further clinical characteristics that could be considered in the differential diagnosis between BP-I and BP-II in ordinary clinical settings is warranted.

## 2. Method

### 2.1. Subjects

Patients who met the diagnostic criteria of the DSM-IV BP-I and BP-II were recruited from outpatient and inpatient units of the Samsung Medical Center between September 2007 and January 2010. The best-estimate diagnosis was independently rendered for each individual by two psychiatrists. The age range was limited between 18 and 60 years and subjects had been required to be clinicly stable, i.e., to have scored 3 (mildly ill) or lower on the Clinical Global Impression of Severity scale (Guy, 1976) at the time of assessment. Subjects were also required to have had no evidence of organic mental disorder, mental retardation, or medical illness related to mental symptoms. Initially, 105 patients, who met above criteria and agreed to participate in the comparative study of clinical features and comorbidity, were enrolled. Among them, 88 patients, who by themselves and whose main care-givers agreed to provide information on detailed family histories within first-degree relatives of the probands, were enrolled in the family study. Demographic characteristics of the subjects and their first-degree relatives ($\geq$18 years) have been summarized in Table 1. Written informed consent was obtained from all subjects after a complete explanation of the study. This study was approved by the institutional review board of the Samsung Medical Center.

### 2.2. Assessment of clinical characteristics

Information was collected through a direct interview with patients, their available care-givers, and their physicians. Patient medical records were also used as an supplementary information source. Direct interviews were performed by psychiatrists (JHB, DYP, JC, and JSK) using the Korean version of the Diagnostic Interview for Genetic Studies (Joo et al., 2004), a semi-structured clinical interview schedule adopting DSM-IV classification and criteria of axis I disorders. All interviewers had at least one-year research experience of using DIGS, and they had several times of consensus-rating meetings in order to improve inter-rater reliability. On the basis of the accumulated information, patients' diagnoses were re-confirmed. Also, illness courses, symptom profiles, lifetime co-occurrence of other DSM-IV axis I disorders, and past history of suicide attempts were evaluated (Tables 2, 3, and 4). For the assessment of clinical course, DIGS asks raters to describe subject's clinical course in detail using a mood chart and it also provides structured items rating number of mood episodes, age at onset of mood episodes, and age at onset of the most severe mood episode.

The age of onset was defined as an age at which any mood episode (manic, hypomanic, mixed or depressive) meeting the DSM-IV criteria had developed. Assessment of symptom profiles of mood episodes was based on lifetime clinical features, i.e., based on the most severe and prominent episode, considering that BPD patients might show different episode features at various times, especially due to the effects of medication (Parker, 2008). Among BP-I patients, 18.3% (13/71) had experienced mixed episode defined by DSM-IV criteria. 'Seasonality' assessed in the current study was not confined to the 'seasonal pattern of depression' by DSM-IV criteria, but rather defined as a tendency to experience seasonal variations in mood, behavior, and vegetative functions, a concept which was adopted from previous studies (Kasper et al., 1989; Hardin et al., 1991). 'Rapid cycling' was assessed based on the DSM-IV criteria for 'rapid-cycling specifier'. 'Antidepressant-related (hypo)mania' was defined as clinically significant treatment-emergent mood elevation meeting the DSM-IV criteria for (hypo)mania or needing intervention by treating clinicians, which had been adopted from a previous large-scale psychopharmacologic study (Sachs et al., 2007).

### 2.3. Assessment of family history

We obtained information about family members through interviews with probands and their main care-givers who