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Preliminary communication

Prevalence of bipolar disorder in panic disorder patients in the Japanese population

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ABSTRACT

Background: We examined the rate of bipolar I (BPD-I) and bipolar II disorders (BPD-II) in panic disorder (PD) patients, and compared clinical and psychological variables between PD patients with and without bipolar disorders (BPD).

Methods: Participants were 649 Japanese patients with PD (215 men and 434 women, 38.49 ± 10.40 years) at outpatient clinics for anxiety disorders. Constructive interviews using the Mini-International Neuropsychiatric Interview (MINI) were conducted to confirm the diagnosis of PD, agoraphobia, and BPD, as well as the presence and severity of suicide risk in each subject. Clinical records were also reviewed to confirm the diagnosis of PD and BPD. Participants then completed several questionnaires, including the State Trait Anxiety Inventory-Trait scale, the Anxiety Sensitivity Index, and the Revised Neuroticism-Extraversion- Openness Personality Inventory (NEO-PI-R).

Results: We found that 22.34% of the PD patients had BPD (BPD-I: 5.24%, BPD-II: 17.10%). PD patients with BPD-I showed higher prevalence and severity of suicide risk, trait anxiety, anxiety sensitivity, and neuroticism, and lower agreeableness (subscales of the NEO-PI-R) than those with BPD-II and those without BPD.

Limitation: First, we could not investigate the order of the onset of PD and BPD. Second, BPD patients without PD were not studied as another control group for PD patients with BPD.

Conclusion: PD patients had high prevalence of BPD. Both PD patients with BPD-I and those with BPD-II had high severity of suicide risk, trait anxiety, anxiety sensitivity, neuroticism, and agreeableness, though these characteristics were more prominent in patients with BPD-I.

1. Introduction

Subjects with panic disorder (PD) might have an elevated risk of bipolar disorder (BPD). This issue is critical not only for etiological studies but also for clinical practices. For example, although antidepressants are considered the first line of treatment for PD,

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they could be contraindicative when BPD is overlapped with PD. Studies have also observed that suicide risk is increased by comorbid PD in individuals with BPD (see review by Kilbane et al. (2009)).

Studies have observed significant elevations in the comorbidity rate of PD in BPD, while the concrete rate must be further studied and discussed (Sala et al., 2012; Castilla-Puentes et al., 2011). A US study estimated a lifetime PD rate of 53.4% in 1600 BPD subjects (Sala et al., 2012). In addition, a Latin-American study observed that 23.1% of 1505 BPD patients had PD at certain emergency departments, while the rate was only 12.3% in patients with non-bipolar mental disorders (Castilla-Puentes et al., 2011).

The comorbidity rate of BPD in PD has been estimated at around 20% in several studies (Birmaher et al., 2002; Bowen et al., 1994; Toni et al., 2008); however, the sample size was small in most of those studies and lower rates were observed (Perugi et al., 1999; Savino et al., 1993). Toni et al. (2008) estimated the comorbidity rate of BPD-II at 16.0% in 326 Italian outpatients with PD, while two other Italian studies found that the rates of BPD-I and BPD-II were 2.1% and 5.0% in 140 outpatients with PD (Savino et al., 1993) and 0.8% and 5.0% in 119 outpatients with PD (Perugi et al., 1999), respectively. Bowen et al. (1994) also reported a rate of 23.1% for BPD or cyclothymic disorder in 108 Canadian subjects with PD (Bowen et al., 1994). Birmaher et al. (2002) found that the rate of BPD was 19.0% in 42 US children and adolescents with PD (aged 5–19 years). In Asian populations, a Taiwanese study observed that 3.6% of 3672 subjects with PD were diagnosed with BPD within the 6 months before and after their first PD diagnosis (i.e., one year in total for each patient), which was significantly higher than in the subjects without a diagnosis of PD in the past 10 years (0.2%, odds ratio=15.5; Chen and Lin, 2011). However, lifetime comorbidity was not studied in Chen and Lin (2011) and no other studies have been conducted in Asian populations to our knowledge. Further studies are therefore required to investigate the comorbidity rate of BPD in PD.

While the detection of comorbid BPD is critically important in the treatment of PD, it might often fail because it is difficult to accurately diagnose in clinical settings such as outpatient clinics or primary care facilities, especially for mild cases. However, studies of the clinical and psychological variables that might be related to the comorbidity of BPD in PD could help in its detection. Previous studies have suggested that neuroticism might be associated with both PD and BPD (Stanković et al., 2006, Carrera et al., 2006, Barnett et al., 2011). Other studies have suggested that suicide risk might be elevated in subjects with both PD and BPD (Dilsaver et al., 1997; Dilsaver and Chen, 2003; Balazs et al., 2006; Frank et al., 2002; Goodwin and Hamilton, 2001). However, few studies have investigated other psychological or clinical variables. One study observed that anxiety sensitivity could contribute to the increased prevalence and severity of PD in BPD (Simon et al., 2005). Agoraphobia and age of onset of PD were also examined, but were found to not be associated with comorbidity of BPD in PD (Savino et al., 1993). This shows that further studies are required.

Thus, we aimed to investigate the comorbidity rate of BPD in PD, as well as find out whether several clinical and psychological variables can help accurately assess comorbidity of BPD in PD. The prevalence of BPD-I and BPD-II were examined in Japanese outpatients with PD, while the clinical and psychological variables were compared between the PD patients with and without BPD.

2. Methods

2.1. Participants

A total of 725 outpatients with PD being treated at two psychiatric clinics majoring in anxiety disorders participated in this study. The clinics were located in Tokyo and Nagoya, Japan. The diagnosis of PD was confirmed according to DSM-IV criteria (American Psychiatric Association, 1994).

Valid data were obtained from 649 PD patients, including 215 men and 434 women. The mean age of the participants was 38.49 ± 10.40 years. The mean age of onset of PD was 28.35 ± 9.82 years, while the mean duration of PD was 10.30 ± 8.38 years. Participants included 368 patients with agoraphobia (56.70%).

2.2. Measures

2.2.1. The Mini-International Neuropsychiatric Interview

The Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) is a brief structured interview for the major axis I psychiatric disorders of the DSM-IV. We used the MINI to confirm the diagnosis of PD and BPD, the presence of agoraphobia, and the presence and severity of suicide risk in the participants in this study. Suicide risk was scored by taking into account the presence of death ideation and suicidal ideation, gestures during the past month, and number of suicide attempts during their whole life (scores ranged from 0 to 33). Suicide risk was first evaluated as "not present" (score=0) or "present" (score=1). In participants for which the answer was "present," severity was evaluated as "mild" (score=1–5), "moderate" (score=6–9) or "severe" (score=10). In the statistical analysis, the stages of the question were merged and suicide risk was rated as "none, mild, moderate, and severe."

2.2.2. State Trait Anxiety Inventory-Trait scale

The State Trait Anxiety Inventory (STAI: Nakazato and Mizuguchi, 1982; Spielberger et al., 1970) is a self-report questionnaire consisting of 40 questions, comprising a state anxiety subscale with 20 items and a trait anxiety subscale with 20 items. We used only the trait anxiety scale (STAI-T) in this study.

2.2.3. Anxiety Sensitivity Index

The Anxiety Sensitivity Index (ASI: Peterson and Reiss, 1992; Maruta et al., 2007) is a reliable and valid 16-item index of the tendency to believe that the physical sensations associated with anxiety are harmful and bear negative physical, social, or psychological consequences. Anxiety sensitivity is defined as excessive fears of anxiety-related sensations based on beliefs that these sensations are harmful (Reiss, 1991), and might be a heritable (Stein et al., 1999) risk factor for the emergence of panic attacks (Plehn and Peterson, 2002; Schmidt et al., 1997), the onset of PD (Gardenswartz and Craske, 2001), and the re-emergence of panic or relapse to medication use in clinical populations (Bruce et al., 1995; Ehlers, 1995).

2.2.4. The Revised Neuroticism-Extraversion-Openness Personality Inventory (Costa and McCrae, 1989, 1992a, 1992b)

The Revised Neuroticism-Extraversion-Openness Personality Inventory (NEO-PI-R) is a self-report questionnaire consisting of 240 questions that provides a comprehensive and detailed assessment of adult personality based on the Five-Factor Model of personality. The NEO-PI-R is made up of five subscales: Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness.

2.3. Procedure

Members of our research team (physicians and clinical psychologists) conducted the constructive interviews using the M.I.N.I. to confirm the diagnosis of PD and BPD, the presence or absence of agoraphobia, and the presence and severity of suicide risk in each participant. The diagnosis of PD and BPD