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Relationships between anxiety severity, diagnosis of multiple anxiety disorders, and comorbid major depressive disorder

Masaki Miyazaki, Aihide Yoshino *, Soichiro Nomura

Department of Psychiatry, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359-8513, Japan

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ABSTRACT

Patients with anxiety disorder (AD) are more likely to be concurrently comorbid with other ADs or major depressive disorder (MDD). However, it is unknown whether such patients show more severe anxiety symptoms than patients with single AD. We compared anxiety severity among patients with single AD, multiple ADs, and multiple ADs plus MDD. Subjects were 136 consecutive outpatients with any AD who were comprehensively diagnosed. Symptom severity of panic disorder (PD), social anxiety disorder (SAD), obsessive–compulsive disorder (OCD), and generalized anxiety disorder (GAD) was measured using self-rating questionnaires, and the scores were compared among the 3 comorbidity conditions (single AD vs. multiple ADs vs. multiple ADs plus MDD). PD and SAD scores in the multiple ADs and the multiple ADs plus MDD conditions were significantly greater than the scores in the single AD condition regardless of diagnosis of PD and SAD. OCD scores did not differ among the 3 conditions while the scores in patients with OCD were significantly greater than those in patients without OCD. GAD scores in the multiple ADs plus MDD condition were significantly greater than those in the single AD and the multiple AD conditions. Moreover, in patients with MDD, the GAD scores in patients with GAD were not greater than those in patients without GAD. The results suggest that symptoms of PD, SAD, and GAD but not OCD are affected by the diagnosis of multiple ADs or comorbid MDD and that diagnosis of comorbid MDD affects GAD symptoms more strongly than diagnosis of GAD.

1. Introduction

More than half of the patients with anxiety disorder (AD) are concurrently comorbid with other ADs or major depressive disorder (MDD) (Miyazaki et al., 2010). The evidence is consistent with the results from previous large epidemiologic studies (Hasin et al., 2005; Regier et al., 1993). Therefore, physicians should pay attention to comorbidity with other ADs and MDD when consulting patients with AD. However, little is known whether patients with multiple ADs or ADs comorbid with MDD show more severe anxiety symptoms than patients with a single AD. We conducted the present study to compare the anxiety severity among patients with single AD, multiple ADs, and multiple ADs plus MDD.

In this study, the severity of anxiety symptoms in patients with single AD was compared with the symptom severity in patients with multiple ADs comorbid with or without MDD using self-rating questionnaires specific for panic disorder (PD), social anxiety disorder (SAD), obsessive–compulsive disorder (OCD), and generalized anxiety disorder (GAD). We also explored the symptomatologic relationships within ADs and between ADs and MDD. For example, among patients with any AD, those with GAD are believed to be most commonly comorbid with MDD (Hasin et al., 2005; Sanderson et al., 1990). In fact, GAD and MDD share a wide range of symptoms. In the DSM-IV, 4 of the 6 diagnostic items of GAD are included in the diagnostic criteria for MDD, and the exclusion criteria of "not occurring only during MDD" maintains GAD as a distinct entity. Therefore, it is important to know how the diagnosis of MDD affects the severity of GAD-related symptoms in patients with GAD and other ADs.

2. Methods

2.1. Self-rating questionnaires

Many self-rating questionnaires have been developed to measure the severity of symptoms in PD, SAD, OCD, and GAD. Out of them, we selected 4 widely used questionnaires whose reliability and discrimination validity against other ADs have been confirmed. We used the Anxiety Sensitivity Index (ASI) for PD, Social Phobia Inventory (SPIN) for SAD, Obsessive–Compulsive Inventory Revised (OCI-R) for OCD, and Penn State Worry Questionnaire (PSWQ) for GAD.

* Corresponding author. Tel.: +81 42 995 1619; fax: +81 42 996 5203.
E-mail address: aihide@ndmc.ac.jp (A. Yoshino).

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ASI (Reiss et al., 1986) consists of 16 question items and has high specificity for PD as discriminating PD from other ADs (Taylor, 1999; Zinbarg et al., 1997). SPIN (Connor et al., 2000) consists of 17 items and clearly distinguishes SAD from PD, agoraphobia, and OCD (Antony et al., 2006). OCI-R (Foa et al., 2002) is a revised version of OCI (Foa et al., 1998) wherein the question items are reduced from 42 to 18 and has the ability to distinguish OCD from other ADs (Abramowitz and Deacon, 2006). PSWQ (Meyer et al., 1990) consists of 16 items to evaluate the generality, excessiveness, and uncontrollability of pathologic anxiety in GAD. It has been reported that PSWQ discriminates GAD from other ADs (Brown et al., 1992). We re-estimated the reliability of each scale using Cronbach's alpha coefficient; 76 healthy volunteers (mean (SD) age, 34.3 (11.4) years; females, 26) were enrolled in this study. The alpha-coefficients of ASI, SPIN, OCI-R, and PSWQ were 0.94, 0.97, 0.97, and 0.95, respectively, indicating that each rating scale had high internal consistency.

2.2. Subjects

This study was approved by the Ethics Committee of the National Defense Medical College. The candidates comprised 353 consecutive psychiatric outpatients who visited our ambulatory unit from January 2006 to December 2007; they were clinically diagnosed to have any AD by attending physicians. All the participants were provided a detailed description of the study, and their written informed consent was obtained. The patients were comprehensively diagnosed using the Mini International Neuropsychiatric Interview (MINI) (Otsubo et al., 2005; Sheehan et al., 1998), a structured interview to diagnose the current 15 psychiatric disorders. The MINI has been confirmed to have high diagnostic concordance rates with ICD-10, DSM-III-R, and DSM-IV (Lecrubier et al., 1997; Sheehan et al., 1998, 1997). The MINI can diagnose 6 ADs, including PD, agoraphobia, SAD, OCD, GAD, and post-traumatic stress disorder (PTSD). In the present study, we considered PD and agoraphobia as a single entity "PD" since both patients with PD without agoraphobia and patients with agoraphobia without history of PD are rare. According to the exclusion criteria for GAD, we did not make a diagnosis of GAD if the patient presented with GAD symptoms only during episodes of MDD. Of the 353 candidates, we excluded 105 who did not have any ADs and 91 who had a history of a psychotic disorder, alcohol and substance use disorder, eating disorder, antisocial personality disorder, manic episode, or hypomanic episode. Since the present study aimed to explore the genuine relationships between ADs and MDD, patients with a history of these disorders were excluded. PTSD was also excluded because there were only 4 patients with PTSD. After 59 patients did not respond to the questionnaire, 158 remained.

A total of 158 participants were classified into the following 4 conditions on the basis of the number of ADs diagnosed and the concurrent comorbidity of MDD: single AD without MDD condition ($N = 66$), multiple ADs without MDD condition ($N = 24$), single AD plus MDD condition ($N = 22$), and multiple ADs plus MDD condition ($N = 46$). Since the number of patients with PD, SAD, and OCD was no more than 4 in the single AD plus MDD condition, we excluded the condition from further analysis and, finally, 136 subjects (mean (SD) age, 38.3 (14.9) years; females, 87) remained (Table 1). Out of the 136 subjects, 59, 67, 44, and 62 were diagnosed to have PD, SAD, OCD, and GAD, respectively (Table 2). The diagnoses of single AD without MDD, of multiple ADs without MDD, and of multiple ADs plus MDD were referred to as single AD, multiple ADs, and multiple ADs + MDD conditions, respectively.

Table 1
Demographic characteristics of the patients with the 3 diagnostic conditions.

	N	Female (%)	Age (SD)
Single AD	66	39 (59.1)	38.3 (16.6)
Multiple ADs	24	18 (75.0)	37.1 (13.5)
Multiple ADs + MDD	46	30 (65.2)	39.1 (13.3)
Total	136	87 (64.0)	38.3 (14.9)

Table 2
The number of subjects with the 3 diagnostic conditions positive for the diagnosis of each AD.

	Single AD	Multiple ADs	Multiple ADs + MDD
PD	18 (10)	15 (11)	26 (18)
SAD	21 (11)	17 (13)	29 (18)
OCD	16 (9)	10 (7)	18 (11)
GAD	11 (9)	12 (10)	39 (24)

Number in parentheses denotes the number of female subjects.

2.3. Statistical analysis

The main aim of this study was to compare the severity of anxiety symptoms among the 3 conditions for each AD. Therefore, each scale score was analyzed using analysis of variance (ANOVA) concerning 2 factors: the AD diagnosis targeted by each scale (for example, ASI targeted PD; positive vs. negative diagnosis) and comorbidity condition (single AD vs. multiple ADs vs. multiple ADs + MDD). Scheffe's method was also used as the post hoc multiple comparison.

3. Results

3.1. PD severity

Fig. 1(a) shows the comparison of mean ASI scores between 6 conditions: patients with PD and patients without PD in each of the single AD, multiple ADs, and multiple ADs + MDD conditions. Mean ASI scores in the patients with PD and without PD were 32.0 (13.2) and 20.1 (11.7), respectively, and the main effect was significant ($F = 16.3$, df = 1/130, $p < 0.0001$). Mean ASI scores in the single AD, multiple ADs, and multiple ADs + MDD conditions were 20.1 (12.8), 29.0 (12.0), and 30.7 (13.2), respectively, and the main effect was significant ($F = 6.0$, df = 2/130, $p < 0.003$). Multiple comparisons revealed that ASI scores in the multiple ADs and multiple ADs + MDD conditions were significantly greater than those in the single AD condition. However, the interaction was not significant ($F = 1.5$, df = 2/130, $p = 0.22$). These results indicated that ASI scores in the patients with PD were higher than those in the patients with other AD and that ASI scores in patients with multiple ADs and ADs comorbid with MDD were higher than those in the patients with a single AD regardless of diagnosis of PD.

3.2. SAD severity

Fig. 1(b) compares mean SPIN scores among the patients with SAD and the patients without SAD in the 3 conditions. Mean SPIN scores in the patients with SAD and without SAD were 38.7 (14.2) and 20.3 (14.9), respectively, and the main effect was significant ($F = 32.0$, df = 1/130, $p < 0.0001$). Mean ASI scores in the single AD, multiple ADs, and multiple ADs + MDD conditions were 23.0 (14.8), 32.6 (16.2), and 36.8 (17.7), respectively, and the main effect was significant ($F = 4.5$, df = 2/130, $p < 0.02$). Multiple comparisons revealed that SPIN scores in the multiple ADs and multiple ADs + MDD conditions were significant greater than those of the single AD condition. However, the interaction was not significant ($F = 0.1$, df = 2/130, $p = 0.89$). These results were similar to those of PD severity.