Distinctive Clinical Features of “Anxious-Depressive Attack”

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Abstract

Background: Anxious-depressive attack (ADA) is a proposed novel symptom complex associated with anxiety and mood disorders. Its main features are (1) sudden intense distressing emotions with no direct psychological cause, (2) intrusive memories of various negative events, (3) worry and agitation about the details of the rumination and (4) various coping behaviors, including acting out. The author has reported five previous cases of ADA. The present study investigates the clinical significance of ADA.

Method: First, to compare clinical characteristics between subjects with and without ADA, 331 consecutive new outpatients were examined (Study I). Second, because of the similarities between ADA and panic attack, the characteristics of ADA were examined in 65 panic disorder (PD) patients (Study II).

Results: The overall incidence of ADA was 43.2%. In PD and social anxiety disorder patients, those exhibiting ADA were significantly younger and had significantly more severe depression and social anxiety than those without ADA (Study I). In PD patients with ADA, ADA preceded panic attacks, and ADA frequency was correlated with the severity of depression and social anxiety but not with panic symptoms (Study II). ADA was often managed with acting out behavior (Study II).

Conclusion: ADA appears to be relatively common among people with anxiety and mood disorders. We found that ADA was correlated with the severity of social anxiety, but not PD. PD patients exhibited a “seesaw” phenomenon between ADA and panic attacks. ADA may be a core symptom complex of a severe form of anxious depression.

Key Words: Anxious-depressive attack, Severe anxious depression, Flashback, Self-harm

[Introduction]

Anxious-depressive attack (ADA) is a proposed novel symptom complex consisting of sudden intense feelings of distressing emotions with no direct psychological cause, followed by intrusive rumination of regretful memories that induce prominent discomfort (Kaiya, 2016). ADA events are typically managed with a range of coping behaviors, including acting out patterns in various disorders involving anxious and/or depressive states (Kaiya, 2016). Thus, ADA seems to manifest as a psychological version of a panic attack.

ADA is distinct from other known syndromes and disorders. ADA does not involve the prominent and various physiological symptoms of panic attack (American Psychiatric
Patients with ADA do not exhibit anticipatory anxiety, and do not commonly visit physicians with this complaint. ADA mimics an agitated depressive state, which is described as “anxious distress” in Specifiers for Depressive Disorders (American Psychiatric Association, 2013). However, ADA differs from this condition in several ways, occurring as an attack and emerging in a particular order as sudden feelings of distress, painful rumination, and consequent coping behavior. Flashbacks are observed in both ADA and post-traumatic stress disorder (American Psychiatric Association, 2013). However, flashbacks in ADA do not contain past experiences of serious trauma, as described in criterion A (DSM-5) of the diagnosis for post-traumatic stress disorder, and the subjects of flashbacks in ADA are various and ever-changing. Ataque de nervios (American Psychiatric Association, 2013), also known as Puerto Rican syndrome, is considered a culture-bound syndrome. This syndrome involves uncontrollable screaming or shouting, crying, trembling, sensations of heat rising in the chest and head, dissociative experiences, and aggressive or suicidal behaviors. Attacks are often associated with a stressful event relating to the subject’s family. The symptoms of ADA are similar to those of Ataque de nervios, including intense emotional outbursts and occasional fit-like paroxysms of emotionality. In ataque de nervios, however, attacks frequently occur as a direct result of a stressful event, whereas ADA has no direct cause. The sudden emotional excitement experienced by patients with schizophrenia can be clearly differentiated from ADA because schizophrenic emotional fits are reactions to a hallucination and/or delusion (American Psychiatric Association, 2013). Thus, ADA is a unique symptom complex that has not been described previously.

Several studies in Western populations have suggested the existence of ADA. For example, Liebowitz and Klein (1979) reported “episodes of abruptly depressive mood” in hysteroid dysphoria (atypical depression). In addition, patients with social anxiety disorder (SAD) have been reported to repeatedly experience excessively negative intrusive images of past unpleasant social incidents (Hackmann et al., 2000). Moreover, approximately 30% of patients with depression suffer from comorbid flashbacks (Felker et al., 2003).

Thus, ADA might be concealed in depressive states and overlooked by physicians for a long period, because patients with ADA seldom report their personal experiences of ADA on their own initiative. Physicians can observe only the externally visible symptoms of ADA, such as acting out behavior resulting from painful rumination. Thus, patients with ADA may be commonly diagnosed patients with Borderline Personality Disorder (American Psychiatric Association, 2013). Elucidating the various characteristics of ADA in a clinical setting may contribute to better understanding of affected patients.

In the current study, two experiments were conducted to examine the clinical characteristics of ADA. Study I clarified the clinical significance of ADA, investigating which types of psychiatric disorders involve ADA, and the incidence of ADA in each disorder. Clinical differences between patients with and without ADA were also examined. Study II examined the characteristics of ADA in panic disorder (PD). As mentioned above, ADA may be a psychological version of panic attack. Thus, it is important to understand the relationship between ADA and panic attack.
[Subjects and Method]

1. Subjects

Subjects were recruited from an outpatient clinic in Nagoya, Japan, specializing solely in anxiety disorders. Patients were diagnosed according to the DSM-IV-TR (American Psychiatric Association, 2000). Primary diagnoses were given for the most clinically urgent conditions for patients, and comorbid mental disorders were diagnosed in addition to the primary diagnosis. Informed consent was obtained from each subject, indicating that they agreed to undergo a detailed evaluation of clinical symptoms for ADA and other related clinical variables. All consenting patients were asked about their life history.

2. Confirmation of ADA

Criteria for ADA were developed according to its characteristics (Table 1). The presence or absence of ADA was assessed using a questionnaire for confirmation of ADA, which we developed according to the criteria of ADA (Appendix I).

3. Psychological assessments

We used the following instruments:

(1) Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) for the diagnosis of mental disorders according to the DSM-IV-TR in Studies I and II.

(2) Structured Clinical Interview for the DSM-IV-TR Axis II Personality Disorders (SCID; First et al., 1997) for the diagnosis of personality disorders according to DSM-IV-TR in Study II.

(3) Hamilton Depression Scale (HAMD) (Nakane & Williams, 2004) for assessment of the severity of depression in Study II.

(4) Self-rating Depression Scale (SDS) (Zung, 1965) for quantitatively assessing depression status in Studies I and II.

(5) Beck Depression Inventory-II (BDI-II) (Beck et al., 1996) for measuring the severity of depression in Studies I and II.

(6) Hamilton Anxiety Scale (HAMA) (Hamilton, 1959) for rating the severity of anxiety in Study II.

(7) Anxious Depression Scale (ADS) (Suyama et al., 2013) for rating the severity of atypical depression in Study I.

(8) Panic and Agoraphobia Scale (PAS) (Bandelow, 1995) for measuring the severity of agoraphobia with or without panic attacks in Studies I and II.

(9) Liebowitz Social Anxiety Scale, Japanese version (LSAS-J) (Liebowitz, 1987) for assessing the range of social interactions and performance situations feared by a patient in Studies I and II.

(10) Social Anxiety Scale (SAS) (Kaiya et al., 2004) for measuring the severity of SAD in Studies I and II.

4. Statistical analysis

All statistical analyses were conducted using the Statistical Package for the Social Sciences, version 19.0 for Windows (SPSS Inc., Tokyo, Japan; 2010). Chi-square tests and Student’s t-tests were employed in Study I. Two-way analysis of variance (ANOVA) was performed, with Group (ADA yes/no) as the first factor, and diagnosis (PD, SAD, depression with atypical features [DAF]) as the second factor, with variables for three depression scales (SDS, BDI-II, ADS) and two social anxiety scales (LSA-J, SAS), followed by post-hoc tests, to examine differences between patients with and without
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ADA.

[Study 1]

1. Subjects
The inclusion and exclusion criteria in Study I were as follows:
Inclusion criteria: Patients aged between 18 and 60 years old who first visited the author’s outpatient clinic consecutively from April 2007 to December 2008.
Exclusion criteria: Intense suicidal ideation or severe aggression towards others. Major physiological diseases requiring medical treatment.

2. Method
All patients were diagnosed according to the DSM-IV-TR at the first visit. If patients experienced two or more ADA during the past year, fulfilling the criteria (Table 1), they were surveyed using the Questionnaire for Confirmation of Anxious-Depressive Attack (Appendix I). The survey was conducted by the author (a psychiatrist) and a clinical psychologist independently at the clinical evaluation. All psychological batteries used in Study I were self-report measures, and were completed before the evaluations at the first visit.

3. Results
There were 613 first-visit patients to the author’s clinic during the research period, 373 of which were invited to participate. Of these, 335 patients consented to take part in the experiment.

The consenting patients consisted of 129 patients with PD, 63 patients with SAD, 46 patients with DAF, and 93 patients with other diagnoses. The incidence of two or more ADAs during the past year was 45.0% in the PD group, 44.4% in the SAD group, and 78.3% in the DAF group (Figure 1). The rate of ADA positive patients among those with other disorders was 22.6% (21/93) (Figure 1): specifically, the rate was 33.3% (12/36) among patients with depression other than DAF, 26.7% (4/15) among patients with generalized anxiety disorder, 66.7% (2/3) among patients with post-traumatic stress disorder, and 33.3% (1/3) among patients with obsessive-compulsive disorder. The kappa coefficient was 0.98 for the assessment of ADA in the 335 patients between the author (psychiatrist) and the clinical psychologist. There were four cases in which the confirmation of ADA between the psychiatrist and the psychologist were discordant (two cases of eating disorders, one case of acute stress dis-

Table 1 Diagnostic criteria of anxious-depressive attack (developed by the author)

|   | A discrete period of intense fear and discomfort, in which symptoms proceed in descending order. |
|---|--------------------------------------------------------------------------------------------------|
| 1 | Abrupt surge of intense discomfort consisting of mixed emotions of anxious and depressive nature with or without being moved to tears. A peak comes within several seconds or minutes. |
| 2 | Intrusion of mostly negative memories, including unpleasant lines of thought or images related to recent or past adverse events (flashbacks), accompanied by rumination continuing for several tens of minutes to several hours. |
| 3 | Mostly intense worry and agitation during rumination. |
| 4 | Various coping behaviors to manage intense discomfort during the rumination occasionally appear as acting out behaviors. |
|   | Physical symptoms (e.g., shortness of breath, palpitations) are extremely modest. |
|   | Anxious-depressive attacks are not caused by the direct psychological effects of any stress. |
order and one case of schizophrenia). These cases were not included in Study I.

A total of 238 patients, including 129 with PD, 63 with SAD, and 46 with DAF were evaluated in Study I. The sex ratio was not significantly different between ADA positive and negative groups ($\chi^2=0.07$, df=1, $p=0.79$). Age was significantly lower among patients with ADA than in those without ADA in PD patients ($t=-3.68$, $p<0.001$) and SAD ($t=-2.41$, $p=0.02$), but not DAF patients ($t=-0.84$, $p=0.41$) (Table 2).

Table 2 shows the mean scores on the depression scales (SDS, BDI-II) according to the presence/absence of ADA. The interaction between the presence/absence of ADA and diagnosis was significant for the BDI-II and ADS. In addition, a simple main effect was significant: BDI-II and ADS scores among patients with PD and SAD with ADA were significantly higher than those without ADA. For the SDS and LSAS-J, the interactions were not significant, but significant main effects of ADA were observed. Among patients with PD and SAD, the SDS, BDI-II, ADS, and LSAS-J scores were significantly higher in those with ADA than those without ADA (Table 2). Multiple comparisons revealed no significant differences in scores on any of the depression scales (SDS, BDI-II, and ADS) between PD and in SAD patients. The frequency and severity of panic attacks and agoraphobia were not significantly different between PD patients with and without ADA (Table 2).

In PD and SAD patients, the comorbidity rate of major depression was significantly higher among patients with ADA than those without ADA (PD, 51.7% vs 23.9%, $\chi^2=10.64$, $p<0.002$; SAD, 50.0% vs 11.4%, $\chi^2=17.04$, $p<0.0001$). The presence/absence of ADA was not affected by the comorbidity of PD (16.7% vs 2.8%, $\chi^2=0.27$, df=1, $p=1.000$) or SAD (44.4% vs 8.3%, $\chi^2=0.67$, df=1, $p=0.488$) in DAF patients.

[Study II]

1. Subjects

A subset of the subjects in Study I who met the following inclusion and exclusion criteria were included in Study II.

**Inclusion criteria:** 1) Revisiting patients aged between 18 and 60 years old, who were examined between October 2006 and December 2008; 2) Patients with a main diagnosis of PD

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Figure 1 Incidence of ADA
PD: panic disorder, SAD: social anxiety disorder; DAF: depression with atypical features
Table 2  Results of psychological batteries of panic disorder, social anxiety disorder and depression with atypical features, and results of analysis of variance in Study I

|                  | PD (n = 129) | SAD (n = 63) | DAF (n = 46) | ANOVA     |
|------------------|-------------|-------------|-------------|-----------|
|                  | ADA+        | ADA−        | ADA+        | ADA−      | Group     | Diagnosis | Interaction | Post hoc tests |
|                  | N (% )      |             | N (% )      |             |           |           |             |              |
| Sex              | Male Female | Male Female | Male Female | Male Female |           |           |             |              |
| N                | 14 44       | 18 53       | 8 20        | 16 19      | 3 7       |           |             |              |
| Age              | 30.4 (10.3) | 37.2 (10.6) | 26.7 (9.3)  | 33.4 (12.2)| 30.5 (9.5)| 33.2 (6.1)| 10.97**     | 2.73 3.00 ADA− > ADA+ |
| SDS              | 55.9 (10.8) | 42.6 (12.0) | 57.5 (6.1)  | 45.5 (13.0)| 59.6 (7.8)| 55.7 (9.3)| 33.51**     | 7.84** 2.44 ADA+ > ADA− DAF > PD, DAF > SAD |
| BDI-II           | 25.3 (11.1) | 14.6 (10.0) | 26.7 (6.6)  | 18.2 (1.25)| 29.6 (8.0)| 29.1 (12.5)| 16.87**     | 10.83** 3.18* PD, SAD : ADA− > ADA− DAF > PD |
| ADS              | 49.2 (16.1) | 32.6 (20.6) | 51.5 (8.0)  | 33.5 (22.7)| 56.1 (13.1)| 59.8 (5.2)| 12.37**     | 14.18** 4.81* ADA− > ADA− DAF > PD, SAD > AD |
| LSAS-J           | 73.7 (37.8) | 41.2 (36.0) | 81.6 (26.7) | 62.2 (26.6)| 78.3 (31.3)| 57.0 (35.3)| 12.23**     | 4.03* 0.85 ADA− > ADA− DAF > PD, SAD > PD |
| SAS              | 63.2 (37.6) | 42.5 (35.8) | 67.4 (23.9) | 61.6 (24.7)| 63.5 (28.7)| 66.3 (31.6)| 1.36        | 3.04* 1.61 SAD > PD |
| Panic Attack frequency | 5.8 (6.5) | 3.9 (7.1) | 6.4 | 2.03 |
| Panic Attack severity | 2.2 (0.9) | 2.2 (1.0) | 2.2 | 0.01 |
| AGO              | 62.3 (18.5) | 59.0 (20.5) | 65.5 (14.0)| 62.6 (14.7)| 66.3 (30.6)| 66.3 (31.6)| 1.36        | 3.04* 1.61 SAD > PD |

Note. Results of ANOVA are expressed as mean (SD), F values and statistical significance: ** p<0.01, * p<0.05
AGO: agoraphobia, ADA: anxious depressive attack, ADS: Anxious Depression Scale, BDI-II: Beck’s Depression Inventory-Second Edition, DAF: depression with atypical features, LSAS-J: Liebowitz Social Anxiety Scale Japanese version, PD: panic disorder, SAD: social anxiety disorder, SDS: Self-Rating Depression Scale; SAS: Social Anxiety Scale.
with or without agoraphobia according to DSM-IV-TR; 3) Patients for whom the psychiatrist and the clinical psychologist agreed fulfilled the criteria for ADA, as shown in Table 1; 4) At least one ADA in the previous month.

The fourth criterion was applied because we aimed to examine the chronological relationship between panic attacks and ADA.

Exclusion criteria: Intense suicidal ideation or severe aggression towards others. Major physiological diseases requiring medical treatment.

2. Method

To examine the comorbidity of PD, the MINI and the SCID were performed in addition to the examinations in Study I. The nature of ADA was evaluated using a structured interview developed by the author, in patients with or without agoraphobia exhibiting ADA.

We measured the monthly frequency of ADA. The occurrence time of ADA was first divided into two by noon, then divided again every 3 hours after noon, because of the convergence of ADA in the afternoon. Reexamination of the presence of ADA was performed 1 year after the initial intake. Patients were asked about the situations in which ADA occurred using the Structured Interview Form of Anxious-Depressive Attack (Appendix II).

3. Results

3–1. Description of subjects
Subjects comprised 65 PD patients (57 females aged 27.3±8.5 years, mean±SD; and eight males aged 32.5±9.0 years).

3–2. Comorbid mental disorders in PD (Table 3)

All subjects had comorbidity with Axis I disorders, and 89.7% of patients (52/58) had other anxiety disorders in addition to PD. Agoraphobia was the most prevalent of the comorbid anxiety disorders (82.7%, 43/58). Of the 58 patients, 54 (93.1%) had a comorbid mood disorder, with atypical features in 32 cases (59.3%, 32/54). The most prevalent comorbidity for Axis II was avoidant personality disorder (35.9%, 14/39).

3–3. Onset and clinical course of PD and ADA
The mean age of onset was 24.0±9.0 years in PD and 22.5±8.4 years in ADA. Therefore, the mean duration of PD (3.8±4.5 years) was shorter than that of ADA (5.2±5.3 years), and
30.8% of patients (20/65) had been experiencing ADAs for more than 5 years. Forty-three patients were followed for more than 1 year of treatment, and 21 patients (48.8%, 21/43) still experienced ADA.

3–4. Situation in which ADA occurred in PD patients (Table 4)

The occurrence of ADA increased with time, from evening to midnight. The most frequent situation in which ADA occurred was when subjects were sitting idle and alone at home. The duration of ADA was <30 min in 16/65 (24.6%) of patients, ≥ 30 min and <60 min in 24/65 (36.9%) of patients, and ≥ 60 min in 25/65 (38.9%) of patients. The frequency (mean ±SD) of ADA was 14.1 ± 14.5 times a month (Table 4).

3–5. Characteristics of ADA in PD patients

Figure 2 shows the incidence of each feeling type during emotional outbursts (Table 1, Criterion A1). Depressive feelings were more frequent than anxious feelings. These emotional outbursts were followed by the intrusion of unpleasant memories. During rumination of memories, 84.6% of patients experienced visual flashbacks. The coping patterns were reported to range from moderate to violent behaviors (Figure 3), especially acting out behaviors, including deliberate self-injury (63.1%), assaulting people (46.2%) or objects (40.0%), and drug overdose (3.1%), were frequent. The average number of types of coping behavior patterns exhibited by each patient was 6.1 ± 2.3. Tearfulness before or after the emotional outburst (Table 1, Criterion A1) was reported in 90.8% of patients.

3–6. Correlation between ADA frequency and PD severity

ANOVA was conducted to examine the relationship between the psychological assessment results and the frequency of ADAs. As the frequency of ADA increased, significantly higher scores were found on the SDS (p<0.01), BDI-II (p<0.01), HAMD-17 (p<0.05), HAMD-21 (p<0.01), SAS (p<0.05), and LSAS (p<0.05), but not the HAMA or PAS (Table 5). Sub-items of the PAS (i.e., number of panic attacks, severity of anticipatory anxiety, and grade of agoraphobia) were not correlated with the frequency of ADA.

[Discussion]

1. The relationship between ADA, depression and social anxiety

The results of Study I suggested that SAD and PD patients exhibiting ADA were more depres-
Figure 2  Incidence of feelings experienced during emotional outbursts in anxious-depressive attacks (ADAs).

Figure 3  Incidence of coping behaviors used to manage anxious-depressive attacks (ADAs).
sive and socially anxious than those without ADA. In addition, Study I revealed that the comorbidity of depression in PD and SAD was higher among patients with ADA than those without ADA. Study II showed that high comorbidity (93.1%) of mood disorders was seen in PD patients with ADA, and that the frequency of ADA was correlated with the severity of depression, but not with that of PD (Table 4). Furthermore, as summarized in Figure 2, which shows the incidence of feeling types during emotional outbursts of ADAs, depressive feelings were more frequent than anxious feelings. Taken together, these findings indicate that ADA in PD and SAD is related to more severe social anxiety and depression.

2. The relationship between ADAs and panic symptoms

Study I demonstrated that the presence of ADA did not affect the severity of panic symptoms in patients with PD. Furthermore, Study II revealed that the severity of panic symptoms was not correlated with the frequency of ADA. These observations do not exclude the possibility of a “seesaw” phenomenon between ADA and panic attacks, which was proposed on the basis of the author’s clinical findings. This hypothesis predicts that ADAs precede the onset of PD, then cease when panic attacks are full-blown and recur when panic attacks give way to depression, as reported in a previous case study (Kaiya, 2016, Case 1).

### Table 5 Results of psychological assessments in Study II

| Frequency of ADA | Group a | Group b | Group c | F value |
|------------------|---------|---------|---------|---------|
|                  | N (18)  | N (23)  | N (24)  |         |
| SDS              | Mean    | SD      | Mean    | SD      | Mean    | SD      | 9.11 ** | c>a, c>b |
|                  | 53.06   | 6.96    | 52.55   | 13.95   | 63.83   | 6.21    |         |         |
| BDI-II           | 23.39   | 8.30    | 23.43   | 8.93    | 33.52   | 9.34    | 9.48 ** | c>a, c>b |
| HAMD-17          | 13.61   | 6.95    | 11.00   | 6.01    | 18.83   | 9.02    | 5.55 *  | c>b     |
| HAMD-21          | 15.78   | 7.62    | 12.65   | 7.11    | 22.52   | 10.64   | 6.63 ** | c>a     |
| PAN              | 21.68   | 9.33    | 24.84   | 6.47    | 25.80   | 7.16    | 1.49 n.s. |         |
| Panic attack     | 4.61    | 2.20    | 5.58    | 2.06    | 5.75    | 2.31    | 1.45 n.s. |         |
| Agoraphobia      | 6.72    | 2.08    | 7.26    | 1.85    | 6.80    | 1.94    | 0.42 n.s. |         |
| Anticipatory Anxiety | 3.78 | 1.59    | 4.16    | 1.42    | 4.45    | 1.73    | 0.85 n.s. |         |
| Disability       | 6.56    | 2.75    | 6.42    | 2.50    | 7.50    | 2.78    | 0.94 n.s. |         |
| Uneasy about health | 1.22 | 1.70    | 1.42    | 1.43    | 1.30    | 1.49    | 0.08 n.s. |         |
| HAMA             | 21.28   | 12.11   | 18.17   | 10.53   | 21.77   | 11.15   | 0.57 n.s. |         |
| SAS              | 52.12   | 24.66   | 67.77   | 28.66   | 79.88   | 36.00   | 4.05 *  | c>a     |
| LSAS-J           | 58.72   | 30.27   | 81.05   | 32.40   | 87.92   | 35.98   | 4.18 *  | c>a     |

* p < .05, ** p < .001
Analyzed with ANOVA. Categorical data were analyzed with Bonferroni.

Note. ADA; anxious depressive attack, BDI; Beck's Depression Inventory, DAF; depression with atypical features, HAMD; Hamilton Depression Scale, LSAS-J; Liebowitz Social Anxiety Scale Japanese version, PAS; Panic and Agoraphobia Scale, SDS; Self-Rating Depression Scale; SAS; Social Anxiety Scale
3. The behavior and significance of ADA

The occurrence rate of ADA among the patients in the present study sample was relatively high (43.2%) and a large number of patients exhibited ADA for a long time before consulting the author. In Study II, the duration of illness of ADA patients was longer than that of PD patients, and continued for more than 5 years in 30.8% of patients. The follow-up examination confirmed the presence of ADA after 1 year in almost half of patients (21/43). Thus, many patients appear to suffer from these stressful events over a long period of time. Study I revealed that patients with PD or SAD exhibiting ADA were younger, and had more severe social anxiety and depression than those without ADA (Study I). Over half of the patients with ADAs coped by using destructive behaviors sometimes regarded as trouble-making (Study II). Thus, ADAs appear to make mood and/or anxiety disorders chronic and complicated. Taken together, these findings indicate that ADA might be a sign of a more severe form of anxious depression (Goldberg, 2014). Increasing recognition among psychiatrists of ADA as a diagnostic entity may help to ease the burden of affected individuals.

4. The Proposed Pathogenesis of ADA

In Table 2, the scores of L-SAS, that indicate social anxiety, were higher in groups with ADA than groups without ADA, in all three disorders (PD, SAD, and DAF). In patients with DAF, only L-SAS scores were significantly higher in the group with ADA than the group without ADA. Moreover, the comorbidity rate of SAD in DAF was 44.4% among patients with ADA and 8.3% among patients without ADA, although this difference did not reach statistical significance. This evidence may indicate that severe social anxiety is related to ADA. It was recently proposed that rejection sensitivity could be a possible cause of depressive symptoms in the course of SAD (Suyama et al., 2014). Rejection sensitivity based on social anxiety may also underlie ADA, having a relationship with depression.

[Limitations]

The current study involved several limitations that should be considered. All participants in the study sample were Japanese. Thus, it is currently unclear whether ADA is also present in non-Japanese populations. Some evidence suggests that ADA may be present to a greater or lesser extent in non-Japanese patients, with several studies in Western populations reporting relationships between rejection sensitivity, DAF, SAD, PD, and avoidant personality disorder (Parker & Crawford, 2007, Posternak & Zimmerman, 2002, Alpert et al., 1997, Koyuncu et al., 2015).

[Conclusion]

(1) Psychological assessments revealed that ADA was related to SAD and depression, mainly with atypical features, but was not related to panic symptoms.

(2) ADA generally occurs earlier than related disorders and can persist for more than several years, causing long-lasting psychological suffering.

(3) In contrast to patients without ADA, patients exhibiting ADA were younger, had more comorbidities, presented a chronic course, had more severe anxiety disorders and/or depression, and predominantly displayed atypical features and troublesome behaviors. Therefore, ADA is likely to be a sign of a more severe form of anxious
depression.

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Appendix I

Questionnaire for Confirmation of Anxious-Depressive Attack
(developed by the author)

(1) When you have not been thinking about something specific, have you ever experienced an abrupt outburst of feelings of violent anxiety or depression? The attack occurs suddenly and captures your entire mind. The feelings are of indescribable discomfort.

(2) Just after the unpleasant feelings, did uncomfortable memories from the past come to your mind unexpectedly? Did you remember various distressing events from the past one by one, almost like a revolving carousel?

(3) Was this psychological situation unbearable for you?

(4) Did you engage in any particular behavior to avoid the painful situation?
   If all questions are answered in the affirmative, anxious-depressive attack is confirmed.

Appendix II

Structured Interview Form for Anxious-Depressive Attack
(developed by the author)

(1) How often have you experienced an ADA in the past week and in the current month? When did you last have an ADA?

(2) Do you experience ADA at a specific time of the day or randomly during the day? If you experience it at a specific time, please specify when.

(3) Generally, how long is an episode of ADA?
   a. < 30 min
   b. ≥ 30 min and < 60 min
   c. ≥ 60 min

(4) Generally, when you experience an ADA, who are you with, where are you, and what are you doing?

(5) Since when have you been frequently experiencing ADA?

(6) Does ADA occur unexpectedly or after a trigger?

(7) If the latter is the case, what is the trigger?

(8) Did you experience an ADA before being diagnosed with panic disorder?
   a. Yes
   b. No

(9) How old were you at the first onset of ADA?

(10) Describe the situation when you first experienced ADA?

(11) Do you experience any of the following symptoms during an ADA?
   a. Anxious/irritable feelings
   b. Sadness
   c. Self-hatred
   d. Despair
   e. Loneliness
   f. Helplessness
   g. Depression
   h. Self-pity
   i. Self-reproach
   j. Envy
   k. Emptiness
   l. Feelings like you are watching yourself or feelings that you are not really there, or that the world around you is unreal.
   m. Fear of losing control or going crazy
   n. Fear of dying
   n. Any other (if yes, please specify):

(12) When you experience an ADA, do you recall sad memories? If yes, provide details:

(13) Does the recalled content appear as intru-
(14) What do you do to manage the pain during an ADA?

a. Do nothing
b. Take medicine
c. Go to bed feeling bad
d. Cry
e. Contact someone
f. Physically assault things
g. Physically assault people
h. Change your location
i. Overeat
j. Drink alcohol
k. Go out
l. Unnecessary shopping
m. Smoke cigarettes
n. Excessive drug consumption (should be combined with b.)
o. Deliberate self-injury
p. Anything else (if yes, please specify):