

REVIEW

Comorbidity in social anxiety disorder: diagnostic and therapeutic challenges

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Abstract

Comorbid disorders are highly prevalent in patients with social anxiety disorder, occurring in as many as 90% of patients. The presence of comorbidity may affect the course of the disease in several ways such as comorbidity in patients with social anxiety disorder (SAD) is related to earlier treatment-seeking behavior, increased symptom severity, treatment resistance and decreased functioning. Moreover, comorbidities cause significant difficulties in nosology and diagnosis, and may cause treatment challenges. In this review, major psychiatric comorbidities that can be

encountered over the course of SAD as well as comorbidity associated diagnostic and therapeutic challenges will be discussed.

Keywords: alcohol use disorder, anxiety, bipolar disorder, comorbidity, major depression, mood disorders, personality disorder, social anxiety disorder.

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Introduction

Social anxiety disorder (SAD) is characterized by persistent and marked fear/anxiety about one or more social or performance situations in social settings. The individual recognizes that the fear or anxiety is excessive and unreasonable, and some individuals fear offending others or being rejected as a result. SAD affects different aspects of a person's life such as social activities, relationships, work, and academic functioning (American Psychiatric Association, 2013).¹⁻³

Epidemiological studies have established that SAD is a common disorder with a current prevalence between 5 and 10%, and lifetime prevalence between 8.4 and 15%.⁴⁻¹⁰ SAD typically begins in early adolescence, and it is usually persistent unless treated effectively. Treatment-seeking behavior is generally rare, delayed, and often accompanied by another psychiatric disorder.⁶⁻¹⁵ In other terms, the presence of comorbidity results in earlier treatment-seeking behavior in patients with SAD.¹⁶⁻¹⁸ Moreover, Crome and colleagues (2015) reported that only around 30% of patients with SAD considered social anxiety as their primary complaint, and among those, 20% of them went to a health facility about these complaints in the past year.⁴

Community studies have reported a high frequency of psychiatric comorbidity in patients with SAD, occurring in as many as 90% of patients.^{9-11,15,19-22} In most cases, SAD

begins earlier than the comorbid disorder.^{15,19,21-23} Moreover, the presence of SAD was found to be a predictor for the development of subsequent major depression (MD) and alcohol use disorder (AUD).^{10,13,19,24-27} Patients with SAD who have comorbid psychiatric disorders are more likely to have increased symptom severity, treatment resistance, and decreased functioning (such as missed days at work or dropping out from school), and they also have higher rates of suicide when compared to ones without comorbidity.^{9,28,29}

Comorbidity is important for several reasons in clinical practice. First, it is highly common and significantly affects the clinical course. The presence of a condition may disguise the other condition or lead to a more complicated clinical presentation. Overlapping symptoms may also increase the risk of misdiagnosis.³⁰ Second, as one disorder can cause the emergence of another or worsen its clinical course, detecting and treating the comorbidity increase the opportunity for early intervention.³¹ Third, comorbidity may result in worse treatment outcomes. This is partially because of the fact that treatment is more difficult when more than one diagnosis exists. In addition, failing to notice one of the comorbid conditions might lead to inadequate treatment and might be misinterpreted as treatment resistance.²⁹

In general, comorbidity in psychiatry is a controversial topic and patients with comorbidities have often been excluded from treatment studies in SAD.³² This also makes it difficult

for clinicians to choose the most appropriate options for treatment. In this review, we will focus on major psychiatric comorbidities that can be encountered over the course of SAD, and how comorbidity affects diagnosis and treatment of SAD, in the light of currently available information. A literature search was conducted in PubMed with the following terms: 'social anxiety disorder', 'social phobia', 'comorbidity', 'major depression', 'bipolar disorder', 'anxiety disorders', 'obsessive-compulsive and related disorders', 'avoidant personality disorder', 'diagnostic difficulties', 'treatment'. References from the articles derived from the literature search were also investigated. Only original articles, brief reports, review articles, and case reports/series that were published in English language were considered for the review.

Mood disorders

Population-based studies have shown that mood disorders are common in patients with SAD.^{4,5,9–11,15,19,21,22} The difficulties in diagnosis and/or treatment derived from comorbidity of commonly encountered mood disorders will be discussed in detail later.

SAD and major depression

MD is the most frequently observed comorbid disorder in clinical studies with comorbidity rates ranging between 35 and 70%,^{33–37} and it may influence several disease-related outcomes. Patients with SAD who have comorbid MD have higher SAD severity, increased risk of relapse, and decreased functionality.^{20,37–39} Especially, lack of social support may cause more severe depressive episodes and higher probability of suicide in patients with SAD.⁴⁰ On the other hand, SAD comorbidity is also prevalent in patients with MD, to the degree that approximately 20–30% of patients with MD also have comorbid SAD.^{19,41–43} In a study of 255 patients with major depression, Fava and colleagues reported that the prevalence of comorbid anxiety disorders and particularly SAD were 50.6 and 27%, respectively. In the same study, the presence of an anxiety disorder was related to earlier onset of MD.⁴⁴

As for the age of onset, symptoms of SAD generally emerge at an earlier age than comorbid mood disorders do,^{5,19,45} such that SAD predated comorbid mood disorders in 69% of the patients.⁵ As reported by Stein and colleagues (2001), the risk of developing MD is increased 3.5 times in patients with SAD.²⁶ In another follow-up study, the risk for subsequent MD was approximately two times (relative risk ranges between 1.49 and 1.85) higher in patients with SAD than in healthy controls.²⁵ In other studies, the presence of SAD in patients with MD increased the risk of subsequent development of depressive symptoms and suicide attempts.^{10,13,19,24–26} There may be several explanations why major depression follows SAD in those cases. Belzer and Schneier (2004) proposed that SAD might contribute to the development of major depression through stressful life events such as job loss, educational difficulties, peer problems, and despair due to poor social functioning.⁴⁰

The comorbidity between SAD and MD may lead to several diagnostic difficulties. It is important to acknowledge that there might be overlapping symptoms between the two disorders. For example, social withdrawal might result from fear of embarrassment in SAD, but it might also be found in patients with MD, usually as a mood-related, temporary phenomenon.⁴⁶ Fear of negative evaluation is the cornerstone of diagnosing SAD, while individuals with MD may also be concerned about being negatively evaluated by others because they feel that they are bad or not worthy of being liked. In contrast, individuals with SAD are worried about being negatively evaluated because of certain social behaviors or physical symptoms.¹ More importantly, social anxiety can be misinterpreted in society as a personality trait such as shyness rather than a disorder; whereas, the onset of major depression is generally more acute and marked.¹⁶ Therefore, it is possible to overlook SAD in the presence of comorbid depression.^{29,45,47} Overlooking one disorder over the course of the other might lead to inadequate treatment of the symptoms, which might be misinterpreted as treatment resistance.²⁹ According to Dalrymple and Zimmerman (2007), almost 75% of patients are willing to accept treatment for social anxiety in addition to treatment for MD, only when asked frankly. Patients with major depression should be carefully assessed in terms of social anxiety, particularly when shyness or a more persistent social withdrawal is suspected.⁴⁷ On the other hand, depression should not be forgotten when the diagnosis of SAD is made because this comorbidity can lead to dramatic outcomes such as increased risk for suicide or a more rapid decline in functioning, besides leading to a need for change in the treatment plan such as prioritizing behavioral activation.

It is also possible that SAD and MD comorbidity will lead to several therapeutic challenges. Interestingly, although SAD and MD have such high comorbidity rates and clinical presentation is more severe, placebo-controlled studies are very limited and most patients with comorbidities have been usually excluded from medication trials.³² In only one double-blind placebo-controlled study on the treatment of this comorbidity, vortioxetine was found to be more effective in alleviating symptoms of both SAD and MD when compared to placebo.³² None of the other antidepressants with efficacy in SAD have been studied in placebo-controlled trials to demonstrate their efficacy in SAD patients with comorbid MD. In an open study conducted with MD patients, treatment with citalopram showed improvement in symptoms of both MD and comorbid social anxiety.⁴⁸ In both studies, MD was reported to have improved earlier than social anxiety. More studies are needed to evaluate the most appropriate treatment options for SAD patients with MD.³²

Some authors suggested that cognitive behavioral therapy (CBT) can be recommended as a treatment of choice in SAD patients with comorbid MD.⁴⁹ However, the results of studies showing how the presence of depressive symptoms affects CBT outcome in patients with SAD are contradictory.⁵⁰ Two studies

reported that patients with SAD who have higher depressive symptoms seemed to benefit less from CBT, especially in the short term.^{51,52} Other studies found that the presence of MD at the beginning of the treatment did not interfere with the outcomes of CBT in patients with SAD,^{53–56} although symptoms of SAD exacerbated during long-term follow-up in one study.⁵⁴

In general, both CBT and antidepressant medications are effective in both conditions, suggesting that they are effective in the case of comorbidity as well. However, this has not been extensively studied in trials with high evidence base. Current evidence regarding to the treatment of comorbid SAD and MD seems insufficient and inconsistent. Therefore, there is a need for comprehensive studies that assess the efficacy of available treatment options as well as for comparative studies that guide clinical decision to select better treatment options among antidepressant alone, CBT alone, or combination treatment of selective serotonin reuptake inhibitor (SSRI) and CBT. Another point is that considering SAD typically predates comorbid disorders, early treatment of SAD might prevent subsequent development of comorbid depression.⁴

SAD and atypical depression

Patients with MD who have atypical features constitute a specific subgroup of depressed patients who have drawn considerable interest with regards to SAD comorbidity. Various studies demonstrated the connection between SAD and atypical depression.^{42,57–63} Rates of atypical MD are especially higher in the generalized type of SAD than in nongeneralized type.⁶⁴ Alternatively, patients with atypical depression showed higher SAD comorbidity than other patients with MD.^{42,62} In a study investigating the impact of atypical MD comorbidity on SAD, Koyuncu and colleagues found that 77.1% of mood episodes (either unipolar or bipolar) included atypical features among individuals with comorbid MD and SAD.⁶³ In the same study, the atypical MD group had higher SAD and depression severity and lower functioning than patients with SAD+MD without atypical features and SAD alone. In addition, age at onset of SAD was earlier in patients with atypical MD.⁶³

Moreover, there are some common features between SAD and atypical depression such as interpersonal sensitivity (IPS). It is included in diagnostic criteria for atypical depression,¹ and it is a core feature related to SAD.^{65,66} The overlap in SAD and atypical depression criteria, specifically IPS, may account for the high rates of comorbidity.⁶⁷ Because IPS is a shared feature between the two disorders, it may lead to difficulties in differential diagnosis. Assessing cautiously whether IPS is a long-standing personality trait as in SAD or a mood-episode-limited phenomenon is important for accurate diagnosis in both atypical depression and SAD patients. Second, it is also important to consider other symptoms that accompany IPS while differentiating between SAD and atypical depression. For example, the presence of other symptoms such as hypersomnia, hyperphagia, and mood reactivity suggests the diagnosis of atypical depression.^{1,46}

Considering the presence of atypical depression in patients with SAD leads to increased symptom severity and more disability,⁶³ atypicality of depression that is overlooked may cause treatment challenges. As atypical depression includes symptoms such as Leiden paralysis and over sleeping, it may be difficult for patients to perform exposure tasks. On the other hand, if the presence of SAD is missed, it is less likely for patients to be referred for a therapy that may be beneficial, such as exposure therapy. In addition, therapy options to improve IPS, which is a shared symptom, can be emphasized in these patients. Earlier findings from treatment studies proposed that monoamine oxidase inhibitors (MAOIs) were highly effective in both disorders.⁶⁸ However, after SSRIs and serotonin–norepinephrine reuptake inhibitors (SNRIs) have been introduced and proved to be effective in both disorders, they become the preferred agents because of their milder side-effect profile.

SAD and bipolar disorder

The rates of bipolar disorder (BD) comorbidity in patients with SAD range between 3.5 and 21%.^{34–37} Only a few studies have investigated how bipolar disorder comorbidity affects patients with SAD. Perugi and colleagues (2001) indicated that patients with SAD who have comorbid MD or BD have higher symptom severity, higher rates of other anxiety disorder comorbidities, and lower functioning than those without mood disorder comorbidity.³⁶ In another study, atypical depression, total number of depressive episodes, and post-traumatic stress disorder (PTSD) comorbidity were higher in the SAD+BD group than in the SAD+MD group. Obsessive-compulsive disorder (OCD) comorbidity was higher in SAD+BD than in patients with SAD who have no comorbid mood disorder.³⁷

Another important point in the relationship between SAD and bipolar is the risk hypomanic/manic switches observed during the treatment of social anxiety.³⁵ In one of the studies, 32 patients with SAD were treated with MAOIs and 14 of the 18 patients remitted with antidepressant treatment switched to hypomania.⁶⁹ It was argued that patients with SAD who switched might belong to the bipolar spectrum, and antidepressant treatment might uncover an underlying bipolarity. Holma and colleagues (2008) also reported that SAD comorbidity might increase the risk of hypomania/mania in MD patients who were treated with antidepressant medications.⁷⁰ Valença and colleagues (2005) mentioned a subgroup of SAD presenting with an explicit hypomanic episode while receiving antidepressants treatment. In this study, patients with SAD and BD-2 patients were found to be similar in terms of past depressive episodes, alcohol abuse, suicide, and family history of BD.⁷¹ It is important for clinicians to be aware of comorbidity rates of SAD and BD, as BD may be commonly missed and may lead to inappropriate treatment choice.

On the other hand, there are more studies assessing SAD comorbidity in patients with a primary diagnosis of BD and reported rates range between 7.8 and 47.2%.^{6,38,72–81} Kessler and colleagues (1994) reported in the National Comorbidity Survey

that SAD comorbidity was found to be higher in patients with BD (odds ratio=4.6) than in patients with MD (odds ratio=3.6).⁶ The presence of an anxiety disorder might be associated with greater BD symptom severity.^{76,78,82} Simon and colleagues (2004) reported that the rate of SAD comorbidity was 22% in 475 patients with bipolar I and II disorder and that anxiety disorder comorbidity was associated with earlier onset of bipolar disorder, more disability, less time spent in euthymia, and greater number of suicidal attempts compared to the nonanxious bipolar patients.⁷⁸ Boylan and colleagues (2003) found that the presence of a comorbid anxiety disorder in bipolar patients led to significantly worse prognosis.⁷⁹ In this study, among other anxiety disorders, SAD and generalized anxiety disorder were the diagnoses with the most adverse effects on the outcome of BD. Pini and colleagues found that 12.7% of bipolar patients fulfilled SAD criteria according to DSM-III-R and the presence of SAD comorbidity was related with an earlier age at onset of bipolar disorder.⁷⁴ Perlis and colleagues (2004) indicated that there was a significant relationship between SAD and early-onset bipolar disorder, while Perroud and colleagues (2007) underlined that SAD comorbidity is an important risk factor for suicidal behavior in bipolar patients.^{83,84}

To the best of our knowledge, no studies examined the treatment of SAD with BD comorbidity specifically. However, studies reported that bipolar patients with higher anxiety had poorer treatment response than the ones with lower anxiety.⁸⁰ Two studies investigated lithium response in bipolar disorder and found that the presence of anxiety was associated with poorer response to treatment with lithium.^{85,86} Henry and colleagues (2003) found that bipolar patients with anxiety responded less to anticonvulsants than bipolar patients without anxiety. However, lithium efficacy did not differ between the two groups in that study.⁷⁷ There are also studies investigating the effects of mood stabilizers in patients with SAD who do not have comorbid mood disorder. Trials with valproate produced inconsistent results.⁷²

Overall, in the comorbidity of bipolar disorder with anxiety disorders, prioritizing the treatment of bipolar disorder is essential and starting mood stabilizer agents as first-line treatment is recommended. Hypomanic/manic switch with antidepressants used for treating SAD may complicate the treatment of SAD. Because of this risk, the potential benefits and risks of antidepressant treatment should be evaluated carefully.⁷¹ and they should be started only with mood stabilizers in comorbidity situation. Benzodiazepines can be used to treat anxiety symptoms; however, it is advisable to be cautious when using alprazolam because of hypomanic switch risk.

In addition, CBT can be considered as a treatment option for anxiety symptoms, especially after stabilization of mood symptoms.⁷² Fracalanza and colleagues (2014) reported that SAD+MD and SAD+BD groups had higher pretreatment symptom severity of SAD than SAD alone and SAD plus other anxiety disorder groups. Although all groups showed improvement with CBT, SAD+MD, and SAD+BD groups remained symptomatic⁸⁷ after treatment.

Other anxiety disorders

Excessive fear, anxiety, and related behavioral disturbances represent shared keystones of all anxiety disorders. Most individuals with one anxiety disorder meet the criteria for additional comorbid anxiety disorders.¹ Both community and clinical studies have reported that approximately one-half of SAD patients had at least one of any other lifetime anxiety disorder comorbidity.^{22,23,28,37} As earlier studies were conducted with DSM-III-R and IV, OCD and PTSD were included in these rates. However, as DSM-5 is being utilized at the time of this review has been written, anxiety disorder comorbidity will be discussed in accordance with the structure of DSM-5.

The most common lifetime anxiety disorder comorbidity in SAD is specific phobia, which ranges between 14.1 and 60.8%.^{11,15,22,28,37} Different from other comorbidities, specific phobia generally begins earlier than SAD does.¹ Panic disorder comorbidity is between 4.7 and 26.9%,^{11,15,22,37,64,88} and agoraphobia is between 8 and 45%.^{11,23} Lifetime-generalized anxiety disorder (GAD) comorbidity rates were found to be between 0.6 and 27%.^{11,22,23,28,37}

Anxiety-related outcomes were found to be influenced by the presence of comorbid anxiety disorders. For example, in a follow-up study of 12 years, patients with SAD showed the lowest rates of recovery among all other anxiety-disordered patients.⁸⁹ In addition to that, the presence of GAD comorbidity in SAD was associated with even decreased chance of recovery and increased risk of recurrence when compared to no GAD comorbidity condition.^{89,90} It should be kept in mind that GAD comorbidity could be the reason behind the treatment resistant in some of the cases. Note that OCD and PTSD were also included in this study, as they used DSM-IV.

Although all anxiety disorders consist of features such as excessive fear, anxiety, and avoidance in common, they also carry dissimilarities from each other such as fear inducing situations, type of avoidance behavior, and accompanied cognitions. Differential diagnosis can be achieved by a thorough examination. Patients with specific phobia may exhibit fear of embarrassment or humiliation because of the reactions given to feared situation; however, according to DSM-5, if social situations are feared because of negative evaluation, social anxiety disorder should be diagnosed instead of specific phobia. Patients with SAD can exhibit panic attacks as well due to fear of negative evaluation, but these are not unexpected panic attacks as seen in panic disorder where the concern is about panic attacks themselves.¹ Social- or performance-related worries are observed as a part of both GAD and SAD; however, while they are restricted to these situations in SAD, GAD is often associated with more expanded worrisome situations and evaluation by others does not usually accompany GAD.¹

As comorbid disorders were generally excluded from treatment studies, evidence is not available with regard to

treatment of comorbid anxiety disorders and SAD. SSRIs and SNRIs are generally considered as first-line pharmacological treatments for anxiety disorders, except specific phobia where efficacy of pharmacotherapy is very limited.⁹¹ On the other hand, CBT has been found to be effective for all anxiety disorders in several randomized controlled studies.⁹² In one study, there was no significant difference in cognitive behavioral group therapy results between SAD patients with and without GAD comorbidity.⁹⁰ It is important to carefully assess patients with SAD for anxiety disorder comorbidities as they would lead patients to receive inappropriate or insufficient treatment if missed. CBT should be tailored to include techniques for comorbid anxiety disorder in addition to SAD.

Obsessive-compulsive and related disorders

OCD comorbidity rates were reported to be between 2 and 19% in patients with SAD.^{11,15,23,28,37} On the other hand, when evaluating the studies conducted with OCD patients, the prevalence of SAD was found to be between 8 and 42%.⁹³ In a study, lifetime history of comorbid OCD was associated with earlier treatment-seeking behavior in patients with SAD.¹⁶ There are studies showing that bipolar disorder and SAD comorbid patients had higher rates of OCD diagnosis compared to SAD group without bipolar disorder.^{36,37}

Body dysmorphic disorder (BDD) is an OCD-related disorder that contains preoccupations about one's physical appearance, where social anxiety and avoidance are common and cause impairment in social functioning. Moreover, the core features related to SAD such as fear of embarrassment and rejection are also common in BDD patients. BDD mostly begins in preadolescence and adolescence, as SAD does. However, in the case of comorbidity, SAD starts earlier than BDD.⁹⁴ While the rate of BDD was found to be 8–12% among patients with SAD,^{94,95} the rate of SAD was about 40% in patients with BDD.⁹⁶

Differential diagnosis of BDD and SAD can be challenging, as social anxiety and avoidance are also common in BDD because of the discomfort related to one's appearance; however, persistent preoccupations about appearance and frequent repetitive behaviors such as checking on the mirror may represent useful cues that favor BDD. Instead, individuals with SAD may be more concerned with the thoughts that others will ridicule or negatively evaluate them because of a mistake they do.¹ Accurate detection of BDD, when comorbid with SAD, would be important, as patients with comorbid BDD may benefit from specific treatment techniques based on CBT for BDD.⁹⁷ BDD treatment would focus more on preventing rituals and avoidance behaviors related to body concerns; whereas, CBT for SAD focuses more on reducing anxiety and avoidance of social situations more generally.

Alcohol use disorder

Epidemiological studies have found high rates of relationship between SAD and AUD.^{14,27,98} The rate of AUD can be up to 50% in patient with SAD.¹⁴ Inpatients with AUD and comorbid SAD had more Axis I and II comorbidity rates compared to AUD inpatients without SAD according to DSM-IV.⁹⁹ Moreover, Perugi and colleagues (2002) also found that the presence of comorbid Bipolar II and AUD predicted a number of important clinical outcomes in social phobia patients.¹⁰⁰

The coexistence of these diseases was associated with heightened severity in both diseases, increased numbers of psychiatric or medical comorbidities and deterioration in functioning when compared to either AUD or BD alone.^{14,99,101–105} Although there are studies showing a strong association between SAD and AUD, the causality and the direction of the relationship between the two disorders are unknown.^{106–108}

SAD generally begins earlier than AUD, and it is considered as a risk factor for later AUD development.^{109–112} Patients with SAD may use alcohol as a self-medication to reduce anxiety. This feature may explain why the risk of alcoholism was increased following SAD.¹¹³ According to another hypothesis, there is often a genetic predisposition to both SAD and AUD. However, only a small proportion of the association of SAD and AUD can be explained by overlapping genetic risk or shared etiology.⁹⁸

Treatment-seeking behavior has been found to decrease in the case of comorbid SAD and AUD, and the patients frequently remain without treatment.^{14,114,115} In treatment, it is important to investigate whether there is SAD in alcohol-dependent patients, and if present, treatment of SAD should not be overlooked.^{46,116} As comorbidity is not included in drug efficacy studies in patients with SAD, it is not known whether similar treatment approaches are effective in SAD and AUD comorbid patients.⁹⁸ Therefore, treatment studies are needed to evaluate this particular comorbidity.

Avoidant personality disorder

According to DSM-5, avoidant personality disorder (AUD) represents a pervasive pattern of social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation.¹ The association between APD and SAD has been a matter of debate since they were first introduced in DSM-III. It has been argued that there is more evidence to support that the two disorders belong to the same continuum where they differ primarily in symptom severity and impairment, rather than representing distinct categories.^{117–120} On the other hand, other studies suggested that besides quantitative differences, there are also qualitative differences between SAD and APD. For example, patients with more APD features have higher levels of social or nonsocial avoidance, more persistent interpersonal problems, feelings of inferiority, and social inadequacy compared to patients with less APD features.^{121–124} While the

discussions are ongoing, the diagnostic distinction of APD and SAD remained unchanged in DSM-5, acknowledging that there is a great deal of overlap between the two disorders, as much as that they may be alternative conceptualizations of the same or similar conditions.¹

APD is particularly overlapping with generalized type of SAD¹²⁵ and comorbidity rates range between 22 and 89% in earlier studies.^{42,126–130} In more recent population-based and clinical studies, comorbidity rates were found to be moderate, around 32–48% of the patients with APD appeared to have both conditions at the same time.^{14,118,121,131–134} There seems to be a shared genetic vulnerability between the two disorders, family studies reported that SAD patients with APD have higher rates of first degree relatives with SAD.¹³⁵ Reichborn-Kjennerud and colleagues (2007) investigated 1427 female twin pairs and found that genetic features of both SAD and APD are similar.¹³³ After following up the same twin pairs for 10 years, it was concluded that the environmental risk factors for the two disorders were highly correlated but distinct.¹³⁶

As for the effect on clinical picture, patients with SAD+APD had higher levels of anxiety, higher rates of comorbidity, and decreased functionality compared to the patients with SAD alone.^{42,121–123,127,130,132,137–141} Several studies conducted on this comorbidity reported that anxiety and avoidance scores of Liebowitz Social Anxiety Scale were higher in SAD patients with APD than those without APD.^{137,141,142} In a study by Lampe et al. (2015), the rates of depression, suicidal ideation, and suicidal attempt were higher in SAD+ADP group than in SAD without APD group.¹³⁴

Even if it has still been debated whether they should be considered as a single disorder, several pharmacological and psychological treatment (e.g. benzodiazepine, SSRIs, MAOI) studies conducted on SAD and APD comorbidity have shown that treatments were effective on symptoms of both SAD and concurrent APD to some degree.^{143,144} There are studies reporting that SAD+APD yielded worse treatment outcomes such as less likelihood of remission, higher symptom severity, and lower functioning at the end of the treatment^{145–147} when compared to SAD alone. CBT for SAD seems to be a useful approach for alleviating the symptoms, but an emphasis on avoidance and inclusion of social skills training have been proposed for patients who have comorbid SAD and APD.¹⁴⁸

Other psychiatric conditions

The rate of PTSD is found to be 3.2–16% in patients with SAD;^{11,22,23,37} however, in veteran and community studies, PTSD and SAD were reported to be frequently comorbid conditions.¹⁴⁹ Zayfert and colleagues (2005) found that SAD comorbidity rate was 43% in primary PTSD patients; whereas, PTSD comorbidity rate was 7% in primary SAD patients.¹⁵⁰ In these studies, PTSD with SAD had higher guilty feeling and childhood abuse than those without SAD.

SAD is the most common anxiety disorder comorbidity in eating disorders (ED), and its rates were detected as high as 60%.^{151,152} In contrast, ED comorbidity is only slightly more prevalent in patients with SAD compared to healthy controls.²³ SAD is hypothesized to play a part in the development of ED as it emerges earlier.¹⁵³

Separation anxiety disorder (SEPAD), such as specific phobia, is a disorder that generally begins earlier than SAD, and comorbidity between them are expected.¹⁵⁴ Studies evaluating the relationship between these two disorders found that the rates of comorbid SAD in child and adult SEPAD patients are 33.4 and 34.5%, respectively.¹⁵⁵ Silove et al. (2010) examined 520 outpatients in an anxiety clinic and reported the rates of comorbid adult SEPAD as 14% in SAD patients.¹⁵⁶

Attention-deficit/hyperactivity disorder (ADHD), another childhood disorder that extends over adulthood, is an overlooked condition that has high rates of comorbidity with SAD.³¹ Only recently increasing evidence suggests that the relationship between the two disorders is closer than that was thought before. Several studies found high rates (up to 60–70%) of childhood ADHD comorbidity, especially predominantly inattentive type, in adults with SAD.^{67,157,158} In addition, follow-up studies showed that the lifetime prevalence of SAD among ADHD patients is higher compared to healthy controls.¹⁵⁹ In treatment studies investigating patients with SAD plus ADHD comorbidity found that ADHD medications such as methylphenidate or atomoxetine could effectively improve symptoms of both disorders at the same time.^{160–163} According to a developmental hypothesis, SAD may be etiologically linked to ADHD in a subgroup of patients, and thus SAD may develop secondary to ADHD.³¹ In other words, ADHD can be considered as a vulnerability factor for later development of SAD.³¹ Further studies are needed to investigate this relationship.

Conclusions

Comorbidity is very common in SAD, particularly in generalized subtype, and its lifetime prevalence has reached up to 90%. These high rates bring the validity of the comorbidity concept into question, suggesting that SAD may be a vulnerability factor for later development of accompanying disorders. In fact, SAD generally begins earlier than the comorbid disorder in many cases, except specific phobia, ADHD, and separation anxiety disorder. SAD particularly increases the risk of subsequent development of major depression, alcoholism, and suicide. On the other hand, SAD comorbidity is expected to be higher in patients with other psychiatric disorders such as OCD, PTSD, and ED and childhood disorders such as ADHD.

Comorbidity affects several SAD-related outcomes, because it increases the chances to observe higher symptom severity, more treatment resistance, and lower functioning compared to comorbidity free conditions. Comorbidity also leads to earlier treatment-seeking behavior in patients with SAD.

Additionally, the presence of comorbid disorders is associated with difficulties in diagnosis and treatment; therefore, a thorough diagnostic examination is necessary to differentiate other psychiatric conditions. Evidence is limited concerning the treatment of patients with SAD who have comorbidities, because these patients are often excluded from the treatment

studies. As comorbidity is more of a rule than an exception, comprehensive studies are needed to identify the best treatment solutions for patients who have SAD and another psychiatric disorder. In addition, follow-up studies investigating causal relationship between SAD and comorbid disorder are warranted.

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