Social Anxiety Disorder Comorbid with Schizophrenia: The Importance of Screening for This Underrecognized and Undertreated Condition

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ABSTRACT

Background: While the presence of comorbid anxiety disorders such as obsessive-compulsive disorder and panic disorder have been well described in schizophrenia, comorbid social anxiety disorder (SAD) has been less emphasized. The goal of this study was to examine the prevalence of SAD in our ambulatory population of patients with schizophrenia.

Methods: A group of 50 outpatients with schizophrenia randomly selected from our public mental health outpatient population was evaluated with the Structured Clinical Interview for DSM-IV (SCID)-schizophrenia section, the Positive and Negative Syndrome Scale (PANSS), the Schizophrenia Quality of Life Scale (SQLS), the Liebowitz Social Anxiety Scale (LSAS) and the Global Assessment of Functioning Scale (GAF). After completion of assessments, a retrospective chart review was conducted on all study patients who met criteria for a diagnosis of SAD in order to determine how many of these patients had been previously given a diagnosis of SAD.

Results: Based on a cutoff score of 29/30 on the total LSAS score, 38% of our sample had a comorbid diagnosis of SAD. Compared to patients who did not suffer from comorbid SAD, patients with schizophrenia and comorbid SAD had lower ratings of quality of life, but similar GAF and PANSS scores. According to the results of the chart review, none of the affected patients had been previously diagnosed with SAD.

Conclusions: According to the results of our study, SAD as a comorbid condition is highly prevalent in schizophrenia and may be under-detected in the outpatient mental health care setting. Furthermore, the presence of SAD may lead to a decreased quality of life for patients with schizophrenia. Further studies should evaluate whether the diagnosis and treatment of comorbid SAD would improve the treatment and quality of life of patients with schizophrenia.

INTRODUCTION

While acute psychotic episodes in schizophrenia generally respond well to treatment with antipsychotic medication, the long-term course is characterized by marked impairment in social and occupational functioning (1). Our lack of success in treating negative symptoms highlights the need for aggressively treating comorbid psychiatric conditions. For example, the current standard of care during the maintenance phase of treatment in schizophrenia is to screen aggressively for concurrent alcohol and drug use, for it is known that these conditions lead to a worsening course in schizophrenia (2). The identification and treatment of comorbid medical and psychiatric conditions in schizophrenia is critically important in preventing relapse and optimizing quality of life.

It has long been recognized that anxiety disorders such as obsessive-compulsive disorder, panic disorder and post-traumatic stress disorder are common in schizophrenia, and multiple studies have demonstrated that treatment of comorbid anxiety symptoms is associated...
with an improved outcome in schizophrenia (2-4). More recently, the implications of comorbid Social Anxiety Disorder (SAD) in schizophrenia have begun to be addressed in the literature. The essential feature of SAD is a marked fear and avoidance of one or more social and/or public performance situations due to an excessive concern about being humiliated while under the scrutiny of others (5). Two subtypes of SAD are recognized: a generalized type, in which a person fears most social or performance situations and a non-generalized type in which fears are typically limited to public speaking or few “performance” activities (5).

Based on the premise that SAD is often under-diagnosed in schizophrenia because of confusion with negative symptoms, Pallanti et al. (6) conducted the first comparison study between outpatients with schizophrenia and concluded that comorbid SAD was common and was strongly associated with increased disability. In the limited number of studies available to date, prevalence rates for comorbid SAD in outpatients with schizophrenia have ranged from 17-36.3% (6-8). Two studies with inpatients showed prevalence rates of 11-17% (9, 10). Clearly, prevalence studies are in their preliminary stages with poor correlation between studies which might be accounted for by disparate treatment settings, as well as other variables including the demographic make-up of the study (age, socio-economic class, and years of education) and the type of antipsychotic agents used (11).

Schizophrenia is characterized by positive symptoms (delusions, hallucinations) and negative symptoms (flat affect and emotions, alogia and avolition). SAD shares common elements with positive and negative symptoms in schizophrenia. Neuropsychiatric studies and functional MRI studies have shown that patients with SAD tend to misinterpret neutral facial expressions as being threatening (12). This misreading of social expression may be seen on a continuum with paranoia and ideas of reference. SAD patients are known to be very sensitive to the scrutiny of others which leads to guarded and withdrawn behavior. The tendency of patients with SAD to suffer from shyness and avoidance may likewise be seen as part of a continuum with apathy and avolition that comprise negative symptom clusters (13). The symptom overlap between SAD and schizophrenia may result in missed diagnosis of comorbid SAD when positive symptoms mask SAD or SAD over-diagnosis if negative symptoms are prominent.

Comorbid SAD in schizophrenia has been associated with more distress and disability, increased rates of substance abuse and a decreased quality of life (6). Consistent with views expressed by experts in the field, it has been our impression that patients with schizophrenia in our large and demographically diverse outpatient population are not systematically screened for the presence of comorbid SAD, and the working hypothesis of this study is that SAD is under-detected in schizophrenia. We aimed to determine the prevalence of SAD in a random cohort of our outpatients with schizophrenia.

METHODS:
Sample: The study was approved by the local Institutional Review Board. Fifty outpatients diagnosed with chronic schizophrenia (n= 45) or schizoaffective disorder (n= 5) were recruited in a random fashion from our public mental health outpatient clinic and were invited to participate in the study after giving written informed consent. The clinic is affiliated with Tel Aviv University and serves an ethnically diverse population in a catchment area of over 120,000 residents. Inclusion criteria were a diagnosis of schizophrenia or schizoaffective disorder according to the Structured Clinical Interview for DSM-IV and age between 18 and 65. Exclusion criteria included difficulty with spoken and written Hebrew, organic brain disease (such as dementia, mental retardation or severe dyslexia), comorbid substance abuse (during the preceding year) and lack of cooperation (e.g., due to the presence of psychotic symptoms or negativism). Patients treated with selective serotonin reuptake inhibitors (SSRI) or serotonin norepinephrine reuptake inhibitors (SNRI) were not excluded from the study.

The study population consisted of 26 men and 24 women. The mean age of the subjects was 45.4 years (S.D. = 13.4). The mean duration of illness was 20.3 years (S.D. =11). All patients were receiving antipsychotic treatment at the time of the evaluation. The mean daily defined dose (D.D.D.) was 1.23 (S.D. =0.7). This is a statistical measure of drug consumption, defined by the World Health Organization (http://www.whocc.no). It is the assumed average maintenance dose per day for a drug used for its main indication in adults and also serves to compare drug use among patients taking different medications.

The mean number of friends was 1.42 (S.D. =1.7) with a minimum of 0 and a maximum of 6 friends. Half of the patients had distinct paranoid features (significant paranoid ideation and paranoid delusions).

Fourteen patients (28%) were taking adjunctive antidepressant medication at the time the study was conducted. Seven patients (14%) had made at least one suicide attempt.
in the past. Four patients (8%) abused drugs in the past and two (4%) abused alcohol in the past.

**Research instruments:** Assessment tools included the following questionnaires:
1. Structured Clinical Interview for DSM-IV (SCID), a structured tool for the diagnosis for schizophrenia (14). All SCID assessments were performed by the last author (I.I.).
2. The self-report version of the Liebowitz Social Anxiety Scale (LSAS-SR) (15), whose objective is to assess the range of social interaction and performance situations which patients with SAD may fear and/or avoid.
3. The Positive and Negative Syndrome Scale (PANSS) (16) measuring symptom severity of patients with schizophrenia with positive, negative and general subscales.
4. The Schizophrenia Quality of Life Scale (SQLS) (17) is a practical and acceptable method of measuring self reported quality of life in people with schizophrenia.
5. The Global Assessment of Functioning scale (GAF) (5). This is a numeric scale (0 through 100) used by mental health clinicians to rate subjectively the social and occupational functioning of adults.

The GAF and the PANSS scores were rated by the clinicians, whereas the LSAS and SQLS were in a self-report format.

**Statistical analysis:** The LSAS-SR questionnaire was used as a screening tool for the presence of SAD using a cutoff of 30 or more (indicating the presence of focused SAD). A secondary measure was for generalized SAD based on a cutoff score of 59/60 on the total LSAS score. 38% of our patients had a diagnosis of SAD (12 males and 7 females). Based on a cutoff score of the total LSAS score of 59/60, 10% of our sample had generalized SAD. None of the patients with schizophrenia+SAD were diagnosed as such by the treating psychiatrist.

**RESULTS**

The scores on the various questionnaires are presented in Table 1. In the majority of cases (78%), the social fears were judged by the clinician to be neurotic (non-psychotic). Based on a cutoff score of 29/30 on the total LSAS score, 38% of our patients had a diagnosis of SAD (12 males and 7 females). Based on a cutoff score of the total LSAS score of 59/60, 10% of our sample had generalized SAD. None of the patients with schizophrenia+SAD were diagnosed as such by the treating psychiatrist.

Table 1 also presents the characteristics of those with and without SAD (based on a cutoff score of 29/30). The two sub-samples had similar age, gender distribution, and clinical characteristics. The Pearson’s correlation coefficients were reviewed between the LSAS and PANSS, between the “fear” subscale of the LSAS and positive symptoms, and between the “avoidance” LSAS subscale and negative symptoms on the PANSS.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total sample (n=50) Mean (S.D.)</th>
<th>SAD Positive (n=19) Mean (S.D.)</th>
<th>SAD Negative (n=31) Mean (S.D.)</th>
<th>Statistical Significance (df= degrees of freedom)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.4(13.4)</td>
<td>43.9(13.8)</td>
<td>46.3(13.3)</td>
<td>p=0.539, t=0.61, df=48</td>
</tr>
<tr>
<td>Duration of Illness (years)</td>
<td>20.3(11)</td>
<td>20.4(10.1)</td>
<td>20.2(11.7)</td>
<td>p=0.939, t=0.07, df=48</td>
</tr>
<tr>
<td>Number of Friends</td>
<td>1.42(1.7)</td>
<td>1.37(1.9)</td>
<td>1.45(1.7)</td>
<td>p=0.872, t=-0.16, df=48</td>
</tr>
<tr>
<td>PANSS total (range 35-100)</td>
<td>62.7(16.8)</td>
<td>67.9(19)</td>
<td>59.6(14.9)</td>
<td>p=0.099, t=-1.68, df=48</td>
</tr>
<tr>
<td>PANSS positive (range 7-23)</td>
<td>13.1(4.8)</td>
<td>14.68(5.7)</td>
<td>12.09(3.9)</td>
<td>p=0.092, t=-1.91, df=48</td>
</tr>
<tr>
<td>PANSS negative (range 7-39)</td>
<td>18.9(6.7)</td>
<td>20.05(7.2)</td>
<td>18.19(6.3)</td>
<td>p=0.345, t=-0.95, df=48</td>
</tr>
<tr>
<td>PANSS general (range 16-49)</td>
<td>30.7(9)</td>
<td>32.94(9.9)</td>
<td>29.29(8.1)</td>
<td>p=0.165, t=-1.41, df=48</td>
</tr>
<tr>
<td>LSAS total (range 0-118)</td>
<td>27.7(24.9)</td>
<td>52(23.1)</td>
<td>12.8(9.3)</td>
<td>p&lt;0.001, t=-8.44, df=48</td>
</tr>
<tr>
<td>SQLS (range 43-113)</td>
<td>78.5(18.1)</td>
<td>87.1(18.7)</td>
<td>73.2(15.8)</td>
<td>p=0.007, t=-2.82, df=48</td>
</tr>
<tr>
<td>GAF (range 35-75)</td>
<td>52.8(8.9)</td>
<td>51.8(6.1)</td>
<td>53.4(10.3)</td>
<td>p=0.533, t=0.59, df=48</td>
</tr>
<tr>
<td>D.D.D. (range 0.4-3.7)</td>
<td>1.23(0.7)</td>
<td>1.09(0.84)</td>
<td>1.2(0.6)</td>
<td>p=0.527, t=-0.63, df=48</td>
</tr>
</tbody>
</table>

Abbreviations: Liebowitz Social Anxiety Scale (LSAS), the Positive and Negative Syndrome Scale (PANSS), the Schizophrenia Quality of Life Scale (SQLS), Global Assessment of Functioning scale (GAF) and Daily Defined Dose (DDD).
duration of illness, number of friends and D.D.D. The group with schizophrenia and SAD included 12 males and 7 females, whereas the group with schizophrenia alone included 14 males and 17 females. This difference in gender distribution (37% females vs 55%, respectively) was not significant (chi square = 1.529, df=1, p=0.22). The subjects with schizophrenia and SAD took antidepressant medications in a similar proportion as the subjects with schizophrenia (26% vs 29%, chi square =0.043, p=1, degrees of freedom=1). Subjects with schizophrenia and SAD had a lower quality of life (the SQLS score is inversely correlated with quality of life).

Correlations: We found significant Pearson correlations between LSAS Fear subscale and PANSS general psychopathology subscale (r=0.28 [p=0.046] and SQLS [r=0.45, p=0.001]), and also between LSAS avoidance subscale and PANSS general psychopathology subscale (r=0.34, p=0.016), PANSS total (r=0.29, p=0.037) and SQLS (r=0.48, p=0.001). No significant correlations were found between LSAS fear subscale and positive PANSS and between LSAS avoidance subscale and PANSS negative. The LSAS (total score) correlated significantly with the PANSS general psychopathology subscale (r=0.31, p=0.024) and with the SQLS (r=0.47, p<0.01). An additional finding was that paranoid patients had lower GAF scores (p=0.017).

Discussion
To date, only a handful of studies have examined the prevalence rates of comorbid SAD in ambulatory patients with schizophrenia. The results of our study show that 38% of our patients met criteria for SAD (based on a score of 30 or greater on the LSAS) and that 10% of our patients met criteria for generalized SAD (based on a score of 60 or greater on the LSAS). The distinction between focused social anxiety and generalized social anxiety disorder is important, as the generalized form is associated with greater disability [20].

Our prevalence rate of 38% for comorbid SAD is consistent with that reported by both Pallanti et al. and Tibbo et al. in their studies of chronic ambulatory patients where prevalence rates were 36.3% and 23.3%, respectively (6, 21). Likewise several studies among first-episode patients have reported rates between 25-32% (22, 23). We note that our prevalence is higher than that reported by Braga et al. (8) who found comorbid SAD in 17% of outpatients (n=53) with schizophrenia. The lower rate reported by Braga may relate to differences in study variables, such as patient selection and choice of screening tools for SAD (SCID vs LSAS-SR). Additionally, several recent studies have examined the prevalence of SAD in acutely hospitalized schizophrenic patients with prevalence rates ranging from 5.7-25% (9, 10, 24). These different rates may be due to the difficulty of administering screening instruments to patients who are not clinically stable and are paranoid.

Consistent with data presented by Pallanti et al. (6), a clear finding of our study was that relative to patients without comorbid SAD, patients with schizophrenia with SAD had a lower overall quality of life (see Table 1). According to Kumazaki et al. (25), the association between social anxiety symptoms and a lower subjective quality of life suggests that it is clinically important to recognize the presence of social anxiety. These authors maintain that anxiety symptoms are often under-diagnosed because clinicians usually pay more attention to psychotic symptoms. In addition, they point out that recent criteria for remission in schizophrenia mainly rely on psychotic symptoms (26, 27) and, therefore, the risk of under-diagnosing anxiety factors is increased. However, this issue is far from simple. Whereas some authors conclude that social anxiety may lead to a decreased quality of life (6), others maintain, for example in community-dwelling patients with remitted schizophrenia, that a lower subjective quality of life might lead to the development of social anxiety symptoms (25), due to life's hardships and a lack of social communication skills.

Contrary to our expectations, we found no significant difference between patients with and without comorbid SAD in terms of the GAF scores. One explanation for this finding is that the GAF provides a relatively rough estimate of the overall severity of psychiatric symptoms and may not be sensitive enough to detect variances in functioning within a group of patients afflicted with schizophrenia. Accordingly, we note that the mean GAF score for both cohorts (with and without SAD) was in the low end of the moderate range showing that all patients had relatively poor functioning.

While the results of our study show that SAD is associated with an impaired quality of life, experts generally agree that the distinction between comorbid SAD and symptoms related to the natural course of schizophrenia is challenging. A major question in this field is that of the ability to differentiate SAD symptoms from positive symptoms (i.e., paranoia, ideas of reference) and negative symptoms (social withdrawal) which are inherent in the disease process of schizophrenia. In the case of a chronic patient who refuses to go to a vocational rehabilitation program, it is mandatory
to discern whether his behavior results from fears that spies will attack him (positive symptoms), avolition (negative symptoms) or fears that in the rehabilitation center he will sweat excessively and therefore will be mocked and will feel embarrassed (possibly SAD). For example, Mazeh et al. (9) concluded that it is difficult to differentiate SAD from positive symptoms, although we note that their study examined a cohort of acutely ill patients in which prominent positive symptoms may confound the assessment of SAD. In concordance with current studies (6, 22), the results of our study show that compared to patients who did not suffer from comorbid SAD, patients with schizophrenia and comorbid SAD had similar rates of negative and positive symptoms (see Table 1). Our results, therefore, support findings by Pallanti et al. (6) and Michail and Birchwood (22) that social anxiety appears to be unrelated to the presence of clinical psychotic symptoms.

In our opinion, screening for SAD in outpatients with schizophrenia may be best accomplished by asking if the patient has a fear of embarrassment or has avoidance in particular social situations (eating in public, going to job interviews or using a public restroom), for the core features of SAD are a fear of embarrassment and an intense apprehension about being negatively evaluated by others which lead to social avoidance. The patient with comorbid SAD complicating schizophrenia will experience the avoidant behavior as ego-dystonic and therefore qualitatively different from avoidant behavior due to anhedonia or lack of social interest. Furthermore, the patient with comorbid SAD is generally motivated to gain control of the anxiety symptoms, whereas avoidant behavior due to negative symptoms is typically accompanied by impaired motivation to change. We note that user-friendly self-report instruments (such as the Mini-SPIN) are available for identifying SAD in the managed care setting and appear to distinguish between the generalized and non-generalized subtypes (19, 28, 29). However, the validity and ease of administration of these tools in patients with schizophrenia deserves further study.

We have provided a synopsis of screening techniques for SAD, for an important finding of our study was that according to the results of the retrospective chart review, the diagnosis of comorbid SAD had been missed in every affected patient. We note that this failure to detect comorbid SAD occurred in a university-affiliated clinical setting which is staffed by experienced senior psychiatrists. We propose that several clinician-related variables contributed to the failure to correctly diagnose the comorbid SAD in our study population including: 1) a lack of knowledge of the high prevalence rates of comorbid SAD in schizophrenia, 2) failure to appreciate the clinical relevance and additional morbidity conferred by the presence of SAD in schizophrenia, 3) lack of knowledge regarding screening procedures, and 4) the tendency (bias) among clinicians to attribute poor social functioning to negative symptoms without exploring other comorbid conditions.

A limitation of our study is the small sample size. Another limitation may be the relative homogeneity of our sample which was composed primarily of patients with chronic schizophrenia, and, therefore, the results of our study may not generalize to a more diverse population including first episode patients. The inclusion of patients with schizoaffective disorder in our study population may also be considered as a limitation of our study, for the presence of affective symptoms may represent a confounding variable in the assessment of SAD. Patients with schizoaffective disorder, however, comprised only a minority of the sample. The inclusion of patients medicated with antidepressant medication may have biased the results, for the pharmacotherapy may have masked symptoms of SAD although we attempted to conduct our study under naturalistic conditions. Furthermore, the use of the LSAS-SR to screen for the presence of SAD (in contrast to the clinician-administered LSAS and the SCID) may have possibly decreased the reliability of our results, although both LSAS scales have been shown to be equivalent in several studies (18, 19). Seedat et al. (24) observed the low agreement between the Mini International Neuropsychiatric Interview (MINI) and a diagnosis of anxiety disorders on symptom status measures. While these authors suggest that existing cutoff scores on these measures may not be appropriate for psychotic individuals, we note that the MINI also is problematic due to its brevity and the possibility that it arouses dissimulation and denial in persons with psychosis.

While the comorbidity rate in our study is much higher than chance alone, its cause is unclear. Is it a result of the fear of stigma and rejection while having a mental disorder or due to a common biological underpinning, or rather a medication-induced side effect? Schizophrenia is associated with excessive dopamine activity, which is related to novelty seeking and exploratory behaviors. Introversion and social anxiety are related to decreased dopamine levels (30) and indeed Pallanti et al. (11) reported that anti-dopaminergic drugs cause SAD symptoms in a higher rate than expected.

We conclude that a failure to systematically screen for comorbid SAD in schizophrenia leads to underdetect-
tion of this potentially treatable disorder. SAD results in patients with schizophrenia in reduced quality of life and perhaps in other impairments. We note that clinicians also need to be aware that the use of atypical neuroleptic medications such as clozapine and olanzapine may lead to the emergence of SAD during treatment (11). Patients with comorbid SAD appear to be sensitive to the social stigma linked to schizophrenia and tend to feel socially marginalized (23).

Whereas a range of effective cognitive behavioral therapies (such as social skills, assertiveness, and empowerment training) and pharmacological therapies now exist for the treatment of SAD (31), there is some progress also in subjects with schizophrenia-SAD comorbidity. Antidepressant agents such as SSRIs have been reported to be efficacious in a small case series (32) and based on the potential role of oxytocin in the management of schizophrenia and also in SAD, this agent may be possibly used in subjects with this specific comorbidity (33, 34). Oxytocin reverses emotional recognition deficit and might restore the sense of trust in patients with schizophrenia and has been shown to attenuate (and normalize) fear-related brain activation and reactivity to emotionally negative cues in SAD. CBT within a group format was also found to be effective in cases with schizophrenia and SAD (35). Five therapeutic techniques could be used in that setting: a psycho-educational component, exposure simulations (gradual confrontation of a feared event/situation), cognitive restructuring (disputation of unhelpful thinking styles), role-play and intra-session assignments (homework). A more specific strategy, Morita therapy is a systematic psychotherapy based on Eastern psychology, named in 1919 after Shoma Morita, a Japanese psychiatrist (36). It involves a structured behavior program to encourage an outward perspective on life, thereby increasing social functioning. A recent review on Morita therapy in patients with schizophrenia revealed that this therapy, in addition to standard treatment, significantly improved daily living, compared with the standard treatment alone (36). Indeed, Kumazaki et al. (25) proposed to examine its efficacy in cases with schizophrenia and SAD comorbidity.

Finally, we suggest that the proper detection and treatment of SAD as a comorbid disorder in schizophrenia may be a prospective way to improve the overall quality of life of these individuals. Further research in this field is warranted with larger samples and sound methodology so as to assess the rate of SAD in schizophrenia and to dissect the similarities and differences of these not so divergent disorders. These studies should also evaluate whether the diagnosis and treatment of comorbid SAD would improve the treatment and quality of life of patients with schizophrenia.

References


