Research Paper

Olfactory performance segregates effects of anhedonia and anxiety on social function in patients with schizophrenia

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Background: Social dysfunction is common among individuals with schizophrenia. While often attributed to anhedonia, social dysfunction could also result from unrecognized anxiety. We examined the contributions of anhedonia and anxiety to social function using olfactory function to examine whether the domains had separate underpinnings. **Methods:** We assessed anhedonia, anxiety and social function as well as olfactory function in well-characterized patients with schizophrenia or schizoaffective disorder and healthy controls. **Results:** We included 56 patients and 37 controls in our study. Patients exhibited significantly higher levels of anhedonia and anxiety than controls, and the domains were highly correlated in patients. The combination of anhedonia and anxiety more strongly predicted social dysfunction than either measure alone. Smell identification was differentially related to the symptoms, with better performance predicting less anhedonia but more social fear in male patients. **Limitations:** The use of self-report measures precludes differentiation between recollected or recounted experience. Aside from smell identification and odour threshold, additional measures of olfaction may be considered for future studies. **Conclusion:** Anhedonia and anxiety were strongly correlated and both negatively impacted social function. The olfactory biomarker results support the conclusion that these domains are separate. Social function in patients with schizophrenia may improve with interventions for anxiety, even in the presence of marked negative symptoms.

Introduction

Social dysfunction is a core feature of schizophrenia. Individuals with the illness are often isolated, without close social or spousal relationships and unable to function independently.[1] Deficits in social function are often subsumed in a category of negative symptoms, which are largely unresponsive to existing treatments and worsen over time, challenging functional improvement for individuals with the disease.[2,3] Anhedonia is the negative symptom that describes the inability to experience pleasure from sensory, social or behavioural experiences. Loss of pleasure diminishes quality of life and may decrease motivation for social interactions.[4] Among samples without psychosis, anhedonia has been associated with social withdrawal and isolation; diminished enjoyment from and reduced need for social contact; and more severe schizotypal, schizoid, paranoid and psychotic-like symptoms at long-term follow-up.[5–7]

Anxiety symptoms and comorbid anxiety disorders are also common in patients with schizophrenia, though less well appreciated.[8,9] Social anxiety may consist of negative self-evaluation, feelings of discomfort and a tendency to withdraw from the company of others.[10] Negative cognition and a sense of shame arising from the stigma of mental illness have been theorized to contribute to social anxiety in individuals with psychosis,[11] but could plausibly arise from the neuropathology of the disease given this temporal association and frequent comorbidity. These symptoms contribute to a greater risk of suicide and relapse as well as a decreased ability to function in a social setting.[12,13]

In examining social anhedonia, social anxiety and schizotypy among a cohort of college students, Brown and colleagues[14] found a moderate association between anhedonia and anxiety, but did not find the 2 to contribute to a general social impairment factor. However, this association has not been well addressed among individuals with schizophrenia. Reduced or absent pleasure from social interactions could produce distorted perceptions, rendering social cues incomprehensible, possibly dangerous, and anxiety provoking.

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Conversely, social anxiety could produce withdrawal and diminish the pleasure of interactions. Alternatively, anhedonia and anxiety may reflect pathology in separate domains, and each could separately contribute to social deficits. A clearer understanding of the contributions of anxiety and anhedonia to social dysfunction in patients with schizophrenia may inform pharmacological and psychotherapeutic interventions.

Repeated meta-analyses by Moberg and colleagues[15,16] have supported ubiquitous deficits across tasks of odour detection, discrimination, hedonics, identification and memory in individuals with schizophrenia compared with healthy controls. Crespo-Facorro and colleagues[17] found individuals with schizophrenia to demonstrate impairment in appreciation of both positive and negative olfactory hedonic extremes, with evidence of accompanying neural circuitry dysfunction, and smell identification deficits have also been linked to diminished social drive in this population.[18] Good and colleagues[19] proposed smell identification test (SIT) performance in patients with early psychosis as a prospective marker for an illness course characterized by negative and cognitive/disorganized symptoms for those with lower scores versus anxiety/depressive symptoms for those with better scores. This suggests that brain impairments associated with SIT deficits are distinct from those producing anxiety/depression and that individuals with psychosis may have a course impacted by one of the singular symptom domains. Both domains, however, are plausibly present and influential of outcome in patients with schizophrenia.

To our knowledge, olfactory studies have not yet jointly considered anxiety and anhedonia (or related negative symptoms). A recent study of college students demonstrated better SIT performance for those with elevated social anhedonia,[20] but another study conversely found lesser performance for individuals with anhedonia, blunted affect and apathy,[21] consistent with the results in patients with schizophrenia. The association between olfaction and anxiety is unstudied in patients with schizophrenia, but SIT deficits have been found in patients with obsessive–compulsive disorder (OCD)[22] and posttraumatic stress disorder (PTSD).[23]

In the present study, we assessed odour sensitivity and SIT using the Smell Threshold Test[24] and the University of Pennsylvania Smell Identification Test (UPSIT),[25] respectively, and focused on quantifiable aspects of anhedonia and anxiety using the Chapman Social and Physical Anhedonia[26] and Liebowitz Social Anxiety (LSAS)[27] scales. Our 3 aims were to compare the presence of anhedonia and anxiety between patients with schizophrenia and healthy controls, to investigate the impact of anhedonia and anxiety on social function so as to shed light on whether anhedonia and anxiety are single or dual pathological domains within schizophrenia influencing social function, and to use olfactory function to explore if the biological underpinnings of anxiety and anhedonia were shared or distinct in patients with chronic schizophrenia. In recent studies addressing this sample, we reported sex-specific differences among patients with schizophrenia between olfaction measures and negative symptoms[28] and diagnosis by sex differences between olfaction measures and cognitive performance.[29] Thus, we examined this data for diagnosis- and sex-specific associations.

Methods

Sample

This study was a component of a larger project to study olfaction and social function conducted at New York State Psychiatric Institute and approved by the Institutional Review Board. Study participants with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder were recruited from inpatient and outpatient research and clinical units initially by a primary care physician to gauge interest and then by the clinical research team. Healthy controls were recruited from medical centre and Internet postings. We excluded individuals if they were younger than 18 and older than 55 years; pregnant; had current alcohol or other substance dependence or abuse; used steroidal contraceptives or allergy medications; or had a history of epilepsy, rhinoplasty, or a major head injury requiring medical treatment. All patients had to have been clinically stable on their current medication regimens for at least 1 month. All patients were assessed for their capacity to consent to this study by clinicians at the masters level or greater, were able to verbalize the relative risks/benefits and purpose of this study, and were deemed "minimal risk," by the human subjects committee. All participants provided written informed consent.

Assessment instruments

Clinical diagnosis

We used the Diagnostic Interview for Genetic Studies (DIGS)[30] to determine current and lifetime psychiatric diagnoses for all study participants. Controls were excluded if they had any personal or family history of psychosis, or if they met criteria for any Axis 1 disorder.

Symptoms

Current (state) symptomatology for each individual was assessed using the Positive and Negative Syndrome Scale (PANSS)[31] and the 24-item Hamilton Rating Scale for Depression (HAMD-24).[32] We used the Schedule for the Deficit Syndrome (SDS)[33] to measure trait-like negative symptoms and identify individuals classified as having the deficit syndrome.

Anhedonia and anxiety

The Liebowitz Social Anxiety Scale[27] assesses anxiety and avoidance of a broad scope of hypothetical social and performance situations. It comprises 4 scale scores (social fear, performance fear, social avoidance and performance avoidance) and a total score. Cutoffs of 30 and 60 have been proposed to provide optimal sensitivity/specificity for social anxiety and generalized social anxiety disorder, respectively.[34] The Chapman Scales for Physical and Social Anhedonia[35] assess deficits in the ability to experience pleasure from typically pleasurable physical stimuli, such as food and sex, as well as social pleasure from nonphysical stimuli, such as talking and exchanging expression of feelings.

Social function

The Social Function Scale[36] examines 7 areas of social

functioning: social withdrawal, interpersonal behaviour, social activities, recreation, independence in performance, independence in competence and employment/occupation.

Odour sensitivity
The Smell Threshold Test[37] (Sensonics Inc.) uses phenyl ethyl alcohol as the olfactory stimulus to determine odour detection threshold. Odour sensitivity reflects the level at which the participant can detect a single odorant applied at increasing concentrations under standard conditions.

Smell identification
The University of Pennsylvania Smell Identification Test[25] is a 40-item scratch-and-sniff multiple choice smell identification test. Participants are required to answer every item and may re-scratch the surface of the odour-impregnated strip if necessary.

Interviewer training and reliability
Mental health professionals carried out all procedures and diagnostic interviews. Training included an initial calibration using training tapes, with internal interview reliability assessments. Interrater reliability was $\kappa = 0.95$ for DSM-IV diagnosis and $\kappa = 0.80$ for individual symptoms.

Statistical analysis

All data and forms were checked for errors and consistency before data entry. We created form-fill databases, and data were entered and verified using the SIR Database Management Software (SIR 2002, SIR Pty Ltd). We examined the descriptive statistics (means ± standard deviations) and distributions of all measures, whether continuous or categorical, to identify key features (non-normal distribution, outliers, skewness) that might impact inferential methods. Age and education level were examined using analysis of variance (ANOVA) to assess for possible diagnostic group (patients and controls) and sex (male and female) effects. We compared age at illness onset between men and women with schizophrenia using the *t* test. The analyses of the LSAS Scales and the Chapman Scales were performed using multivariate ANOVAs assessing for the main effects of diagnostic group, sex and their interaction. The LSAS Total (the total of the 4 subscales) was analyzed using ANOVA. We examined partial correlations of total anhedonia and anxiety scales with social function as well as the interaction between anhedonia and anxiety on social function by sex and diagnosis.

As an integrative procedure, we performed 4 separate multiple regression analyses stratified by diagnosis and sex, regressing anhedonia and anxiety subscales on olfactory measures to identify those most salient in predicting SIT scores and odour sensitivity. In these regressions, age was entered as a control measure. During this procedure, variables are entered into the model 1 at a time based on the smallest criteria probability level until no other variables meet the criteria. We performed an additional multiple regression analysis with SFS total as the outcome measure, patient age as a control measure and forward-stepping of the anhedonia and anxiety subscales.

Results

Participants

We included 56 patients — 43 with schizophrenia and 13 with schizoaffective disorder (7 with depression and 6 with bipolar type) — and 37 healthy controls in the present study. All study participants were 18–55 years of age. Preliminary analyses (Table 1) showed similar mean ages and sex composition for the patient and control groups. There were significant effects of diagnostic group and sex for education, with patients significantly less educated than controls and women in both groups attaining a higher level of education than men. Mean SIT scores did not differ by diagnostic groups, but women in each group performed significantly better than men ($F = 4.40$, $p = 0.039$). As to odour sensitivity, the groups were not significantly different, but patients exhibited greater variability than controls (Levine test, $F = 3.40$, $p = 0.022$), particularly the female patients. The controls had negligible symptom levels on all PANSS and HAMD-24 measures, and these were not further examined. Patients did not show sex differences for the PANSS or HAMD-24.

Anhedonia and anxiety

The examination of anhedonia and anxiety scale scores by a multivariate ANOVA (Table 2) showed significant group and sex effects without any interactions. Patients had significantly more anhedonia than controls, and male patients had more severe symptoms than female patients. Female controls had the lowest levels of anhedonia, while male patients exhibited the highest levels. The groups differed significantly on the social subscales from the LSAS (Wilks' λ, $F_{4,78} = 6.80$, $p < 0.001$), without significant sex or group × sex interactions. All 4 subscales demonstrated group differences, and patients demonstrated significantly higher levels of fear and avoidance. Likewise, the LSAS total showed a similarly significant effect of diagnosis ($F_{1,81} = 28.00$, $p < 0.001$), with no significant sex effect or interaction.

Among individuals with schizophrenia, social anhedonia was significantly associated with every subscale of the LSAS: social fear ($r_{49} = 0.435$, $p = 0.002$), performance fear ($r_{49} = 0.345$, $p = 0.014$), social avoidance ($r_{49} = 0.514$, $p < 0.001$) and performance avoidance ($r_{49} = 0.519$, $p < 0.001$). In male patients the effects were similarly robust and significant between social anhedonia and all LSAS subscales and total LSAS (all $r > 0.465$, all $p < 0.019$). Female patients comparably demonstrated a significant association between social anhedonia and social avoidance ($r_{24} = 0.509$, $p = 0.009$), performance avoidance ($r_{24} = 0.417$, $p = 0.038$) and total LSAS ($r_{24} = 0.417$, $p = 0.038$). For healthy controls, social anhedonia was associated with performance avoidance in both men ($r_{15} = 0.505$, $p = 0.046$) and women ($r_{17} = 0.473$, $p = 0.047$), and no other associations were significant.

Among patients, physical anhedonia was associated only with social avoidance ($r_{49} = 0.316$, $p = 0.025$), but sex-specific analyses showed this was owing to the men, who uniquely demonstrated associations between physical anhedonia with

both social avoidance (r_{24} = 0.416, p = 0.038) and performance avoidance (r_{24} = 0.403, p = 0.046). Physical anhedonia did not have this predictive capacity among female patients, male controls or female controls.

Association between anhedonia and anxiety and social function

The association between both anhedonia (using Chapman scales) and social anxiety (using the total LSAS score) and social function were examined separately and in combination. Among patients, the interaction of anhedonia and anxiety scales was more strongly associated with social function (t = 4.68, p < 0.001) than anhedonia (t = 1.85, p = 0.07) and anxiety (t = 3.20, p = 0.003) alone. In the controls there was also a large effect of combined anhedonia and fear in social dysfunction (t = 2.93, p = 0.007), even though neither anhedonia (t = 1.30, p = 0.21) nor anxiety (t = 2.01, p = 0.06) alone were associated with social function among controls.

Additional regressions within diagnosis × sex analyses were performed to more finely probe the components of the anhedonia and anxiety subscales that predicted social function. Among patients, separate from sex, performance avoidance most negatively influenced social function (t = 4.54, p < 0.001); comparably, in the male subgroup of patients those with lower performance avoidance had the highest social function scores (t = 2.94, p = 0.008). In female patients, who demonstrated better social functioning than male patients (t = 2.41, p = 0.020), both social anhedonia (t = 2.46, p = 0.023) and social fear (t = 2.706, p = 0.014) independently predicted social functioning. Among controls, independent of sex, performance fear negatively influenced social function (t = 2.39, p = 0.024). No anxiety or anhedonia measure predicted social function in male controls examined separately. Female controls demonstrated better overall social function than their male counterparts (t = 2.59, p = 0.016); in particular, those with lower performance fear had the highest social functioning (t = 2.56, p = 0.026).

Olfactory measures

Analyses were used to identify which of the anhedonia and anxiety scales were most saliently associated with SIT and odour sensitivity. Better SIT scores correlated with less physical anhedonia in patients with schizophrenia (r_{50} = –0.361, p = 0.009), although not in controls (r_{32} = –0.216, p = 0.22). Among male patients, better SIT independently predicted greater social fear (t = 2.84, p = 0.010) and lesser physical anhedonia (t = 2.61, p = 0.017), showing the measures were dissociated by the olfactory task. Also in male patients, increased odour sensitivity was associated with lesser social anhedonia (t = 2.15, p = 0.046). For female patients, increased odour sensitivity was associated with younger age (t = 2.27, p = 0.035). Though significant, the associations observed among patients with odour sensitivity would not survive Bonferroni correction. Among male controls, no anhedonia or anxiety scales were predictive of odour sensitivity or SIT. In the female control group, increased odour sensitivity was associated with younger age (t = 4.09, p = 0.003) and less social avoidance (t = 3.30, p = 0.009) and independently with higher performance avoidance (t = 2.31, p = 0.047).

Other considerations

Post hoc we examined the influence of the deficit syndrome and schizoaffective disorder on the measures, as these are potential markers of heterogeneity in the illness. Patients with the deficit syndrome (n = 6) had lower overall social function (t = 3.59, p = 0.001), greater social anhedonia (t = 2.59, p = 0.014) and greater physical anhedonia (t = 3.94, p < 0.001)

Table 1: Demographic and clinical characteristics and measures of olfaction in healthy controls and patients with schizophrenia, by sex

	Controls; mean ± SD*		Patients; mean ± SD*		Group; statistic,† p value		
Characteristic	Men n = 18	Women n = 19	Men n = 29	Women n = 27	Diagnosis	Sex	Diagnosis × sex
Age, yr‡	29.5 ± 8.3	35.8 ± 14.5	32.2 ± 10.3	33.0 ± 8.3	F = 0.00, p = 0.98	F = 2.61, p = 0.11	F = 1.59, p =0.21
Age at illness onset, yr	—	—	22.9 ± 6.4	25.2 ± 7.0	—	t = 1.26, p = 0.21	—
Education (category)‡	4.4 ± 0.92	5.0 ± 0.78	3.2 ± 1.6	4.1 ± 1.3	F = 15.70, p < 0.001	F = 7.34, p = 0.008	F = 0.67, p = 0.42
Olfaction							
Smell identification	n = 17 31.5 ± 3.6	n = 19 33.4 ± 4.5	n = 28 30.4 ± 4.0	n = 26 32.2 ± 4.4	F = 1.66, p = 0.20	F = 4.40, p = 0.039	F = 0.01, p = 0.93
Odour sensitivity‡	n = 17 4.63 ± 1.5	n = 16 4.73 ± 1.0	n = 23 4.29 ± 1.4	n = 23 5.16 ± 2.2	F = 0.01, p = 0.91	F = 1.67, p = 0.20	F = 1.06, p = 0.31
PANSS symptoms	—	—	n = 27	n = 25	—	λ = 0.05, p = 0.99	—
Positive total	—	—	12.0 ± 5.3	12.2 ± 7.9	—	F = 0.02, p = 0.88	—
Negative total	—	—	13.7 ± 5.5	13.2 ± 5.6	—	F = 0.10, p = 0.76	—
General total	—	—	25.5 ± 5.9	25.6 ± 9.3	—	F = 0.00, p = 0.97	—
HAMD-24	—	—	7.6 ± 6.0	9.2 ± 7.3	—	t = 0.92, p = 0.36	—

HAMD-24: 24-item Hamilton Rating Scale for Depression; PANSS = Positive and Negative Symptom Scale; SD = standard deviation.
*Unless otherwise indicated.
†Test statistic: analysis of variance. Clinical symptoms were examined across sex using a multivariate analysis of variance statistic for the PANSS scales and the t test statistic for the HAMD-24 and the Young Mania Rating scales.
‡For age, education and odour sensitivity, the equality of variances test was significant.

than their non–deficit syndrome counterparts (n = 33). Compared with individuals carrying the diagnosis of schizophrenia, those with schizoaffective disorder demonstrated higher levels of social fear (t = 2.63, p = 0.011), social avoidance (t = 2.76, p = 0.008), performance avoidance (t = 2.38, p = 0.023) and a higher LSAS total (t = 3.18, p = 0.003).

Discussion

This study demonstrated greater levels of anhedonia and anxiety in a group of individuals with schizophrenia. The domains of psychopathology were significantly correlated in the patients, and both independently and together anhedonia and anxiety significantly impacted social function. The domains could be distinguished by use of olfactory testing, with better SIT scores predicting less physical anhedonia but more social fear.

The most robust findings of this research are the significantly more severe anhedonia and anxiety symptoms in the patients and the high intercorrelation of these domains, which was not observed in the controls. Social anhedonia was significantly associated with each of the 4 social anxiety subscales in patients: social fear, performance fear, social avoidance and performance avoidance. In controls, only performance avoidance was associated with social anhedonia.

The interaction between total anhedonia and total anxiety scores on social function was significant in both patients and controls, demonstrating that symptoms in both domains impact social capacity. Unexpectedly, among patients, total anxiety alone predicted a greater decline in social function than the anhedonia measures. This suggests that, in the schizophrenia population, not only may anxiety play a larger role than expected as a determinant of social function, when present to a high degree it may also be a principal determinant, despite negative symptoms. Of note, recent studies of high-risk, prodromal and early psychosis populations have identified negative symptoms as the strongest predictors of social function.[38,39] Our sample, however, consisted of individuals with chronic illness, further emphasizing the importance of phase-specific investigation of symptoms and their impact.

Breaking down the measures into subscales, performance avoidance was the sole independent negative predictor of social function among patients, whereas performance fear emerged as the negative determinant of social function in healthy controls. Interestingly, in patients we observed an association between anhedonia and performance avoidance but not between anhedonia and performance fear, as demonstrated in controls. This again suggests a heightened interplay between the 2 constructs unique to individuals with schizophrenia. Future work can explore the extent to which faulty reward circuitry could explain the greater performance avoidance with diminished pleasure.

The question of whether anhedonia and anxiety were variations of the same underlying construct was disentangled with the use of olfactory biomarkers, particularly in men with schizophrenia, who demonstrated the highest levels of every subscale of anhedonia and anxiety and the lowest social function. More negative symptoms and worse functional outcome is well-documented in male patients, as are greater structural and neurophysiological abnormalities.[40,41]

In this study, among men with schizophrenia, better SIT scores predicted both increased social fear and decreased physical anhedonia. Use of this olfactory probe among individuals with severe disease therefore demonstrated that despite the

Table 2: Anhedonia and anxiety measures in healthy controls and patients with schizophrenia, by sex

	Controls; mean ± SD*		Patients; mean ± SD*		Group; statistic,† p value		
Measure	Men	Women	Men	Women	Diagnosis	Sex	Diagnosis × sex
Chapman Scales	n = 17	n = 18	n = 27	n = 26	$\lambda_{2,83}$ = 3.44, p = 0.037	$\lambda_{2,83}$ = 4.54, p = 0.013	$\lambda_{2,83}$ = 0.59, p = 0.56
Physical anhedonia	16.0 ± 7.6	9.4 ± 5.6	17.9 ± 7.6	14.7 ± 8.4	F = 4.84, p = 0.031	F = 8.97, p = 0.004	F = 1.06, p = 0.31
Social anhedonia	10.5 ± 6.2	7.3 ± 5.4	13.4 ± 6.6	11.0 ± 6.6	F = 5.88, p = 0.017	F = 4.16, p = 0.045	F = 0.06, p = 0.80
LSAS	n = 17	n = 17	n = 26	n = 25	$\lambda_{4,78}$ = 6.80, p < 0.001	$\lambda_{4,78}$ = 0.79, p = 0.54	$\lambda_{4,78}$ = 0.57, p = 0.69
Social fear	3.5 ± 4.3	5.9 ± 6.2	12.3 ± 8.2	12.0 ± 7.6	F = 23.00, p < 0.001	F = 0.46, p = 0.50	F = 0.76, p = 0.39
Performance fear	3.9 ± 4.2	6.2 ± 5.0	12.7 ± 7.7	12.2 ± 8.3	F = 23.76, p < 0.001	F = 0.34, p = 0.56	F = 0.78, p = 0.38
Social avoidance	3.4 ± 3.8	5.0 ± 6.3	13.1 ± 9.6	10.4 ± 7.2	F = 21.31, p < 0.001	F = 0.10, p = 0.75	F = 1.74, p = 0.19
Performance avoidance	3.4 ± 4.7	4.5 ± 5.3	12.5 ± 8.1	10.5 ± 7.5	F = 24.68, p < 0.001	F = 0.09, p = 0.77	F = 1.06, p = 0.31
LSAS total (ANCOVA)	14.2 ± 13.5	21.6 ± 21.7	50.6 ± 31.2	45.2 ± 27.7	F = 28.00, p < 0.001	F = 0.03, p = 0.86	F = 1.29, p = 0.26
Social Function Scale total	835 ± 49	868 ± 24	755 ± 79	802 ± 58	F = 31.96, p < 0.001	F = 9.91, p = 0.002	F = 0.30, p = 0.58

ANCOVA = analysis of covariance; LSAS = Liebowitz Social Anxiety Scale; SD = standard deviation.
*Unless otherwise indicated.
†Multivariate analysis of variance.

intercorrelation of anhedonia and anxiety, they may act through distinct neurobiological pathways. This may account for the discord in the model of anxiety, anhedonia and social dysfunction previously mentioned, as described by Brown and colleagues.[14] Therefore, despite overlap on common structures associated with anxiety, the circuitry of anhedonia appears separate from that of anxiety, as assessed through olfaction.

The association between physical anhedonia and poor smell identification was unique to patients with schizophrenia. It cannot be excluded that olfactory dysfunction may be a direct cause of anhedonia. An individual's sense of smell, closely tied to taste and memory, is a component of many pleasurable experiences, such as enjoying a meal or smelling a rose. As mentioned, this association reached significance in men with schizophrenia, but a similar effect was observed among female patients. Links between loss of smell, anhedonia and reduced quality of life have been recently described,[42,43] as has an association between anhedonia and decreased performance on smell identification.[21]

Increased ability to identify the origins of odours may heighten vigilance and produce fear in individuals unable to use higher-level processes to evaluate the context of the sensory experience. The amygdala plays central roles in both odour perception and response to aversive stimuli and in the awareness and expression of fear.[44,45] Individuals with schizophrenia show increased amygdala activation to neutral perceptual stimuli.[46] A heightened sense of fear with smell identification might thus be possible, noted here in male patients, with the attendant limbic and prefrontal dysfunction of schizophrenia attaching too much danger to an odour identity.

Of note, post hoc analyses showed patients with the deficit syndrome to carry increased negative symptoms, as expected, in addition to a lower level of social functioning. Patients with schizoaffective disorder demonstrated increased fear, avoidance and social anxiety compared with patients with schizophrenia. Taken as a whole, the majority of patients had notable symptomatology in both the negative symptom and anxiety domains.

Limitations

Measures of self-report, such as the Chapman Anhedonia Scales, preclude the disentanglement of impaired recollection versus impaired experience in the moment, and thus remain an estimation of hypothetical anhedonia. Though an important distinction,[47] this measure likewise cannot be used to differentiate the experience of anticipatory from consummatory pleasure, nor can it contribute to emerging literature on anhedonia versus amotivation. Furthermore, the self-report social function scale used cannot differentiate between indifference to versus active avoidance of social engagement. Future studies in this area would benefit from the use of emotion-induction paradigms among individuals with schizophrenia compared with controls. In addition, shared variance among scales may have contributed to the correlations observed (i.e., SFS social withdrawal and LSAS social avoidance).

Individuals with active substance abuse/dependence were excluded in this study. Limiting the study population in this regard, though important for olfactory investigation, does notably limit generalizability of these findings, as high comorbid substance use is found in individuals with schizophrenia. Further, cigarette use was not included as a variable in this study and may have impacted the olfactory function of study participants.

We used smell identification and odour sensitivity to illuminate potential biological underpinnings; however, use of additional measures, namely odour discrimination, memory and, importantly here, hedonics, may have expanded the scope of our results. Though major findings highlighted in the discussion remained significant after correction, given the limited size of this investigation and multiple analyses conducted, prospective studies with larger samples and use of mediation analysis, not formally tested here, should solidify and expound upon the novel correlations presented in this study.

Conclusion

Our study demonstrated that individuals with schizophrenia display significantly greater anxiety and anhedonia than their healthy counterparts, indicating that these are important components of the largely heterogeneous disease. The association between anhedonia and anxiety was amplified in the schizophrenia population, with implications for a joint effect on social function, though with potentially distinct neurobiological circuitry. Nonetheless, we cannot glean a causal relationship between these domains. Patients may be avoidant because they do not enjoy social interactions, or rather, may not enjoy social interaction because they are avoidant or fearful and thus do not have the opportunity to associate interactions with pleasure.

Importantly, owing to the heightened correlation of anhedonia and anxiety among those with schizophrenia and the demonstrated robust effect of anxiety on social function both alone and combined with anhedonia in such patients, the role of anxiety should not be overlooked in the disease course. Targeted anxiety interventions, including cognitive behavioural therapy, benzodiazepines and selective serotonin reuptake inhibitors, have been shown to positively impact quality of life and symptom severity among individuals with schizophrenia.[48–51] As negative symptoms are historically difficult to treat in schizophrenia, identification and treatment of underlying anxiety has the potential to drastically improve functional outcomes in these individuals. These findings suggest that social dysfunction may improve with interventions for anxiety in some individuals with schizophrenia, even in the presence of anhedonia.

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