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Social anxiety and risk factors in patients with schizophrenia: Relationship with duration of untreated psychosis

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ABSTRACT

Social anxiety is commonly reported as a comorbid condition among people with schizophrenia. The aims of this study were to elucidate the associations between demographic/clinical features and social anxiety. A total of 207 outpatients with schizophrenia underwent assessments for social anxiety, psychiatric symptoms, social cognition, cognitive function, social functioning, and quality of life (QOL). To confirm the prediction model for social anxiety, we conducted multiple linear regressions using the Liebowitz Social Anxiety Scale (LSAS) score as an outcome variable and demographic/clinical variables as predictors. Of the 207 patients, 30 (14.5%) met the criteria for social anxiety disorder and 109 (52.7%) had a mean LSAS score higher than 30, suggesting that their social anxiety symptoms had reached a clinical level. Social anxiety was significantly correlated with psychiatric symptoms, social functioning, and QOL, whereas significant correlations with social cognition and cognitive function were not observed. A multiple regression analysis identified social functioning, gender, age of onset, and duration of untreated psychosis (DUP) as predictors that were most closely associated with the LSAS score. We confirmed that social anxiety symptoms were highly prevalent among outpatients with schizophrenia and were closely associated with social functioning and DUP, rather than social cognitive impairments.

1. Introduction

Recovery is a possible, but still challenging, goal for most patients with schizophrenia (Harvey et al., 2012). In general, recovery requires the amelioration of psychotic symptoms, cognitive impairment, and social dysfunction (Andreasen et al., 2005; Van Eck et al., 2017). Therefore, improvements in social functioning that are related to the long-term outcome are considered a treatment goal for patients with schizophrenia considering the achievement of self-support, the formation of better relationships with others, and a return to social activities (Bromley and Brekke, 2010; Kern et al., 2009; Nemoto et al., 2014). In clinical practice, however, most patients with schizophrenia are unwilling to even engage in social interactions or feel anxious about maintaining relationships with others (Braga et al., 2013).

Recent studies have revealed that social anxiety, including the fear or avoidance of social interactions, is commonly reported as a comorbid condition among people with schizophrenia and could be an obstacle to recovery or remission (Bosanac et al., 2016; Braga et al., 2013; Gorun et al., 2015; Karpov et al., 2016; Temmingh and Stein, 2015; Wetherell et al., 2003). Social anxiety has serious effects on role functioning and quality of life (Keller, 2006). We previously revealed a significant correlation between a low subjective wellbeing and an exacerbation of social anxiety symptoms in remitted outpatients with schizophrenia (Kumazaki et al., 2012). Therefore, the significance of identifying social anxiety symptoms should be highlighted in terms of achieving personal recovery as well as clinical and functional recovery (Chan et al., 2017).

It has been argued that social anxiety might emerge from some cognitive processing biases, such as deficits in social cognition and neurocognitive impairment, which are core features of schizophrenia (Kingsep et al., 2003; Voges and Addington, 2005). In particular, theory of mind (ToM) and the recognition of emotional facial expressions have been reported as key factors in the development of social anxiety symptoms (Hezel and McNally, 2014; Lysaker et al., 2010; Michail and Birchwood, 2009). However, in patients with schizophrenia, the results of studies examining the association between these social cognitive factors and social anxiety symptoms remain controversial (Achim et al., 2013, 2016; Sutliff et al., 2015). The perception of social rank, that is, how participants perceive themselves in relation to others, was reduced in schizophrenia patients with social anxiety disorder (Sutliff et al., 2015). However, a better performance in some areas of social cognition,

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such as social knowledge, was revealed in schizophrenia patients with social anxiety disorder when compared with the performances of patients without social anxiety disorder (Achim et al., 2013), although non-psychotic patients with primary anxiety disorders tended to present with social cognition biases (Plana et al., 2014).

The psychopathology of social anxiety symptoms in schizophrenia patients also remains unclear. Pallanti et al. (2004) insisted that social anxiety in psychotic patients was not qualitatively different from that in non-psychotic patients; however, social anxiety symptoms such as shyness and avoidance seem to share common elements with negative symptoms, such as apathy and avolition (Blanchard et al., 1998).

In addition, whether the presence or development of social anxiety in patients with schizophrenia is likely to be associated with the patient's background such as the age of onset, illness duration, and delay in first treatment, which might modify social and functional outcome, remains unclear (Bosanac et al., 2016; Marshall et al., 2005), although Vrbova et al. (2017) reported that schizophrenia patients with comorbid social anxiety had an earlier onset of illness. Especially, the duration of untreated psychosis (DUP) has been considered a key determinant of patient outcome, and shortening the DUP is a treatment target (Ito et al., 2015; Marshall et al., 2005).

As mentioned above, social anxiety symptoms appear to be a critical factor in the treatment of patients with schizophrenia; however, many issues remain controversial. Consequently, the aims of this study were to elucidate the demographic/clinical features of schizophrenia patients with social anxiety using a large sample and a large battery of measures and to identify determinant variables that are closely related to social anxiety symptoms. We hypothesized that the presence of social anxiety symptoms among patients with schizophrenia might be associated with social cognition, social functioning, quality of life (QOL), and specific clinical factors, such as age of onset, illness duration, and the DUP, and some of these factors might be key determinants of social anxiety symptoms.

2. Methods

2.1. Participants

Although 214 outpatients with schizophrenia under the age of 40 years were recruited at the Toho University Omori Medical Center, Tokyo, a total of 7 patients (3.3%) dropped out of the study because of exacerbation (2 patients) or the withdrawal of agreement (5 patients). Therefore, a total of 207 patients were registered in this study.

All the participants provided written informed consent before study enrollment. If the participant was under 20 years old, written informed consent was also obtained from the participant's parent or guardian. The Institutional Review Board of the Toho University School of Medicine approved the study procedure. The study was carried out in accordance with the latest version of the Declaration of Helsinki.

Patients who met the DSM-IV criteria for schizophrenia (295.10, 295.20, 295.30, 295.60, 295.90) were included in the present study. Patients who had an IQ below 70, as estimated using the Japanese National Adult Reading Test (JART; Matsuoka et al., 2006), were excluded.

2.2. Measures

The participants were assessed for social anxiety disorder (SAD) using the Mini International Psychiatric Interview (MINI; Otsubo et al., 2005; Sheehan et al., 1998). The MINI has been shown to have a high reliability and validity when compared to other structured clinical interviews for DSM-IV diagnoses (Sheehan et al., 2009). The severity of social anxiety symptoms was measured using the Liebowitz Social Anxiety Scale (LSAS; Asakura et al., 2002; Liebowitz, 1987). This clinician-administered scale consists of 24 items, 13 describing performance situations and 11 describing social interaction situations. Each of the items is separately rated for “fear” and “avoidance” using a 4-point categorical scale. Receiver operating curve analyses have shown that an LSAS score of 30 is the best cutoff point for distinguishing between individuals with and those without SAD (Ballenger, 2001; Mennin et al., 2002). The severity of positive/negative symptoms and depressive symptoms was rated using the Positive and Negative Syndrome Scale (PANSS; Igarashi et al., 1998; Kay et al., 1987) and the Calgary Depression Scale for Schizophrenia (CDSS; Addington et al., 1993; Kaneda et al., 2000).

ToM was examined using a battery consisting of four cartoon tasks: first-order false belief, second-order false belief, reality question, and tactical deception (Inoue et al., 2004). The subjects were asked to put the four pictures in order. The subjects were given a verbal description of each picture as follows: “A woman catches a bee in a paper bag (first picture); she presents the paper bag to the monkey (second picture); the monkey curiously reaches into the paper bag (third picture); the monkey is stung by the bee (fourth picture).” After the description, the subjects were asked to answer the first-order false belief question (Q1), followed by the reality question (Q2). After that, the subjects were asked the reality question again (Q3). Finally, the subjects were asked a tactical deception question (Q4). A correct answer was given 1 point for each question, and the points were summed. Therefore, the subjects were rated on a scale from 0 (all the questions answered incorrectly) to 4 (all the questions answered correctly).

Recognition of emotional facial expression was assessed according to the Japanese and Caucasian Facial Expressions of Emotion (JACFEE; Matsumoto and Ekman, 1988). The JACFEE is a highly standardized and reliable 56 color image set that shows actors from two different ethnicities portraying one of seven basic emotions including happiness, anger, fear, sadness, disgust and surprise. All of the facial emotions are rated using the Facial Action Coding System (Ekman and Friesen, 1978), and JACFEE photos have been validated and have shown multiculture reliability (Biehl et al., 1997).

Neurocognitive performance was evaluated using the Brief Assessment of Cognition in Schizophrenia (BACS), which assesses five different domains of cognitive function such as verbal memory, working memory, motor speed, verbal fluency, and reasoning and problem solving (Kaneda et al., 2007; Keefe et al., 2006). The composite BACS score was used for the analyses in this study.

Social functioning and QOL were evaluated using the Social Functioning Scale (SFS; Birchwood et al., 1990; Nemoto et al., 2008), the Sheehan Disability Scale (SDISS; Leon et al., 1997; Yoshida et al., 2004), the Global Assessment of Functioning Scale (GAF; American Psychiatric Association, 1994; Takizawa, 2015), the Subjective Well-Being Under Neuroleptics–Short Version (SWNS; Naber et al., 2001; Watanabe and Matsumura, 2003), and the World Health Organization-Quality of Life 26 (WHO-QOL; Tazaki and Nakane, 1997; WHOQOL Group, 1993). The SFS asks about the abilities and the performance of patients with schizophrenia in seven social functioning areas. We used the total score on the SFS in the present study. The SWNS consists of 5 subscales: emotional regulation, self-control, mental functioning, social integration, and physical functioning. The total scores for the functional measures were used in this study. The SDISS is a patient-rated tool evaluating functional disability in work, social, and family life, and the total score was used in this study. The WHO-QOL was used to measure the patients’ subjective sense of well-being in a comprehensive manner; it is composed of 26 items classified into four domains: physical health, psychological health, social relationships, and environment. The total average score was used in this study.

Patient insight and attitude toward treatment were measured using the Scale to Assess Unawareness of Mental Disorder (SUMD; Amador et al., 1994; Sakai et al., 2002) and the Drug Attitude Inventory 10-term version (DAI-10; Miyata, 2015; Nielsen et al., 2012). The SUMD evaluates present and past awareness of having a mental disorder, social consequences, need for treatment, and attribution of symptom to disorder. The DAI-10 assesses patient attitude towards medication with 10

dichotomous items.

The psychometric characteristics of the Japanese version of the clinical measures are as follows: for the LSAS, the Cronbach's alpha coefficient for the total score was 0.95 and the intra-class correlation coefficient (ICC) for individual items ranged from 0.86 to 0.92 (Asakura et al., 2002); for the PANSS, the Cronbach's alpha coefficient for the positive, negative, and general psychopathology subscales were 0.84, 0.87 and 0.76, respectively, and the ICC for the subscales were 0.85, 0.83 and 0.75, respectively (Igarashi et al., 1998); for the CDSS, the ICC was 0.98 (Addington et al., 1993; Kaneda et al., 2000); for the SFS, the Cronbach's alpha was 0.84, and the ICC for the total score was 0.87 (Nemoto et al., 2008); for the SDISS, the Cronbach's alpha was 0.84 (Yoshida et al., 2004); for the GAF, the ICC was over 0.8 (Takizawa, 2015); for the SWNS, the Cronbach's alpha of the total score was 0.87 (Watanabe and Matsumura, 2003); for the WHO-QOL, the Cronbach's alpha ranged from 0.64 to 0.84 (Tazaki and Nakane, 1997); for the SUMD, the Cohen's kappa coefficient was over 0.75 (Sakai et al., 2002); for the DAI-10, the Cronbach's alpha was 0.97, and the ICC for the total score was 0.81 (Miyata, 2015). In the Japanese versions of these measures, the reliability and validity were satisfactory and were similar to those obtained in the antecedent studies. The variables and their abbreviations are shown in Table 1.

2.3. Statistics

We compared the demographic and clinical variables between participants who met the MINI criteria for SAD (SAD +) and those who did not (SAD-) and between those who had social anxiety symptoms at a clinical level (LSAS ≥ 30; LSAS +) and those who did not (LSAS < 30; LSAS-) using independent *t*-tests for continuous variables and the chi square test for categorical variables. The Spearman rank-order correlation (r) was also used to examine the association between the LSAS score and demographic/clinical variables. We adopted the Spearman's order correlation coefficient because of the many variables included in the analysis and the robustness of this method (Spearman, 1904). This decision was described in the Statistical Analysis Plan before the database for this study was locked. We used stepwise multiple linear regressions using the LSAS score as an outcome variable and the clinical variables described in Table 1 as well as gender, age, age of onset, illness duration, and the DUP as predictors. All the tests were two-tailed, and results with a probability of less than 5% were regarded as significant.

Table 1
List of measures.

Category	Acronym	Measures
Social anxiety	LSAS	Liebowitz Social Anxiety Scale
Psychiatric symptoms	PANSS	Positive and Negative Syndrome Scale
	CDSS	Calgary Depression Scale for Schizophrenia
Social cognition	ToM	Theory of Mind
	JACFEE	Japanese and Caucasian Facial Expressions of Emotion
Cognitive function	BACS	Brief Assessment of Cognition in Schizophrenia
	JART	Japanese National Adult Reading Test
Social functioning	SFS	Social Functioning Scale
	SDISS	Sheehan Disability Scale
	GAF	Global Assessment of Functioning Scale
Quality of life	SWNS	Subjective Well-Being Under Neuroleptics-Short Version
	WHO-QOL	World Health Organization-Quality of Life 26
Others	SUMD	Scale to Assess Unawareness of Mental Disorder
	DAI-10	Drug Attitude Inventory 10-term version

Table 2
Background of participants.

	mean	SD
Sex (male/female)	101/106	
Age (years)	29.3	7.0
Age of onset (years)	22	6.4
Illness duration (years)	6.8	5.6
Duration of untreated psychosis (months)	9.8	18.5
Dose of antipsychotics (mg/day, CP equivalent)	444.2	334.9

CP: chlorpromazine.

3. Results

3.1. Clinical characteristics of participants

As shown in Table 2, of the 207 patients with schizophrenia who agreed to participate, 106 patients (51.2%) were female. The mean age of all the participants was 29.3 years, the mean age of onset was 22.0 years, and the mean illness duration was 6.8 years. Their mean DUP was 9.8 months, and 75 participants (36.2%) had some form of psychiatric family history. Their mean dose of antipsychotics was 444.2 mg/day (chlorpromazine equivalent).

According to the MINI, 30 of the 207 patients (14.5%) met the criteria for SAD. The mean total LSAS score was 38.3 (SD = 30.4) (fear: 21.2 [SD = 16.3]; avoidance: 17.1 [SD = 15.1]), and 109 participants (52.7%) had a mean LSAS score higher than 30, suggesting that their social anxiety symptoms had reached a clinical level.

Comparisons between the SAD + and the SAD- groups and comparisons between the LSAS + and LSAS- groups are presented in Table 3. No differences in ToM, JACFEE, or DAI-10 were seen between the SAD + and the SAD- groups or between the LSAS + and the LSAS- groups. The SAD + group had significantly higher LSAS, PANSS, CDSS, and SDISS scores and significantly lower SFS, GAF, SWNS, and WHO-QOL scores than the SAD- group. Similar trends were observed when the LSAS + and LSAS- groups were compared.

3.2. Social anxiety symptoms and other clinical variables

As shown in Table 4, the LSAS score was correlated with the age of onset, the DUP, psychiatric symptoms, social functioning, and QOL. Regarding the subscales of the PANSS, both the positive symptoms ($r = 0.355$, $P < 0.001$), negative symptoms ($r = 0.261$, $P < 0.001$), and general psychopathology ($r = 0.393$, $P < 0.001$) were significantly correlated with the LSAS score. On the other hand, there were no significant correlations with social cognition and cognitive function.

A multiple regression analysis showed that a lower SFS, a female gender, a younger age of onset, and a longer DUP contributed significantly to a more severe LSAS score (Table 5).

4. Discussion

The results revealed that social anxiety was significantly correlated with the age of onset, DUP, psychiatric symptoms, social functioning, and QOL. Furthermore, social functioning, gender, age of onset, and DUP were identified as determinant variables most closely associated with the severity of social anxiety symptoms.

The findings for the associations between social anxiety and psychiatric symptoms and QOL were consistent with the results of previous studies (Lowengrub et al., 2015; Mazeh et al., 2009). Social anxiety symptoms often remain untreated because of their confusion with negative symptoms in schizophrenia patients (Pallanti et al., 2004). Clinical attention should be focused on social anxiety in the differentiation of negative symptoms, although inter-correlations do exist as seen in the present study. Some studies have suggested significant overlap between social anxiety and paranoia (Birchwood, 2007;

Table 3
Demographic and clinical assessment scores of patient groups.

		SAD- N = 177		SAD + N = 30			LSAS- N = 98		LSAS + N = 109		
Variables		mean	SD	mean	SD	*P*	mean	SD	mean	SD	*P*
Age (years)		29.6	7.0	27.5	6.6	n.s.	30.0	7.1	28.7	6.8	n.s.
Age of onset (years)		22.6	6.5	18.4	4.1	< 0.0001	22.8	6.3	21.3	6.5	n.s.
Illness duration (years)		6.5	5.4	8.6	6.6	n.s.	6.6	5.6	6.9	5.6	n.s.
Duration of untreated psychosis (months)		9.7	18.8	10.0	17.5	n.s.	7.6	14.2	11.8	21.7	n.s.
LSAS	Fear	18.2	14.1	39.2	16.9	< 0.0001	8.4	5.9	32.8	13.7	< 0.0001
	Avoidance	14.4	13.4	33.0	15.3	< 0.0001	4.8	4.2	28.1	12.7	< 0.0001
	Total	32.6	26.4	72.2	30.9	< 0.0001	13.2	9.2	60.9	24.4	< 0.0001
PANSS	Total	71.7	16.8	84.4	16.9	0.0007	67.6	17.4	78.7	15.5	< 0.0001
CDSS		4.5	4.0	10.3	4.6	< 0.0001	3.2	3.0	7.2	4.9	< 0.0001
ToM		2.4	1.0	2.4	1.0	n.s.	2.4	1.0	2.3	1.0	n.s.
JACFEE	Total	32.0	4.2	32.1	5.7	n.s.	31.7	4.3	32.3	4.5	n.s.
BACS	Verbal Memory	−1.3	1.4	−1.8	1.3	0.0414	−1.2	1.3	−1.4	1.4	n.s.
	Working Memory	−1.0	1.3	−1.3	1.2	n.s.	−1.1	1.3	−1.0	1.4	n.s.
	Motor Speed	−2.2	1.3	−2.3	1.5	n.s.	−2.3	1.2	−2.2	1.4	n.s.
	Verbal Fluency	−0.7	1.0	−0.9	1.2	n.s.	−0.7	0.9	−0.8	1.1	n.s.
	Attention and Processing Speed	−1.1	1.0	−1.6	1.0	0.0244	−1.0	1.0	−1.3	1.1	n.s.
	Reasoning and Problem Solving	−0.9	1.8	−1.3	2.0	n.s.	−0.9	1.7	−1.1	1.9	n.s.
	Composite Score	−4.5	3.5	−5.6	4.0	n.s.	−4.4	3.4	−4.9	3.8	n.s.
JART		26.0	10.1	26.7	8.9	n.s.	24.6	9.8	27.4	9.9	0.0406
SFS	Withdrawal	10.6	2.2	9.1	2.4	0.0028	11.0	2.0	9.8	2.3	0.0001
	Interpersonal	7.8	2.8	6.5	3.2	0.0468	8.4	2.6	6.9	3.0	0.0001
	Prosocial activities	15.1	9.2	14.4	9.7	n.s.	16.8	9.6	13.3	8.6	0.0070
	Recreation	20.3	7.0	18.0	5.8	n.s.	20.6	6.9	19.4	6.8	n.s.
	Independence-competence	35.6	3.8	33.2	6.2	0.0457	36.6	3.0	34.1	4.9	< 0.0001
	Independence-performance	27.6	7.2	24.7	6.3	0.0295	29.6	6.2	25.0	7.3	< 0.0001
	Employment	5.7	3.0	5.7	3.3	n.s.	6.6	2.9	4.8	3.0	< 0.0001
	Total	122.6	25.0	111.4	24.1	0.0272	129.6	22.7	113.3	24.8	< 0.0001
SDISS	Work/School	3.3	2.7	5.5	2.5	< 0.0001	2.5	2.6	4.6	2.5	< 0.0001
	Social life	2.9	2.7	5.8	2.6	< 0.0001	2.1	2.4	4.5	2.8	< 0.0001
	Family life	2.0	2.2	4.4	2.8	< 0.0001	1.5	2.0	3.2	2.6	< 0.0001
GAF		54.3	14.0	47.5	12.6	0.0112	58.4	14.5	48.8	11.8	< 0.0001
SWNS	Total	75.6	17.1	54.4	13.6	< 0.0001	82.6	14.6	63.7	16.4	< 0.0001
WHO-QOL	Physical	22.6	4.8	18.6	3.7	< 0.0001	24.2	4.2	20.1	4.6	< 0.0001
	Psychological	18.8	4.6	13.9	3.1	< 0.0001	20.1	4.3	16.2	4.4	< 0.0001
	Social	9.5	2.2	7.7	1.7	< 0.0001	9.9	2.0	8.6	2.3	< 0.0001
	Environmental	27.8	5.2	23.3	4.2	< 0.0001	29.1	5.2	25.5	4.9	< 0.0001
	Overall	5.9	1.7	4.5	1.3	< 0.0001	6.4	1.6	5.2	1.7	< 0.0001
SUMD	Awareness of disease - present	4.6	2.5	5.0	2.9	n.s.	4.8	2.5	4.4	2.6	n.s.
	Awareness of disease - past	6.3	4.1	5.8	3.0	n.s.	6.3	3.9	6.2	4.0	n.s.
	Awareness of symptoms - present	14.8	15.2	13.9	9.8	n.s.	14.9	17.7	14.4	11.0	n.s.
	Awareness of symptoms - past	26.1	17.6	19.0	11.0	0.0053	25.9	17.6	24.4	16.5	n.s.
	Attribution of symptoms - present	13.5	9.3	16.8	11.3	n.s.	11.6	9.0	15.9	9.8	0.0021
	Attribution of symptoms - past	19.3	10.8	21.9	12.6	n.s.	18.5	10.8	20.9	11.4	n.s.
DAI-10		3.4	4.3	2.3	4.3	n.s.	3.7	4.3	2.8	4.2	n.s.

We compared the demographic and clinical variables between participants who met the MINI criteria for social anxiety disorder (SAD +) and those who did not (SAD-) and between those who had social anxiety symptoms at a clinical level (LSAS ≥ 30; LSAS +) and those who did not (LSAS < 30; LSAS-). LSAS: Liebowitz Social Anxiety Scale; PANSS: Positive and Negative Syndrome Scale; CDSS: Calgary Depression Scale for Schizophrenia; ToM: Theory of Mind; JACFEE: Japanese and Caucasian Facial Expressions of Emotion; BACS: Brief Assessment of Cognition in Schizophrenia; JART: Japanese National Adult Reading Test; SFS: Social Functioning Scale; SDISS: Sheehan Disability Scale; GAF: Global Assessment of Functioning Scale; SWNS: Subjective Well-Being Under Neuroleptics-Short Version; WHO-QOL: World Health Organization-Quality of Life 26; SUMD: Scale to Assess Unawareness of Mental Disorder; DAI-10: Drug Attitude Inventory 10-term version.

Lysaker et al., 2010; Michail and Birchwood, 2009). Actually, the Delusion item (P1) and the Suspiciousness item (P6) in the Positive symptoms subscales of the PANSS were both significantly associated with the LSAS score (r = 0.398, $P < 0.001$; r = 0.434, $P < 0.001$, respectively). However, Gorun et al. (2015) reported that social anxiety was unrelated to the PANSS scores, with a few exceptions. Sutliff et al. (2015) reported that the severity of social anxiety symptom ratings were correlated with certain PANSS scores not in schizophrenia patients who met the criteria for SAD, but in patients who did not. Further investigation is needed.

In the present study, while 109 participants (52.7%) had LSAS scores higher than 30, suggesting that their social anxiety symptoms had reached a clinical level, only 30 of the 207 patients (14.5%) met the MINI criteria for SAD. Although the LSAS rates “fear” and “avoidance” for each of 24 items using a 4-point categorical scale in detail, the MINI simply asks the subjects directly as to whether social fears have disrupted the subjects’ normal work or social functioning or have caused subjects significant distress, possibly resulting in an under-detection. Short structural interviews may underestimate the diagnosis of anxiety disorders (Balestrieri et al., 2007), and a clinical interview supplemented with another scale for social anxiety symptoms appears to be more useful for the diagnosis of social anxiety disorder.

Regarding gender and social functioning, although almost all subtypes of anxiety disorders are substantially more prevalent in women, social anxiety disorder appears to affect both sexes equally (Bekker and van Mens-Verhulst, 2007). However, social anxiety has been reported to be more severe in women (Turk et al., 1998). Bosanac et al. (2016) also showed that a female gender and social dysfunction were highly

Table 4
Correlation coefficient between LSAS and demographic/clinical variables.

Variables	r
Age of onset	−0.176*
Illness duration	0.063
Duration of untreated psychosis	0.151*
PANSS	0.379**
CDSS	0.537**
ToM	−0.027
JACFEE	0.058
BACS	−0.042
JART	0.176*
SFS	−0.367**
SDISS	0.491**
GAF	−0.274**
SWNS	−0.625**
WHO-QOL	−0.516**
SUMD	0.127
DAI-10	−0.113

LSAS: Liebowitz Social Anxiety Scale; DUP: Duration of Untreated Psychosis; PANSS: Positive and Negative Syndrome Scale; CDSS: Calgary Depression Scale for Schizophrenia; ToM: Theory of Mind; JACFEE: Japanese and Caucasian Facial Expressions of Emotion; BACS: Brief Assessment of Cognition in Schizophrenia; JART: Japanese National Adult Reading Test; SFS: Social Functioning Scale; SDISS: Sheehan Disability Scale; GAF: Global Assessment of Functioning Scale; SWNS: Subjective Well-Being Under Neuroleptics-Short Version; WHO-QOL: World Health Organization-Quality of Life 26; SUMD: Scale to Assess Unawareness of Mental Disorder; DAI-10: Drug Attitude Inventory 10-term version.

* $P < 0.05$.

** $P < 0.01$.

associated with all domains of anxiety among Australian people with psychotic disorders. The present results showed that the severity of social anxiety was associated with a female gender among schizophrenia patients. Women have reported greater fear than men when talking to authority figures, speaking before an audience, and working while being observed (Bekker and van Mens-Verhulst, 2007), and this appears to be true among patients with schizophrenia as well.

The prevalence of any anxiety disorder as a comorbid condition in schizophrenia is estimated to be as high as 38%, and SAD, which is characterized by a difficulty with interpersonal relationships, is the most prevalent among anxiety disorders (Temmingh et al., 2015). Patients with a younger onset of schizophrenia have fewer opportunities to develop social skills. This may explain why the age of onset was a predictor of the LSAS score in the multiple regression analysis.

As far as we know, this is the first report to show an association between social anxiety and the DUP in patients with schizophrenia. This observed association may also support the importance of early intervention for psychosis and avoiding the development of social anxiety, as the presence of social anxiety can be correlated with a poorer social outcome and a lower subjective quality of life during later life (Judd, 1994; Katzelnick et al., 2001). Actually, a long DUP was reportedly associated with social withdrawal and a poor social network in several studies examining first-episode psychosis (Fraguas et al., 2014; Barnes et al., 2008; Yamazawa et al., 2008). Social anxiety is a significant comorbidity in first-episode psychosis (Michail and Birchwood, 2009). Although social anxiety disorder has been suggested to develop after the onset of psychosis (Birchwood et al., 2007), subclinical social anxiety might be present before the onset of psychosis (Michail and Birchwood, 2009). Therefore, a long period of untreated psychosis may progressively lead to fear and the avoidance of social situations and relationships. Actually, our results revealed an association between social anxiety and the DUP that seems to have clinical implications for the real-world treatment of schizophrenia. Schizophrenia patients with a long DUP should be reconsidered from the viewpoint of social anxiety. Reversely, the presence of social anxiety may be suggestive of a delay in the first treatment for psychosis. These findings indicate that close attention to social anxiety is needed during the prodromal phase of schizophrenia. Cooper et al. (2016) reported that social anxiety occurred even during the premorbid phase of schizophrenia, and social anxiety was separable from but also significantly associated with attenuated psychotic symptoms.

Regarding our finding of a lack of correlation between the social anxiety symptom level and social cognition (ToM and JACFEE), one plausible explanation is that cognitive aberration might not have a significant relationship with the symptom level, but with the functional level, as if basic neurocognition is not associated with symptoms, but rather the functional outcome (Green et al., 2000). A meta-analysis revealed that people with SAD showed attributional biases, while people with posttraumatic stress disorder showed deficits in mentalizing and emotion recognition (Plana et al., 2014). Further investigations are needed to examine the bias of social cognitive functioning in schizophrenia patients with social anxiety symptoms.

The present results showed a higher prevalence of social anxiety symptoms that had reached a clinical level (52.7%) among patients with schizophrenia than in previous studies. Some studies, which had a smaller sample size, reported that 38–43% of patients suffered from SAD (Gorun et al., 2015; Lowengrub et al., 2015; Sutliff et al., 2015). *Taijin-kyofu-sho* (TKS), which is a culture-bound disorder of social anxiety, is known to be common in Japan (Asakura et al., 2012; Nakamura et al., 2002). In addition to the sample size, cultural differences may have also affected the prevalence (Kumazaki et al., 2012).

Some methodological limitations of our study should be considered. This study had a cross-sectional design; however, a strength of our study was that social anxiety was comprehensively evaluated using both psychological and cognitive measures in a large-scale sample of outpatients with schizophrenia.

In this study, the participants had a somewhat short illness duration. In our previous study in which the illness duration of schizophrenia patients was over 25 years, although social anxiety symptoms were commonly reported among elderly patients with remitted schizophrenia, an increase in social anxiety symptoms was not associated with psychotic symptoms or social functioning, but with subjective quality of life (Kumazaki et al., 2012).

In conclusion, we confirmed that social anxiety symptoms are highly prevalent among outpatients with schizophrenia and are closely associated with social functioning, gender, age of onset, and DUP,

Table 5
Multiple regression model coefficients for LSAS as independent variable.

	Unstandardized		95%C.I. for B		Standardized		
Variables	B	Std. Error	Lower	Upper	beta	t	*P*
SFS	−0.51	0.08	−0.66	−0.36	−0.42	−6.73	< 0.001
Male	−13.04	3.77	−20.47	−5.60	−0.22	−3.46	< 0.001
Age of onset	−0.81	0.29	−1.37	−0.25	−0.18	−2.84	0.005
DUP	0.21	0.10	0.01	0.41	0.13	2.11	0.036

($F = 17.31$, $P < 0.001$, $R^2 = 0.270$, adjusted $R^2 = 0.255$).

LSAS: Liebowitz Social Anxiety Scale; SFS: Social Functioning Scale; DUP: Duration of Untreated Psychosis.

rather than social cognitive impairments. Optimal intervention from the early stage of psychosis and intensive treatment for social anxiety seem essential for the achievement of patients' goals and recovery.

Declaration of interests

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Authors' contributions

S.A., H.K., T.N., S.M., N.M., and M.M. conceived the idea and methodology of this study. S.A., T.N., and S.M. managed the study. S.A., T.N., T.Y., N.K., N.T. and M.M. were involved in subject recruitment, clinical and diagnostic assessments. Y.W. provided clinical and demographic tests. S.A., H.K., and T.N. undertook the literature searches and wrote the first draft of the manuscript. S.A. and T.N. revised the manuscript. All authors contributed to and have approved the final manuscript.

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References

Achim, A.M., Ouellet, R., Lavoie, M.A., Vallieres, C., Phillip, L.J., Roy, M.A., 2013. Impact of social anxiety on social cognition and functioning in patients with recent-onset schizophrenia spectrum disorders. Schizophr. Res. 145 (1–3), 75–81.
Achim, A.M., Sutliff, S., Samson, C., Montreuil, T.C., Lecomte, T., 2016. Attribution bias and social anxiety in schizophrenia. Schizophr. Res. Cogn. 4, 1–3.
Addington, D., Addington, J., Maticka-Tyndale, E., 1993. Assessing depression in schizophrenia: the Calgary Depression scale. Br. J. Psychiatry Suppl. 22, 39–44.
Amador, X.F., Flaum, M., Andreasen, N.C., Strauss, D.H., Yale, S.A., Clark, S.C., Gorman, J.M., 1994. Awareness of illness in schizophrenia and schizoaffective and mood disorders. Arch. Gen. Psychiatry 51 (10), 826–836.
American Psychiatric Association, 1994. Diagnosis and Statistical Manual of Mental Disorders, fourth ed. American Psychiatric Association, Washington, DC.
Andreasen, N.C., Carpenter Jr., W.T., Kane, J.M., Lasser, R.A., Marder, S.R., Weinberger, D.R., 2005. Remission in schizophrenia: proposed criteria and rationale for consensus. Am. J. Psychiatry 162 (3), 441–449.
Asakura, S., Inoue, T., Kitagawa, N., Hasegawa, M., Fujii, Y., Kako, Y., Nakato, Y., Hashimoto, N., Ito, K., Tanaka, T., Nakagawa, S., Kusumi, I., Koyama, T., 2012. Social Anxiety/Taijin-Kyofu Scale (SATS): development and psychometric evaluation of a new instrument. Psychopathology 45 (2), 96–101.
Asakura, S., Inoue, S., Sasaki, F., Sasaki, Y., Kitagawa, N., Inoue, T., Denda, K., Ito, M., Matsubara, R., Koyama, T., 2002. Reliability and validity of the Japanese version of the Liebowitz Social Anxiety Scale. Clin. Psychiatry 44 (10), 1077–1084 (in Japanese).
Balestrieri, M., Baldacci, S., Bellomo, A., Bellantuono, C., Conti, L., Perugi, G., Nardini, M., Borbotti, M., Viegi, G., 2007. Clinical vs. structured interview on anxiety and affective disorders by primary care physicians. understanding diagnostic discordance. Epidemiol. Psichiatr. Soc. 16 (2), 144–151.
Ballenger, J.C., 2001. Treatment of anxiety disorders to remission. J. Clin. Psychiatry 62 (suppl 12), 5–9.
Barnes, T.R., Leeson, V.C., Mutsatsa, S.H., Watt, H.C., Hutton, S.B., Joyce, E.M., 2008. Duration of untreated psychosis and social function: 1-year follow-up study of first-episode schizophrenia. Br. J. Psychiatry 193 (3), 203–209.
Bekker, M.H.J., van Mens-Verhulst, J., 2007. Anxiety disorders: sex differences in prevalence, degree, and background, but gender-natural treatment. Gend. Med. 4 (suppl B), s178–s193.
Biehl, M., Matsumoto, D., Ekman, P., Hearn, V., Heider, K., Kudoh, T., Ton, V., 1997. Matsumoto and Ekman's Japanese and Caucasian Facial Expressions of Emotion (JACFEE): reliability data and cross-national differences. J. Nonverbal Behav. 21 (1), 3–22.
Birchwood, M., Smith, J., Cochrane, R., Wetton, S., Copestake, S., 1990. The Social Functioning Scale. The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. Br. J. Psychiatry 157, 853–859.
Birchwood, M., Trower, P., Brunet, K., Gilbert, P., Iqbal, Z., Jackson, C., 2007. Social anxiety and the shame of psychosis: a study in first-episode psychosis. Behav. Res. Ther. 45, 1025–1037.
Blanchard, J.J., Mueser, K.T., Bellack, A.S., 1998. Anhedonia, positive and negative affect, and social functioning in schizophrenia. Schizophr. Bull. 24, 413–424.
Bosanac, P., Mancuso, S.G., Castle, D.J., 2016. Anxiety symptoms in psychotic disorders: results from the Second Australian National Mental Health Survey. Clin. Schizophr. Relat. Psychoses 10, 93–100.
Bromley, E., Brekke, J.S., 2010. Assessing function and functional outcome in schizophrenia. Curr. Top. Behav. Neurosci. 4, 3–21.
Braga, R.J., Reynolds, G.P., Siris, S.G., 2013. Anxiety comorbidity in schizophrenia. Psychiatry Res. 210 (1), 1–7.
Chan, R.C.H., Mak, W.W.S., Chio, F.H.N., Tong, A.C.Y., 2017. Flourishing with psychosis: a prospective examination on the interactions between clinical, functional, and personal recovery processes on well-being among individuals with schizophrenia spectrum disorders. Schizophr. Bull (Epub ahead of print).
Cooper, S., Klugman, J., Heimberg, R.G., Anglin, D.M., Ellman, L.M., 2016. Attenuated positive psychotic symptoms and social anxiety: along a psychotic continuum or different constructs? Psychiatry Res. 235, 139–147.
Ekman, P., Friesen, W.V., 1978. Facial Action Coding System. Consulting Psychologists Press, Palo Alto.
Fraguas, D., Del, Rey-Mejías, A., Moreno, C., Castro-Fornieles, J., Graell, M., Otero, S., Gonzalez-Pinto, A., Moreno, D., Baeza, I., Martínez-Cengotitabengoa, M., Arango, C., Parellada, M., 2014. Duration of untreated psychosis predicts functional and clinical outcome in children and adolescents with first-episode psychosis: a 2-year longitudinal study. Schizophr. Res. 152 (1), 130–138.
Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr. Bull. 26 (1), 119–136.
Gorun, A., Cieslak, K., Harkavy-Friedman, J., Deptula, A., Goetz, D., Goetz, R., Malaspina, D., 2015. Frequent comorbidity and predictors of social anxiety in persons with schizophrenia: a retrospective cohort study. Prim. Care Companion CNS Disord. 17 (5).
Harvey, P.D., Heaton, R.K., Carpenter Jr., W.T., Green, M.F., Gold, J.M., Schoenbaum, M., 2012. Functional impairment in people with schizophrenia: focus on employability and eligibility for disability compensation. Schizophr. Res. 140 (1–3), 1–8.
Hezel, M.D., McNally, R.J., 2014. Theory of mind impairments in social anxiety disorder. Behav. Ther. 45, 530–540.
Igarashi, Y., Hayashi, N., Yamashina, M., Otsuka, N., Kuroki, N., Anzai, N., Kazamatsuri, H., 1998. Interrater reliability of the Japanese version of the Positive and Negative Syndrome Scale and the appraisal of its training effect. Psychiatry Clin. Neurosci. 52 (5), 467–470.
Inoue, Y., Tonooka, Y., Yamada, K., Kanba, S., 2004. Deficiency of theory of mind in patients with remitted mood disorder. J. Affect. Dis. 82 (3), 403–409.
Ito, S., Nemoto, T., Tsujino, N., Ohmuro, N., Matsumoto, K., Matsuoka, H., Tanaka, K., Nishiyama, S., Suzuki, M., Kinoshita, H., Ozawa, H., Fujita, H., Shimodera, S., Kishimoto, T., Matsumoto, K., Hasegawa, T., Mizuno, M., 2015. Differential impacts of duration of untreated psychosis (DUP) on cognitive function in first-episode schizophrenia according to mode of onset. Eur. Psychiatry 30 (8), 995–1001.
Judd, L.L., 1994. Social phobia: a clinical overview. J. Clin. Psychiatry 55, 5–9.
Kaneda, Y., Omori, T., Addington, D., 2000. The Calgary Depression Scale for Schizophrenia Japanese Version (JCDSS). Brain Nerve 52 (2), 163–166 (in Japanese).
Kaneda, Y., Sumiyoshi, T., Keefe, R., Ishimoto, Y., Numata, S., Ohmori, T., 2007. Brief assessment of cognition in schizophrenia: validation of the Japanese version. Psychiatry Clin. Neurosci. 61 (6), 602–609.
Karpov, B., Joffe, G., Aaltonen, K., Suvisaari, J., Baryshnikov, I., Naatanen, P., Koivisto, M., Melartin, T., Oksanen, J., Suominen, K., Heikkinen, M., Paunio, T., Isometsa, E., 2016. Anxiety symptoms in a major mood and schizophrenia spectrum disorders. Eur. Psychiatry 37, 1–7.
Katzelnick, D.J., Kobak, K.A., DeLeire, T., Henk, H.J., Greist, J.H., Davidson, J.R., 2001. Impact of generalized social anxiety disorder in managed care. Am. J. Psychiatry 158, 1999–2007.
Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13 (2), 261–276.
Keefe, R.S.E., Poe, M., Walker, T.M., Harvey, P.D., 2006. The relationship of the Brief Assessment of Cognition in Schizophrenia (BACS) to functional capacity and real-world functional outcome. J. Clin. Exp. Neuropsychol. 28 (2), 260–269.
Keller, M.B., 2006. Social anxiety disorder clinical course and outcome: review of Harvard/brown Anxiety Research Project (HARP) findings. J. Clin. Psychiatry 67 (Suppl 12), 14–19.
Kern, R.S., Glynn, S.M., Horan, W.P., Marder, S.R., 2009. Psychosocial treatments to promote functional recovery in schizophrenia. Schizophr. Bull. 35 (2), 347–361.
Kingsep, P., Nathana, P., Castle, D., 2003. Cognitive behavioural group treatment for social anxiety in schizophrenia. Schizophr. Res. 63, 121–129.
Kumazaki, H., Kobayashi, H., Niimura, H., Kobayashi, Y., Ito, S., Nemoto, T., Sakuma, K., Mizuno, M., 2012. Lower subjective quality of life and the development of social anxiety symptoms after the discharge of elderly patients with remitted schizophrenia: a 5-year longitudinal study. Compr. Psychiatry 53 (7), 946–951.
Leon, A.C., Olfson, M., Portera, L., Farber, L., Sheehan, D.V., 1997. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. Int. J. Psychiatry Med. 27 (2), 93–105.
Liebowitz, M.R., 1987. Social Phobia. Mod. Probl. Pharm. 22, 141–173.
Lowengrub, K.M., Stryjer, R., Birger, M., Iancu, I., 2015. Social anxiety disorder comorbid with schizophrenia: the importance of screening for this under recognized and under treated condition. Isr. J. Psychiatry Relat. Sci. 52 (1), 40–45.

Lysaker, P.H., Salvatore, G., Grant, M.L.A., Procacci, M., Olesek, K.L., Buck, K.D., Nicolo, G., Dimaggio, G., 2010. Deficits in theory of mind and social anxiety as independent paths to paranoid features in schizophrenia. Schizophr. Res. 124 (1–3), 81–85.
Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., Croudace, T., 2005. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. Arch. Gen. Psychiatry 62 (9), 975–983.
Matsumoto, D., Ekman, P., 1988. Japanese and Caucasian facial expressions of emotion (JACFEE) (Slides). Intercultural and Emotion Research Laboratory, Department of Psychology, San Francisco State University, San Francisco, CA.
Matsuoka, K., Uno, M., Kasai, K., Koyama, K., Kim, Y., 2006. Estimation of premorbid IQ in individuals with Alzheimer's disease using Japanese ideographic script (Kanji) compound words: Japanese version of National Adult Reading Test. Psychiatry Clin. Neurosci. 60 (3), 332–339.
Mazeh, D., Bodner, E., Weizman, R., Delayahu, Y., Cholostoy, A., Martin, T., Barak, Y., 2009. Co-morbid social phobia in schizophrenia. Int. J. Soc. Psychiatry 55 (3), 198–202.
Mennin, D.S., Fresco, D.M., Heimberg, R.G., Shneier, F.R., Davies, S.O., Liebowitz, M.R., 2002. Screening for social anxiety disorder in the clinical setting: using the Liebowitz Social Anxiety Scale. J. Anxiety Disord. 16 (6), 661–673.
Michail, M., Birchwood, M., 2009. Social anxiety disorder in first-episode psychosis: incidence, phenomenology and relationship with paranoia. Br. J. Psychiatry 195 (3), 234–241.
Miyata, R., 2015. DAI. In: Yamauchi, T., Kashima, H. (Eds.), The Handbook of Psychiatric and Psychological Assessment. Nakayama Shoten, Tokyo (in Japanese).
Naber, D., Moritz, S., Lambert, M., Rajonk, F., Holzbach, R., Mass, R., Andresen, B., 2001. Improvement of schizophrenic patients' subjective well-being under atypical antipsychotic drugs. Schizophr. Res. 50, 79–88.
Nakamura, K., Kitanishi, K., Miyake, Y., Hashimoto, K., Kubota, M., 2002. The neurotic versus delusional subtype of taijin-kyofu-sho: their DSM diagnoses. Psychiatry Clin. Neurosci. 56 (6), 595–601.
Nemoto, T., Fujii, C., Miura, Y., Chino, B., Kobayashi, H., Yamazawa, R., Murakami, M., kashima, H., Mizuno, M., 2008. Reliability and validity on the Social Functioning Scale Japanese version (SFS-J). Jpn. Bull. Soc. Psychiatry 17, 188–195 (in Japanese).
Nemoto, T., Niimura, H., Ryu, Y., Sakuma, K., Mizuno, M., 2014. Long-term course of cognitive function in chronically hospitalized patients with schizophrenia transitioning to community-based living. Schizophr. Res. 155 (1–3), 90–95.
Nielsen, R.E., Lindström, E., Nielsen, J., Levander, S., 2012. DAI-10 is as good as DAI-30 in schizophrenia. Eur. Neuropsychopharmacol. 22 (10), 747–750.
Otsubo, T., Tanaka, K., Koda, R., Shinoda, J., Sano, N., Tanaka, S., Aoyama, H., Mimura, M., Kamijima, K., 2005. Reliability and validity of Japanese version of the Mini-International Neuropsychiatric Interview. Psychiatry Clin. Neurosci. 59, 517–526.
Pallanti, S., Quercioli, L., Hollander, E., 2004. Social anxiety in outpatients with schizophrenia: a relevant cause of disability. Am. J. Psychiatry 161 (1), 53–58.
Plana, I., Lavoie, M.A., Battagia, M., Achim, A.M., 2014. A meta-analysis and scoping review of social cognition performance in social phobia, posttraumatic stress disorders. J. Anxiety Disord. 28, 169–177.
Sakai, Y., Kim, Y., Akiyama, T., Kurita, H., 2002. Reliability and validity of the scale to assess unawareness of mental disorder Japanese version (SUMD-J). Clin. Psychiatry 44 (5), 491–500 (in Japanese).
Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl. 20), 22–33.
Sheehan, D., Janavs, J., Harnett-Sheehan, K., Sheehan, M., Gray, C., 2009. The Mini International Neuropsychiatric Interview Version 6.0 (M.I.N.I.6.0).
Spearman, C., 1904. The proof and measurement of association between two things. Am. J. Psychol. 15 (1), 72–101.
Sutliff, S., Roy, M.A., Achim, A.M., 2015. Social anxiety disorder in recent onset schizophrenia spectrum disorders: the relation with symptomatology, anxiety, and social rank. Psychiatry Res. 227 (1), 39–45.
Takizawa, R., 2015. GAF. In: Yamauchi, T., Kashima, H. (Eds.), The Handbook of Psychiatric and Psychological Assessment. Nakayama Shoten, Tokyo (in Japanese).
Tazaki, M., Nakane, Y., 1997. WHO QOL 26 Japanese Version. Kaneko Shobo. (in Japanese).
Temmingh, H., Stein, D.J., 2015. Anxiety in patients with schizophrenia: epidemiology and management. CNS Drugs 29, 819–832.
Turk, C.L., Heimberg, R.G., Orsillo, S.M., Holt, C.S., Gitow, A., Street, L.L., Schneier, F.R., Liebowitz, M.R., 1998. An investigation of gender differences in social phobia. J. Anxiety Disord. 12, 209–223.
Van Eck, R.M., Burger, T.J., Vellinga, A., Schirmbeck, F., de Haan, L., 2017. The relationship between clinical and personal recovery in patients with schizophrenia spectrum disorders: a systematic review and meta-analysis. Schizophr. Bull (Epub ahead of print).
Voges, M., Addington, J., 2005. The association between social anxiety and social functioning in first episode psychosis. Schizophr. Res. 76, 287–292.
Vrbova, K., Prasko, J., Ociskova, M., Holubova, M., 2017. Comorbidity of schizophrenia and social phobia - impact on quality of life, hope, and personality traits: a cross sectional study. Neuropsychiatr. Dis. Treat. 13, 2073–2083.
Watanabe, M., Matsumura, H., 2003. Reliability and validity of subjective well-being under neuroleptic drug treatment short form, Japanese version (SWNS-J). Jpn. J. Clin. Psychopharmacol. 6, 905–912 (in Japanese).
Wetherell, J.L., Palmer, B.W., Thorp, S.R., Patterson, T.L., Golshan, S., Jeste, D.V., 2003. Anxiety symptoms and quality of life in middle-aged and older outpatients with schizophrenia and schizoaffective disorder. J. Clin. Psychiatry 64 (12), 1476–1482.
WHOQOL Group, 1993. Measuring Quality of Life: The development of the World Health Organization Quality of Life Instrument (WHOQOL). World Health Organization, Geneva.
Yamazawa, R., Nemoto, T., Kobayashi, H., Chino, B., Kashima, H., Mizuno, M., 2008. Association between duration of untreated psychosis, premorbid functioning, and cognitive performance and the outcome of first-episode schizophrenia in Japanese patients: prospective study. Aust. NZ J. Psychiatry 42 (2), 159–165.
Yoshida, T., Otsubo, T., Tsuchida, H., Wada, Y., Kamijima, K., Fukui, K., 2004. Reliability and validity of Japanese version of the Sheehan disability scale (SDISS). Jpn. J. Clin. Psychopharmacol. 7 (10), 1645–1653 (in Japanese).