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# Serotonin Transporter Polymorphism and Depressive-Related Symptoms in Schizophrenia

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**A role for the serotonin transporter (5-HTT) gene polymorphism in mental illnesses and anxiety-traits has been implicated. The contribution of genetic factors in personality traits and the manifestation of specific symptoms in psychiatric illnesses have yet to be elucidated. Anxious-depressive symptoms are a significant component in a pattern of schizophrenic symptoms. This study focused on the relation between 5-HTT polymorphism and clinical presentations of schizophrenia, specifically those related to the affective spectrum. Using clinical and psychological analyses, we tested the genetic association between the 5-HTTLPR polymorphism (5-HTT gene-linked polymorphic region) and anxiety- and depressive-related symptoms emerged in schizophrenia. In 260 patients with an ICD-10 diagnosis of schizophrenia (broad definition), we studied the 5-HTTLPR genotype (insertion-deletion polymorphism), the Positive and Negative Syndrome Scale (PANSS), and self-rated inventories (EPI, MMPI, STAI) scores. Patients with the "ss" genotype (deletion variant) scored significantly higher on "Guilt feelings" and "Depression" items, as compared with those of the "ll" genotype (insertion variant) ($P = 0.016$, 0.039, respectively). The frequency of the "ss" genotype was reduced in patients with no depression or guilt feelings, or in those patients exhibiting questionable symptoms. In contrast, the "ss" genotype carriers prevailed among the patients with mild, moderate, or severe ratings of the symptoms. The scores on all anxiety- and depression-related traits, self-rated by the patients, did not significantly differ by genotype. Our finding may contribute to understanding of molecular genetic features underlying an appearance of psychopathological symptoms emerged in schizophrenia.**


**KEY WORDS: clinical symptoms; PANSS; personality traits; serotonin transporter**

## INTRODUCTION

Schizophrenia is a multifactor disorder with a complex pattern of inheritance, and of unclear etiology. Multiple linkage studies, as well as association analyses, have been carried out in an attempt to find a major gene for the disease, or genes, which may predispose to its manifestation. Genes predisposing to the manifestation of the disease are likely to be of small effect and contribute to the variance of continuously measurable traits, for example, psychological and clinical characteristics, rather than to categorical features, such as a diagnosis. In this view, the genes for neurotransmitters appear to receive a lot of attention, as they might contribute to pathophysiological processes.

Serotonin plays a pivotal role in central nervous system development and functioning. A vast body of literature addresses a relationship between genes involved in serotonin metabolism and various psychiatric disturbances. The serotonin transporter gene (5-HTT) regulates neurotransmission and it is the initial target for several antidepressant drugs.

Within this gene, two polymorphic variants have been described and used in association studies: (1) a 17-bp variable tandem-repeat (VNTR-17) located in the second intron with one rare (9 repeats) and two common (10 or 12 repeats) alleles [Lesch et al., 1994]; and (2) polymorphism in the 5-HTT gene-linked polymorphic region (5-HTTLPR) located approximately 1-kb upstream of

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the transcription initiation site [Lesch et al., 1997]. The latter polymorphism is represented by long (l) and short (s) alleles. These alleles have been reported to determine differences in 5-HTT expression that might contribute to the serotonin (5-HT) function in neurotransmission.

Numerous studies of 5-HTT polymorphism in various psychiatric diseases, that is, autism, attention deficit hyperactivity disorder, panic and obsessive-compulsive disorders, affective disorders [for a review, see Lesch and Mossner, 1998], yielded conflicting results. The most interesting finding proved to be an association between the "s" 5-HTT allele responsible for reduced 5-HTT function and higher expression of anxiety-related personality characteristics in psychiatrically well subjects [Lesch et al., 1997; Greenberg et al., 2000]. As was found earlier, anxiety-related traits, such as neuroticism, contribute to the risk of depression [Kendler et al., 1993a,b]. Based on these information, Benjamin et al. [2001] articulated the hypothesis that "some of the genes affecting personality may be heuristic "endophenotypes" for major psychiatric disorders."

There are several lines of evidence for a role of the 5-HTT in schizophrenia pathophysiology due to a dysfunction in serotoninergic signaling. Reduced 5-HT reuptake sites were detected in the postmortem brains of schizophrenics [Joyce et al., 1993; Naylor et al., 1996] and a significant increase in 5-HTT RNA was found in the frontal and temporal cortex of schizophrenic subjects [Hernandez and Sokolov, 1997]. Recently, Kaiser et al. [2001] found an association between the "ll" 5HTTLPR genotype and schizoaffective psychoses. To the contrary, extensive literature reports a lack of association between the 5-HTT gene polymorphism and schizophrenia [Mendes de Oliveira et al., 1998; Stoeber et al., 1998; Rao et al., 1999; Tsai et al., 2000; Kaiser et al., 2001; Serretti et al., 2002].

The negative results may be explained assuming that allelic variants account for expression of certain disease symptomology, but not for disease development per se. Attempts have been made to find an association between 5-HTT variants and such characteristics as aggression [Nolan et al., 2000] or attempted suicide [Chong et al., 2000] in the patients with schizophrenia. Serretti et al. [1999, 2002] investigated 5-HTTLPR polymorphism in relation to symptomologic factors of major psychoses assessed by the Operational Criteria for Psychotic Illness (OPCRIT), which were represented by mania, depression, delusion, and disorganization as phenotype definitions. No evidence of a relationship between 5-HTT-polymorphism and any of the above factors was observed in their sample of 261 schizophrenia patients. Also, no association was found between the 5-HTT genetic variants and clinical symptoms being assessed using the Brief Psychiatric Rating Scale in 90 treatment-resistant schizophrenics [Tsai et al., 2000].

An anxious-depressive component is believed to contribute to schizophrenia symptoms [Kay and Sevy, 1990; Lindenmayer et al., 1994; Wolthaus et al., 2000; Lykouras et al., 2000]. Therefore, a relationship between 5-HTT polymorphism and clinical presentations of schizophrenia, conferring to affective spectrum, needs further investigation.

The present study aims at seeking an association between 5-HTTLPR polymorphism and anxiety- and depressive-related symptoms emerged in schizophrenia using the Positive and Negative Syndrome Scale (PANSS) and self-rated inventories for psychological assessment. We assumed that using both clinical and psychopathological evaluation of anxiety- and depression-related symptoms would be helpful for comparison of scores obtained with 5-HTT genotypes.

## MATERIALS AND METHODS

### Patients

Two hundred sixty patients have been included in this study. All were inpatients of clinical departments of the Research Center of Mental Health. The inclusion criterion was a diagnosis of schizophrenia and spectrum disorders defined according to the International Diagnostic Checklist for ICD-10. Patients with organic brain disorders or severe somatic diseases were not included. Once an initial diagnosis was established by a psychiatrist, the diagnosis was confirmed by the senior researchers (V.G.K. and L.I.A.).

After being informed about the goals of the investigation, each patient gave a written informed consent to participate in the study.

Sample characteristics are given in Table I.

### Psychopathological Assessment

The PANSS [Kay et al., 1987] is a widespread instrument proven to be valid and suitable for evaluation of positive, negative, and general psychopathological items, that is, depression and anxiety. It includes three subscales measuring positive, negative, and general psychopathological symptoms on 30 items—7 for positive symptoms, 7 for negative, and 14 for general psychopathological ones. Each symptom has 7 ratings (1: symptom is absent, 2: questionable, 3: mild, 4: moderate, 5: severe, 6: markedly severe, 7: extremely severe). The PANSS interviews, completed by a trained researcher, were conducted 1 week before the patient's discharge from the hospital. The inter-rater reliability for each item met conventional levels.

TABLE I. Sample Characteristics (n = 260)

| | |
|---|---|
| Age, years (SD) | 35.1 (16.5) |
| Age at onset, years (SD) | 22.9 (17.5) |
| Duration of illness, years (SD) | 12.1 (10.1) |
| Gender, n (%) | |
| Male | 160 (61.5) |
| Female | 100 (38.5) |
| ICD-10 diagnoses, n (%) | |
| Paranoid schizophrenia (code F20.0) | 159 (61.2) |
| Catatonic schizophrenia (code F20.2) | 7 (2.7) |
| Undifferentiated schizophrenia (code F20.3) | 8 (3.0) |
| Post-schizophrenic depression (code F20.4) | 1 (0.4) |
| Simple schizophrenia (code F20.6) | 2 (0.8) |
| Unspecified schizophrenia (code F20.8) | 1 (0.4) |
| Schizotypic disorder (code F21) | 22 (8.4) |
| Schizoaffective disorder (code F25) | 60 (23.1) |

### Psychological Questionnaires

Translated and adapted versions of the Eysenck Personality Inventory (EPI) [Rusalov, 1987]; Minnesota Multiphasic Personality Inventory (MMPI) [Beresin et al., 1976], and the State Trait Anxiety Inventory (STAI) [Khanin, 1978] were administered to measure anxiety-related personality traits. EPI (57 items) encompasses personality traits on two scales: extraversion and neuroticism. MMPI (377 item version) comprised three validity scales (L, F, K) and ten clinical diagnostic scales: hypochondriasis, depression, hysteria, psychopathic deviate, masculinity-femininity, paranoia, psychasthenia, schizophrenia, hypomania, and social introversion. STAI consists of 20 items measuring trait anxiety. To reduce an influence of affected status on personality trait evaluation, the patients were asked to complete the inventories *after* an improvement of their clinical state being assessed as 1 or 2 or 3 with Global Clinical Impression scale. The patients completed the questionnaires themselves or with the assistance of an examiner or psychologist (M.V.A.). The patients scoring above 90 on scale F (MMPI) were excluded, because of marked personality changes.

### Genotyping and Statistics

Each participant was asked to donate venous blood for DNA extraction, after being informed about the goals of the investigation. Primers for genotyping the 5-HTTLPR locus and PCR performance were as described elsewhere [Lesch et al., 1996]. Because of rank characteristics of PANSS ratings, an association between PANSS scores and the 5HTTLPR genotype was assessed by applying Mann–Whitney test. A difference between genotype frequencies in the patient's groups, being divided according to a degree of severity of each of the PANSS item, was evaluated using $\chi^2$-statistics. One-way ANOVA was used to compare subjects with different 5HTTLPR genotypes on personality inventory scales. Two-way ANOVA was conducted to evaluate the contribution of genotype and depression in psychological trait variability. Spearman's correlations between personality traits and clinical symptoms have been calculated in correlation analysis.

## RESULTS AND DISCUSSION

Genotype frequencies did not differ significantly between different diagnostic groups (see Table I), that is, between the patients with schizophrenia and schizoaffective disorder ($P = 0.1$).

The mean scores on all the positive, negative, and general psychopathological items of the PANSS by 5HTTLPR genotype are shown in Table II. The data demonstrate that the patients, regardless of genotype, had higher mean scores (above 3) on the all items, but "Grandiosity" of the positive symptom subscale, and on the all items, with the exception of "Difficulty in abstract thinking," on the negative symptom subscale. In the terms of negative and positive schizophrenia subtypes, one can consider the sample studied as a "mixed" one [Dollfus et al., 1996].

No difference by 5HTTLPR genotype has been found between mean scores for positive and negative symptoms. In terms of general psychopathological symptoms, the patients with the "ss" genotype scored significantly higher on "Guilt feelings" and "Depression" items, as compared to those with the "ll" genotype ($P = 0.016$ and 0.039, respectively). The frequencies of "ll" and "ss" genotypes were evaluated in the patient's groups divided according to the degree of severity of each item (symptoms are absent or questionable, mild, moderate, severe, very severe). Here, we combined the patients scored as 1 or 2 and the patients scored as 6 and 7. As shown in Figures 1 and 2, the frequency of the patients with "ss" genotype was significantly lower in the group with the absence of depression and guilt feelings, and tended to increase in the groups with moderate to extremely severe depression and mild or severe guilt feelings ($\chi^2 = 5.0$, $P = 0.03$ and $\chi^2 = 6.8$, $P = 0.02$).

Carriers of different genotypes were examined for personality self-rating characteristics, measuring the anxiety-related traits and depression, such as neuroticism (EPI), hypochondriasis, depression, psychasthenia (MMPI), and trait-anxiety (STAI). Only 152 out of 260 schizophrenia patients studied were able to complete at least one questionnaire. The results are shown in Table III. The levels of all traits measured did not significantly differ by 5HTTLPR genotype. When comparing the clinical and subjective ratings in the total sample, significant correlations between the PANSS scores, evaluating clinically emerged depression and psychological traits studied, with the exception of Hypochondriasis, were found.

The sample was then divided into two groups, according to the absence or presence of depression, and two-way ANOVA used, with PANSS depression and 5HTTLPR genotype as independent factors. A significant contribution of clinically evaluated depression in all psychological traits was found. Patients with an absence of depressive appearance scored significantly lower on all self-rating scales, as compared to those exhibiting symptoms of depression. Genotype influence, as well as interaction effect, proved to be insignificant.

Therefore, the schizophrenia patients with the "ss" 5HTTLPR genotype scored significantly higher on the PANSS items measuring depression and depressive-related trait—guilt feelings—as compared to the patients with the "ll" genotype. The frequency of the "ss" genotype was reduced in the patients with the absence of depression or guilt feelings, or in those patients exhibiting questionable symptoms. In contrast, the "ss" genotype carriers prevailed among patients with mild, moderate, or severe ratings of the symptoms.

This finding, to some extent, supports evidence for a "ss" 5HTTLPR genotype association with anxiety-related traits, because anxiety and depression are considered as correlative psychopathological symptoms. We did not, however, find a relationship between 5HTTLPR polymorphism and PANSS item for anxiety in the present investigation. There are a few studies, which reported an association between depression level and 5HTTLPR polymorphism, for example, the "ss" genotype frequency was higher in the patients with

TABLE II. Mean (SD) Scores of the PANSS Items by 5HTTLPR Genotype

| PANSS items | 5HTTLPR genotype [mean (SD)] | | |
|---|---|---|---|
| | "ll" (n = 82) | "ls" (n = 119) | "ss" (n = 59) |
| Positive symptoms | 23.9 (7.7) | 24.0 (7.9) | 22.9 (8.0) |
| Delusions | 4.3 (1.4) | 4.2 (1.5) | 4.1 (1.5) |
| Conceptual disorganization | 3.9 (1.3) | 3.9 (1.4) | 3.8 (1.3) |
| Hallucinatory behavior | 3.0 (1.8) | 3.2 (1.7) | 2.8 (1.6) |
| Excitement | 3.0 (1.6) | 3.3 (1.4) | 3.1 (1.7) |
| Grandiosity | 2.6 (1.7) | 2.6 (1.5) | 2.5 (1.6) |
| Suspiciousness/persecution | 4.0 (1.5) | 3.8 (1.5) | 3.7 (1.6) |
| Hostility | 3.2 (1.5) | 3.0 (1.5) | 3.1 (1.4) |
| Negative symptoms | 23.3 (7.6) | 22.8 (8.0) | 22.2 (7.0) |
| Blunted affect | 3.6 (1.2) | 3.4 (1.3) | 3.6 (1.1) |
| Emotional withdrawal | 3.5 (1.3) | 3.3 (1.3) | 3.4 (1.2) |
| Poor rapport | 3.7 (1.4) | 3.4 (1.3) | 3.5 (1.3) |
| Passive/apathetic social withdrawal | 3.4 (1.3) | 3.3 (1.5) | 3.2 (1.2) |
| Difficulty in abstract thinking | 2.7 (1.3) | 2.7 (1.3) | 2.5 (0.9) |
| Lack of spontaneity | 3.2 (1.6) | 3.3 (1.4) | 3.1 (1.4) |
| Stereotyped thinking | 3.1 (1.4) | 3.1 (1.5) | 3.0 (1.3) |
| General psychopathological symptoms | 48.5 (12.3) | 48.6 (9.7) | 49.4 (12.3) |
| Somatic concern | 2.4 (1.5) | 2.2 (1.3) | 2.2 (1.3) |
| Anxiety | 2.8 (1.5) | 2.7 (1.5) | 3.0 (1.5) |
| Guilt feelings | 1.7 (1.2) | 1.9 (1.3) | 2.2 (1.3)[a] |
| Tension | 3.7 (1.5) | 3.6 (1.4) | 3.6 (1.4) |
| Mannerism and postering | 3.2 (1.2) | 2.9 (1.3) | 2.9 (1.3) |
| Depression | 2.5 (1.6) | 2.5 (1.7) | 3.1 (1.7)[b] |
| Motor retardation | 2.7 (1.3) | 2.7 (1.4) | 2.9 (1.4) |
| Uncooperativeness | 3.2 (1.5) | 2.9 (1.5) | 3.0 (1.6) |
| Unusual thought content | 3.7 (1.6) | 3.8 (1.5) | 3.8 (1.5) |
| Disorientation | 1.6 (0.9) | 2.0 (1.3) | 1.6 (0.9) |
| Poor attention | 3.6 (1.2) | 3.6 (1.1) | 3.6 (1.0) |
| Lack of judgment and insight | 4.5 (1.3) | 4.5 (1.3) | 4.4 (1.3) |
| Disturbance of volition | 3.4 (1.2) | 3.3 (1.2) | 3.2 (1.1) |
| Poor impulse control | 2.9 (1.6) | 2.6 (1.5) | 2.6 (1.6) |
| Preoccupation | 4.1 (1.2) | 4.0 (1.2) | 4.0 (1.2) |
| Active social avoidance | 3.8 (1.3) | 3.6 (1.2) | 3.6 (1.3) |

[a]Mann–Whitney test ("ll" vs. "ss"), $P = 0.016$.
[b]Mann–Whitney test ("ll" vs. "ss"), $P = 0.039$; ("ls" vs. "ss"), $P = 0.02$.

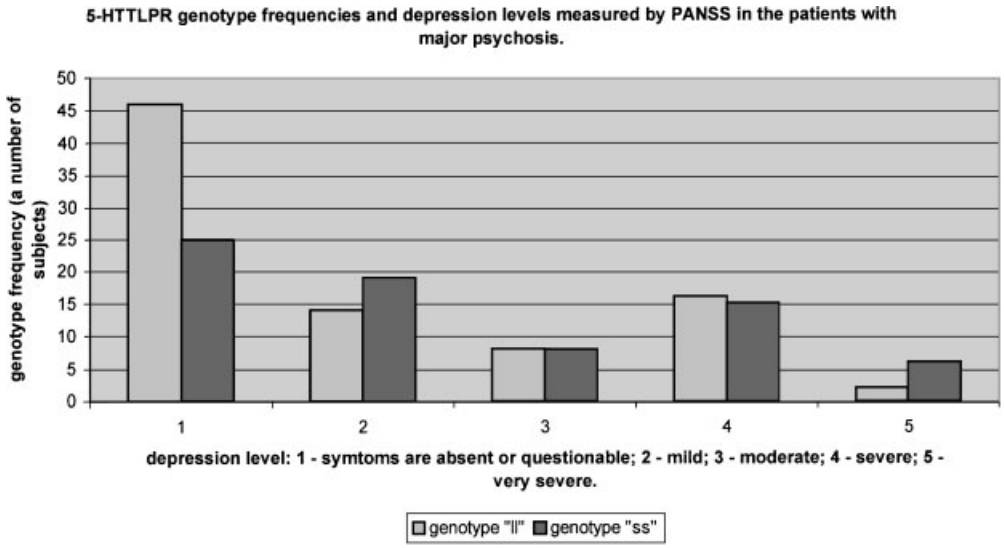


Fig. 1. 5HTTLPR genotype frequencies and depression levels measured by PANSS in the patients with major psychosis (schizophrenia and spectrum disorders). Y-axis, a number of subjects; X-axis, depression level: 1—symptoms are absent or questionable; 2—mild; 3—moderate; 4—severe; 5—very severe. Left column—"ll" genotype, right column—"ss" genotype.

TABLE III. Scores on Anxiety-Related Scales by 5HTTLPR Genotype

| | 5HTTLPR genotypes [mean (SD)] | | |
|---|---|---|---|
| Variable | ll (n = 46) | ls (n = 78) | ss (n = 28) |
| Neuroticism (EPI) | 13.4 (5.2) | 13.6 (5.1) | 13.1 (5.7) |
| Hypochondriasis (MMPI) | 58.5 (12.9) | 58.3 (11.6) | 54.2 (10.2) |
| Depression (MMPI) | 61.5 (16.2) | 57.9 (14.5) | 53.9 (9.9) |
| Psychasthenia (MMPI) | 66.1 (14.5) | 64.8 (14.3) | 56.4 (16.0) |
| Anxiety (STAI) | 48.1 (8.9) | 49.9 (10.4) | 48.0 (9.1) |

Parkinson's disease, who scored higher on the Hamilton depression scale [Menza et al., 1999; Mossner et al., 2001]. When studying behavioral responses to tryptophan depletion in healthy women, 5HTTLPR "ss" genotype was associated with an increased risk of depressive symptom development [Neumeister et al., 2002]. In other studies, an association was confirmed between genetic variants and bipolar [Bellivier et al., 1998] or unipolar [Furlong et al., 1998; Steffens et al., 2002] disorders. It should also be mentioned that a number of similar-designed investigations revealed the opposite results [Gutierrez et al., 1998; Frisch et al., 1999; Moreno et al., 2002; Serretti et al., 2002].

Association studies of clinical presentations in schizophrenia dependent on 5HTTLPR genotype so far have not yielded any consistent results. Serretti et al. [1999, 2002] failed to find any significant relationship between 5HTTLPR polymorphism and symptomologic factors of major psychosis, namely, delusion, disorganization, mania, and depression, extracted from OPCRIT. Using a Brief Psychiatric Rating Scale (BPRS), Malhotra et al. [1998] reported a prevalence of the "ll" genotype in the patients with higher density of hallucinations, but this association was not confirmed in the present study.

To our knowledge, a relationship between 5HTTLPR polymorphism and depressive symptoms measured with the use of the PANSS in schizophrenia patients has never been investigated, thus we are unable to compare our findings with the literature data. One may assume the association is accounted for by the validity of the PANSS assessment or peculiarities of the sample used. To evaluate the validity of the PANSS assessment used in the present study, we compared our results with those of former investigations administering PANSS for measuring symptoms in schizophrenia samples. The data shown in the Table IV indicate a high degree of concordance between scores on PANSS items obtained in the present study and in those reported for 253 schizophrenic patients by Mass et al. [2000] and by Dollfus et al. [1996] for 48 patients. These are featured by higher scores on the most positive, negative, and general psychopathological items (correlation coefficients were 0.7, $P < 0.0001$ and 0.6, $P < 0.0004$, respectively). The accordance with former studies argues for objective evaluation of psychopathological symptoms undertaken in the present investigation.

In regards to an evaluation of anxiety and depression rated by the patients themselves, no genotype differences emerged on the psychological scales used in the study. At the same time, depressive mood exerted an influence on a patient's subjective ratings of depression and anxiety, because the patients with depressive symptoms scored significantly higher on all scales. Therefore, in the sample studied, the "ss" genotype is more likely to be associated with clinically rated depression and related traits, than with corresponding characteristics rated subjectively by schizophrenia patients.

Depressive symptoms are recognized to be common in schizophrenia. Factor analyses conducted with PANSS data consistently extracted the depression component in this disease [Kay and Sevy, 1990; Lindenmayer et al., 1994; Lancon et al., 2000; Lykouras et al., 2000; Wolthaus et al., 2000; El Yazaji et al., 2002]. Not all schizophrenic patients exhibit depressive symptoms

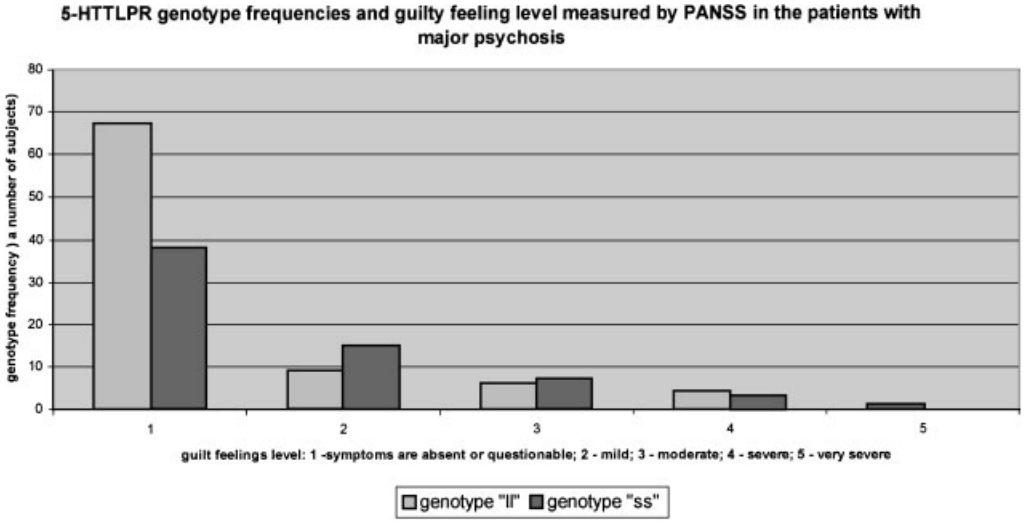


Fig. 2. 5HTTLPR genotype frequencies and guilt feeling levels measured by PANSS in the patients with major psychosis (schizophrenia and spectrum disorders). Y-axis, a number of subjects; X-axis, guilt feeling level: 1—symptoms are absent or questionable; 2—mild; 3—moderate; 4—severe; 5—very severe. Left column—"ll" genotype, right column—"ss" genotype.

TABLE IV. Synopsis of the Studies Measuring Distribution Characteristics of the PANSS Items

| | Mean (SD) | | |
|---|---|---|---|
| PANSS items | Present study (n = 260) | (n = 253) [Mass et al., 2000 ] | (n = 48) [Dollfus et al., 1996] |
| Delusions | 4.2 (1.4) | 2.9 (1.5) | 4.1 (1.5) |
| Conceptual disorganization | 3.9 (1.4) | 3.1 (1.4) | 2.8 (1.8) |
| Hallucinatory behavior | 3.1 (1.7) | 2.3 (1.4) | 3.6 (1.8) |
| Excitement | 3.1 (1.6) | 2.5 (1.6) | 1.3 (0.7) |
| Grandiosity | 2.7 (1.6) | 2.0 (1.4) | 1.9 (1.4) |
| Suspiciousness/persecution | 3.7 (1.6) | 2.8 (1.5) | 3.6 (1.2) |
| Hostility | 3.1 (1.5) | 1.9 (1.2) | 1.6 (1.2) |
| Blunted affect | 3.6 (1.2) | 3.1 (1.4) | 3.9 (1.3) |
| Emotional withdrawal | 3.5 (1.2) | 3.3 (1.5) | 4.1 (1.1) |
| Poor rapport | 3.5 (1.3) | 3.1 (1.5) | 2.6 (1.1) |
| Passive/apathetic social withdrawal | 3.5 (1.3) | 3.1 (1.5) | 4.6 (1.4) |
| Difficulty in abstract thinking | 2.9 (1.3) | 3.1 (1.6) | 3.5 (1.7) |
| Lack of spontaneity | 3.2 (1.5) | 2.8 (1.4) | 2.7 (1.4) |
| Stereotyped thinking | 3.2 (1.4) | 3.3 (1.7) | 1.7 (1.1) |
| Somatic concern | 2.3 (1.5) | 2.4 (1.6) | 2.1 (1.6) |
| Anxiety | 2.7 (1.5) | 2.8 (1.4) | 2.7 (1.1) |
| Guilt feelings | 2.0 (1.3) | 2.2 (1.4) | 1.4 (0.9) |
| Tension | 3.4 (1.6) | 2.6 (1.4) | 2.2 (1.2) |
| Mannerism and postering | 2.9 (1.3) | 2.5 (1.6) | 2.3 (1.5) |
| Depression | 2.6 (1.6) | 2.5 (1.3) | 2.7 (1.5) |
| Motor retardation | 2.7 (1.4) | 2.4 (1.3) | 2.7 (1.4) |
| Uncooperativeness | 2.9 (1.5) | 2.0 (1.5) | 1.5 (1.2) |
| Unusual thought content | 3.7 (1.5) | 3.2 (1.7) | 3.3 (1.7) |
| Disorientation | 2.1 (1.3) | 1.2 (0.5) | 1.3 (0.7) |
| Poor attention | 3.3 (1.3) | 2.8 (1.2) | 2.6 (1.0) |
| Lack of judgment and insight | 4.4 (1.4) | 3.1 (1.4) | 3.7 (1.8) |
| Disturbance of volition | 3.5 (1.3) | 2.8 (1.4) | 2.3 (1.2) |
| Poor impulse control | 2.8 (1.5) | 2.2 (1.5) | 1.8 (1.4) |
| Preoccupation | 3.8 (1.4) | 3.3 (1.6) | 2.6 (1.3) |
| Active social avoidance | 3.6 (1.3) | 2.8 (1.4) | 2.7 (1.4) |

in the disease course; this might be accounted for by predisposing factors. In that sense, our finding may contribute to understanding of molecular genetic features, underlying an appearance of the numerous psychopathological symptoms emerged in schizophrenia.

Limitations of the study concern mainly a type I error occurrence. Because many comparisons have been executed, some significant associations could occur by chance. Two possibilities appear to reduce a chance of an inflation of type I error: to apply a correction for multiple comparison, for example, Bonferroni, and to obtain the results in the predicted direction. In our study, we cannot withstand Bonferroni correction but the fact that the association between "ss" 5HTTLPR genotype and depressive-related traits has been reported in other studies increases a probability for obtaining true results.

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