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Gender differences in cognitive function of patients with chronic schizophrenia

Abstract

Schizophrenic patients have cognitive impairments, but gender differences in these cognitive deficits have had limited study. This study assessed cognitive functioning in 471 subjects including 122 male and 78 female schizophrenic patients and 141 male and 130 female healthy controls. We found that immediate memory, language, delayed memory and total RBANS scores were significantly decreased in schizophrenia compared with healthy controls for both genders. Male patients had significant lower immediate memory, delayed memory and total RBANS scores than female patients, and healthy controls showed a similar gender difference. The RBANS showed modest correlations with PANSS scores, duration of illness and antipsychotic dose (chlorpromazine equivalents). Almost all RBANS scores in the schizophrenics and healthy controls showed significant positive correlations with education. Thus, patients of both sexes with schizophrenia experienced more deteriorated performance than healthy controls on cognitive domains of immediate memory, language and delayed memory. Furthermore, male schizophrenic patients had more serious cognitive deficits than female patients in immediate and delayed memory, but not in language, visuospatial and attention indices.

Keywords

cognitive, differences, schizophrenia, gender, chronic, patients, function, CMMB

Disciplines

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Gender differences in cognitive function of patients with chronic schizophrenia

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Running title: Sex difference in cognition in schizophrenia

Abbreviations: RBANS, the repeatable battery for the assessment of neuropsychological status; PANSS, positive and negative syndrome scale; ANOVA, analysis of variance.

Abstract

Schizophrenic patients have cognitive impairments, but gender differences in these cognitive deficits have had limited study. This study assessed cognitive functioning in 471 subjects including 172 male and 78 female schizophrenic patients and 141 male and 130 female healthy controls. We found that immediate memory, language, delayed memory and total RBANS scores were significantly decreased in schizophrenia compared with healthy controls for both genders. Male patients had significant lower immediate memory, delayed memory and total RBANS scores than female patients, and healthy controls showed a similar gender difference. The RBANS showed modest correlations with PANSS scores, duration of illness and antipsychotic dose (chlorpromazine equivalents). Almost all RBANS scores in the schizophrenics and healthy controls showed significant positive correlations with education. Thus, patients of both sexes with schizophrenia experienced more deteriorated performance than healthy controls on cognitive domains of immediate memory, language and delayed memory. Furthermore, male schizophrenic patients had more serious cognitive deficits than female patients in immediate and delayed memory, but not in language, visuospatial and attention indices.

Keywords: schizophrenia; RBANS; PANSS; cognitive deficits; correlation; gender difference

1. Introduction

Neuropsychological studies of patients with schizophrenia have demonstrated cognitive deficits as core features of the illness. Cognitive deficits rather than clinical diagnostic categories may better represent the underlying pathogenesis of schizophrenia (Gur et al., 2007). Several studies have focused on gender differences in the cognitive deficits of schizophrenia and showed gender differences in cognitive domains in both schizophrenia and healthy populations (Goldstein et al., 2002; Halari et al., 2006; Phillips and Silverman, 1997; Ragland et al., 1999; Wisner et al., 2011). Furthermore, gender differences in schizophrenia' cognitive deficits are evident in the prodromal symptoms, acute psychotic episodes, illness course, and clinical response to antipsychotic treatment (Grigoriadis and Seeman, 2002; Hughes et al., 2003; Rubin et al., 2008).

The explanations and hypotheses about the gender differences in cognitive tasks in both schizophrenia and healthy populations include abnormalities in brain structure and volume, abnormal function of neurotransmitter systems, gonadal hormone differences and genetic effects (Antonova et al., 2004; Friston et al., 1991; Stefansson et al., 2009; Wegesin and Stern, 2007). However, the evidence is still not clear whether gender differences occur in the cognitive deficits of schizophrenia patients. For example, some studies have reported that male patients appear to have more cognitive impairment than females (Goldstein et al., 1998; Seidman et al., 1997), while others have found that female schizophrenics exhibit greater cognitive deficits than males (Lewine et al., 1996). Moreover, some studies failed to find any sex differences in cognitive deficits of schizophrenia (Goldberg et al., 1995; Hoff et al., 1998). These conflicting results suggested that further study of the sex differences in the cognitive deficits of schizophrenia might benefit from examination in another non-Western culture such as China.

The inconsistency of gender differences in cognitive deficits relate to variations in illness severity, inadequate sample size, sampling bias, and lack of normal healthy controls of females for statistically robust comparisons (Goldstein et al., 1998; Halari et al., 2006; Walker and Lewine, 1993). This study was specifically designed to test for the gender differences in cognitive functioning in a large sample of schizophrenia and healthy controls. To our knowledge, this is the first study examining gender differences in cognition in Chinese schizophrenic population. Also, the samples were taken so that the gender, age and education of the schizophrenic subjects matched the healthy controls.

The purpose of this study was to determine: (1) whether Chinese patients with chronic schizophrenia had cognitive deficits compared to healthy controls; (2) whether cognitive functioning in schizophrenia showed gender differences; (3) whether cognitive

deficits correlated with symptoms of schizophrenia, duration of illness, or antipsychotic treatments (chlorpromazine equivalents).

2. Methods

2.1. Subjects

We compared 200 (122 males, 78 females) physically healthy Chinese patients who met DSM-IV for schizophrenia to 271 (141 males, 130 females) healthy controls. All schizophrenic patients were inpatients of Beijing Hui-Long-Guan Hospital, a Beijing City owned psychiatric hospital and were chronic with at least 5 years of illness and were between 25 and 70 years old. They had been receiving stable doses of oral neuroleptic medications for at least 12 months prior to entry into the study. Their antipsychotic treatment consisted mainly of monotherapy with clozapine (n=101), risperidone (n=43), and other typical antipsychotics (n=56) including haloperidol (n=20), perphenazine (n=15), sulpiride (n=14) and chlorpromazine (n=7). In addition, 58 patients received antiparkinsonian drugs.

For comparison, healthy controls were recruited from the community, and group matched for age, education and gender. All subjects were Han Chinese recruited at the same period from the Beijing area. The patients and healthy subjects had a similar socioeconomic status and dietary patterns. We obtained a complete medical history and physical examination from all subjects, and any subjects with serious medical abnormalities were excluded. Neither the patients with schizophrenia nor the control subjects suffered from drug abuse or dependence. A psychiatrist ruled out any mental disorders among healthy controls by direct psychiatric interview; however, he did not use a structured interview instrument. All subjects provided signed, informed consent to participate in this study, which was approved by the Institutional Review Board, Beijing Hui-Long-Guan Hospital.

2.2. Clinical assessment

Two psychiatrists who had over five year clinical practice and who were blind to the clinical status and treatment conditions assessed the patient's psychopathology using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). To ensure consistency and reliability of rating, the two psychiatrists simultaneously attended a training session for standardizing their use of the PANSS prior to the start of the study. Thereafter, they maintained an intraclass correlation coefficient of greater than 0.8 on the PANSS at repeated assessments during the course of this study.

2.3. Cognitive measures

We individually administered The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) to measure cognitive function (Duff et al., 2008).

The RBANS is comprised of 12 subtests that are used to calculate 5 age-adjusted index scores and a total score (Abe et al., 2009). Test indices are immediate memory (comprised of list learning and story memory tasks); visuospatial/constructional (comprised of figure copy and line orientation tasks); language (comprised of picture naming and semantic fluency tasks); attention (comprised of digit span and coding tasks); and delayed memory (comprised of list recall, story recall, figure recall, and list recognition tasks). Our group previously translated RBANS into Chinese and the clinical validity and its test-retest reliability established among controls and schizophrenic patients (Zhang et al 2009). To ensure consistency and reliability of rating, the two clinical psychologists simultaneously attended a training session for standardizing their use of the RBANS prior to the start of the study. Thereafter, they maintained an intraclass correlation coefficient of 0.92 on the RBANS at repeated assessments.

Each subject came in the testing room on a separate day to have a research member introduce our research center and be given a training session to allow the individual to become acclimated to the testing environment and computerized tasks. In order to reduce or eliminate the withdrawal effect of smoking, participants who smoked were allowed to smoke cigarettes prior to testing and during breaks. The subjects took breaks for smoking at the end of each domain test of the RBANS, in order to prevent participants from being in a state of nicotine withdrawal (Zhang et al 2012). The RBANS test was performed within the same timeframe for patients and controls.

2.4. Statistical analysis

Group comparisons on demographic and clinical variables used chi squared or Fisher exact tests for categorical variables and Student *t*-tests or analysis of variance (ANOVA) for continuous variables. For the RBANS comparisons, we also included age, education and smoking as covariates in multivariate analyses of covariance for significant gender differences across the dependent measures from the RBANS total score and its five cognitive domains, with independent predictors being gender (male vs. female), diagnosis (patients vs. healthy controls) and the gender-by diagnosis interaction. Effect sizes were also calculated for the two-way comparisons and represented the mean difference, in standard deviation units, between groups of interest. Correlations between variables used Pearson product moment correlations with Bonferroni corrections applied to adjust for multiple testing. Multiple regression models were used to quantify the amount of variance in cognitive functioning explained by psychopathological variables, after controlling for several potential confounders, e.g., gender, age, years of education, and clinical variables. SPSS version 15.0 was used to do all statistical analysis. Data were presented as mean \pm SD. All *p* values were 2 tailed at the significance level of ≤ 0.05 .

3. Results

3.1. Sample characteristics

Table 1 shows no significant differences between schizophrenics and healthy controls in age, sex and education. However, there was a significant difference in smoking rates between the patients (50.5%) and normal controls (37.3%) ($\chi^2 = 8.22$, $df=1$, $p<0.005$). Furthermore, smoking was more common in male than female schizophrenic patients and in male than female controls (both P values $<.001$). Furthermore, significantly more male chronic schizophrenic patients than older male controls smoked (79.5% vs 61.7%); however, fewer female chronic schizophrenic patients than older female controls currently smoked (5.1% vs 10.8%) (both P values $<.01$). Thus, we controlling for smoking in the following analyses.

In addition, we found no significant differences between male and female patients in any of PANSS scores, duration of illness, or antipsychotics dose (equivalent to chlorpromazine) (Table 2). Furthermore, there were no gender differences in the ratio of first generation antipsychotics to second generation antipsychotics ($p=0.55$) or in the use of anti-Parkinson's medication between patients on these two types of medication ($p=0.66$) (Table 2). We also found no difference in medication compliance between the two types of antipsychotics. In addition, there were no gender differences in antipsychotic monotherapy versus polytherapy ($p<0.05$). However, there was a significant gender difference in the times and duration of hospitalization (Table 2), which we controlled for in the following analyses.

3.2. Cognitive performance in schizophrenia and healthy controls

Table 3 showed cognitive test scores in schizophrenic compared to control subjects on the RBANS total scores and all five indexes. After controlling for age, education and smoking, multivariate analysis of covariance revealed statistically significant differences between schizophrenic patients and controls for all cognitive domains ($F_{1,464}=28.6$, $P<.0001$). Furthermore, diagnosis (patient vs control) differences were significant for the RBANS total scores and all index scores (all P values $<.001$), except for the RBANS visuospatial/constructional index ($p=.097$) (Table 3). Pair-wise post hoc comparisons showed significant differences in the RBANS total score and all index scores (all $p<0.001$) between the male patients and male controls (all $p<0.05$ - $p<0.001$) with effect sizes ranging from 0.27 to 1.07 except for the visuospatial/constructional index, and between the female patients and female controls (all $p<0.05$ - $p<0.001$), with effect sizes ranging from 0.25 to 0.93. After controlling for age, education, and smoking, multivariate analysis of covariance also revealed overall main effects for gender in RBANS immediate memory ($F_{1,464}=28.82$, $P<.001$; effect size=0.37), delayed memory ($F_{1,464}=24.66$, $P<.001$; effect size=0.54), and total score ($F_{1,464}=15.31$,

$P < .001$; effect size = 0.36) domains. Women performed better than men on these domains.

Further multivariate analysis of covariance showed a gender \times diagnosis interaction effect on for all cognitive domains ($F_{1,464} = 2.25$, $p < 0.05$). In order to decompose the two-way interaction, we examined patients and controls grouped by gender separately. Male patients performed worse than female patients on immediate memory, delayed memory, and RBANS total score (all $p < 0.05$) (Table 3). After controlling for hospitalization and smoking separately, or together with duration of illness, clinical symptoms as assessed using the PANSS, antipsychotic medication (type, dosage and duration of treatment) and anti-Parkinson's medication, these differences still remained significant (all $p < 0.05$). However, only the immediate memory result passed the Bonferroni test. In the control group, the males and females showed significant differences only in immediate memory ($p < 0.05$) (Table 3). However, this result did not pass the Bonferroni test.

3.3. Relationship between cognitive performance and clinical phenotypes in schizophrenia

Using multivariate regression analysis the following variables were independently associated with the RBANS total score: education ($\beta = 0.24$, $t = 4.02$, $p < 0.001$), PANSS negative symptom score ($\beta = -0.28$, $t = -3.71$, $p < 0.001$), and age ($\beta = -0.15$, $t = -2.39$, $p < 0.05$) and gender ($\beta = 0.12$, $t = 2.02$, $p < 0.05$). These factors together predicted 23% of the variance of the RBANS total score.

Further, data for the women and men with schizophrenia were analysed separately to assess gender differences in clinical characteristics associated with cognitive impairment. We hypothesized that the clinical predictors for cognitive function were different in the male and female CS patients. In male patients, Pearson correlation analysis showed significant negative associations between all examined cognitive variables and the negative symptom scale or PANSS total score (all $p < 0.01$) (Table 4). Moreover, immediate memory, language and delayed memory were significantly and negatively associated with the general psychopathology scale (all $p < 0.01$). In addition, the duration of illness had a significantly negative association with immediate memory, attention, delayed memory, and RBANS total score (all $p < 0.01$). The RBANS total score had a significant negative relationship with antipsychotic dose (chlorpromazine equivalents) (Table 4). Finally, smoking was significantly and negatively associated with RBANS total score ($r = -0.24$, $p < 0.05$) and the Visuospatial/Constructional index ($r = -0.35$, $p < 0.01$). Further multivariate regression analyses showed that the following variables were independently associated with the RBANS total score: years of education ($\beta = 0.29$, $t = 3.62$, $p < 0.001$), PANSS negative symptom score ($\beta = -0.25$, $t = -2.41$, $p < 0.05$), and smoking ($\beta = -0.22$, $t = -2.29$, $p < 0.05$).

In female patients, Pearson correlation analysis showed significant positive correlations between the positive symptom scale and immediate memory, visuospatial, and total score (all $p < 0.05$) (Table 4). Except for the attention index, the other cognitive domains were negatively associated with the negative symptom scale (all $p < 0.05$) (Table 4). Immediate memory was positively associated with the general psychopathology scale ($p < 0.05$). Only the language index was negatively associated with the duration of illness ($p < 0.05$). Finally, we found a positive association between RBANS total score and antipsychotic dose (all $p < 0.05$) (Table 4). Further multivariate regression analyses showed that the following variables were independently associated with the RBANS total score: the PANSS negative symptom score (beta=-0.26, $t=-2.30$, $p=0.024$), the PANSS positive symptom score (beta=0.32, $t=2.20$, $p=0.031$) and age (beta=-0.21, $t=-2.01$, $p=0.049$).

4. Discussion

This study had five major findings. (1) Significantly lower cognitive scores on the RBANS total score and nearly all of its subscales except for the visuospatial/ constructional index were found in schizophrenia than normal controls. (2) More specifically, male schizophrenics had significantly lower immediate memory, delayed memory and total RBANS scores than female schizophrenics. (3) The RBANS showed modest correlations with the PANSS scores, duration of illness and antipsychotic dose. (4) Lower education, higher negative symptoms, older age and male gender were associated with cognitive impairments in schizophrenia. (5) We found gender differences in the associations of specific cognitive impairments with various clinical characteristics and symptom assessments.

In this study, we found significant cognitive impairments for patients with schizophrenia. To our knowledge, this is the first report of cognitive deficits in immediate memory, language and delayed memory for Chinese patients with schizophrenia. These results are consistent with other phenomenological studies (Goldstein et al., 1998, Sota and Heinrichs, 2003, Halari et al., 2006). For example, abnormalities in the frontal lobe and hippocampal volume are associated with cognitive deficits in executive functioning, working memory, verbal fluency and immediate memory among schizophrenics (DeLisi et al., 1991, Antonova et al., 2004), suggesting that the cognitive deficits of schizophrenia may be associated with these brain abnormalities. Also, the cognitive deficits of schizophrenia were found to be associated with abnormal neurotransmitter systems in the brain and with genetic mutations (Friston et al., 1991; Stefansson et al., 2009). Abnormal expression of neurotransmitter receptors occurs among schizophrenia

in those brain regions that are related to cognitive deficits in verbal memory and attention (Crook et al., 2000; Newell et al., 2007; Sumiyoshi et al., 1996). For example, a reduction in M1 receptor protein in the hippocampus, superior temporal gyrus, and anterior cingulate cortex in schizophrenic subjects has been reported (Crook et al., 2000; Deng and Huang, 2005; Zavitsanou et al., 2004). A genetic study indicated that the homozygous risk AA genotype of ZNF804 performed significantly better on the cognitive tasks of verbal memory and spatial working memory than the homozygous CC genotype group (Walters et al., 2010). These studies suggest that multiple and complex mechanisms contribute to cognitive deficits in schizophrenia.

Male and female patients with schizophrenia did not differ on any PANSS scores, but immediate memory and delayed memory were worse in male than female schizophrenia, which we also found in our healthy controls. These discordant deficits in the clinical and cognitive domains of schizophrenics also were consistent with a previous study (Hughes et al., 2003). Similarly, these sex differences in cognitive domains are consistent with previous studies (Antonova et al., 2004; Halari et al., 2006; Sota and Heinrichs, 2003), and have been suggested as due to differences in brain structure for the two sexes and to differences in neural lateralization (Antonova et al., 2004). One study indicated greater right hemispheric specificity for males' and bilateral representations for females' brains (Gur et al., 2000) and greater leftward asymmetry of frontal lobe fractional anisotropy in females than males (Szeszko et al., 2003).

This female advantage in immediate and delayed memory may also reflect gonadal hormone effects on cognitive functioning. Estrogen and testosterone may influence cognitive functioning through dopamine and serotonin effects in specific brain regions (Fink et al., 1999; Hafner et al., 1991). For example, estrogen can decrease dopamine concentrations and modulate sensitivities and numbers of dopamine receptors in the striatum and hippocampus (Di Paolo, 1994; Karakaya et al., 2007; McEwen and Woolley, 1994). Therefore, females may have better immediate and delayed memories than males. Female patients also may show better improvements in cognitive deficits with antipsychotic treatments potentially through normalizing estrogen's activity in the brain (Grigoriadis and Seeman, 2002; Rubin et al., 2008). However, not all studies have found sex differences in memory tasks and several have found sex differences in visuospatial and attention deficits in patients with schizophrenia (Goldstein et al., 1998; Halari et al., 2006).

Almost all cognitive indices were negatively correlated with the negative PANSS symptom scale in both sexes and with the general psychopathology scale and total PANSS scale in males. Fewer negative symptoms are perhaps not surprisingly associated with less impairment on cognitive tasks. The other significant negative

associations between duration of illness and immediate memory, attention and delayed memory in male patients are perhaps intuitively obvious in suggesting that the more chronic patients perform worse on all these cognitive tasks. Whether this association is a pernicious effect of long term institutionalization, long-term medication side effects, or the course of this illness, which was originally called “dementia precox,” cannot be determined from our data.

The more interesting positive associations are between immediate or visuospatial memory and positive symptoms in females. Does being paranoid improve the patient's capacity for these types of cognitive functions in female patients with schizophrenia? Perhaps it does, as the patient becomes hyper-vigilant and focused on specific tasks such as these cognitive tests rather than simply being unable to concentrate on anything. However, this is only speculation; we do not have evidence to support this hypothesis, which deserves further investigation. Overall, the relationships between the cognitive tasks and PANSS scales and duration of the illness in schizophrenia are very complex. Furthermore, effects of antipsychotic drugs make these relationships more complex, since antipsychotic drug may can improve clinical symptoms and cognitive performance of schizophrenia, while controversially also having side effects on performance during cognitive tasks (Daban et al., 2005; Stip, 2006; Terry and Mahadik, 2007). For example, a study has showed that cognitive tasks may be potentially impaired after patients with schizophrenia were treated long-term using antipsychotic drugs (Terry and Mahadik, 2007). However, other studies have not indicated that antipsychotics impair cognitive function in schizophrenia (Daban et al., 2005). More work is clearly needed on this topic with better controlled longitudinal studies. We are starting such studies in China.

Some studies indicate that cigarette smoking or nicotine may ameliorate some of the cognitive deficits in schizophrenic patients (Smith et al, 2002; George et al., 2002; Hahn et al, 2012), suggesting that cigarette smoking or nicotine serves as a form of self-medication. However, in our present study, we found that smoking was negatively associated with RBANS total score and the Visuospatial/Constructional index in male patients. Furthermore, the female patients, who overall had much lower rates of smoking than the males, had better cognitive functioning than the male patients. Thus, smoking may be taken up and sustained by those with more cognitive impairment. Whether smoking then relatively improves their cognition would require a longitudinal study and cannot be addressed in our cross-sectional design.

This study has some limitations. First, our subjects were all inpatients and may represent more serious clinical profiles including more serious cognitive deficits than outpatient schizophrenics. Second, our patients are all chronic and might show gender differences due to long term gender differences in antipsychotic drug effects rather than

pathophysiological differences between the genders. Third, we had no data for medication free periods with these patients, which may affect the results of the cognitive performances. Thus, gender differences might be overestimated in this study. Fourth, psychiatric disorders were ruled out among healthy controls by an unstructured psychiatric evaluation, and no specific instrument was used to rule out diagnoses.

In conclusion, patients with chronic schizophrenia performed worse than healthy controls in immediate and delayed memory and language. Furthermore, among patients males have more serious cognitive impairments than females in immediate memory and delayed memory, but not in language, visuospatial and attention.

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Table 1
Demographics of schizophrenia and healthy controls grouped by gender*

Groups	Gender	Age (years)	Education (years)
Schizophrenia	Male (n=122)	51.6±8.7	9.4±2.4
	Female (n=78)	53.5±7.7	9.9±2.5
Healthy control	Male (n=141)	48.6±10.9	9.4±3.2
	Female (n=130)	50.1±10.0	9.3±3.5

*Patient group did not differ from control group on any characteristic by χ^2 test and ANOVA.

Table 2**Characteristics of male and female patients with schizophrenia**

	Male	Female	t or X ²	p-value
Duration of illness (months)	144.8±101.2	128.1±114.4	1.08	0.28
Antipsychotic types (typicals/atypicals)	36/86	20/58	0.35	0.55
Antipsychotic dose (CPZ equivalents)	523.9±672.7	548.6±635.3	-0.26	0.80
Duration of current antipsychotic treatment	53.8±51.4	53.5±72.6	0.036	0.97
Antiparkinsonian drug (Yes/No)	34/88	24/54	0.19	0.66
Hospitalization times	4.3±3.0	3.4±2.9	2.39	<0.01
Duration of hospitalization (years)	10.8±9.8	8.7±8.5	2.13	<0.05
Score on positive symptom scale	12.5±5.0	13.4±6.7	-1.09	0.31
Score on negative symptom scale	22.1±7.0	20.6±7.3	1.41	0.16
Score on general psychopathology scale	26.4±5.2	27.4±6.2	-1.17	0.24
Total PANSS score	60.9±13.1	61.3±14.7	-0.20	0.84
Fasting glucose	5.3±0.8	5.5±1.0	-1.91	0.06

Note: Mean ± SD. CPZ=Chlorpromazine; PANSS= the Positive and Negative Syndrome Scale

Table 3**The levels of cognitive function in schizophrenia and healthy controls**

RBANS	Schizophrenia		Healthy control		Diagnose F (p value)	Gender F (p value)	Diagnose*Gender F (p value)
	Male (n=122)	Female (n=78)	Male (n=141)	Female (n=130)			
Immediate memory	59.9±18.1 ^{***}	66.7±19.6 ⁺⁺	73.0±16.6*	80.3±18.2	69.48(<.001)	21.85(<.001)	0.22(0.64)
Visuospatial/constructional	81.4±18.5	85.6±19.1	80.2±14.7	80.5±15.8	3.81(0.059)	2.37(0.12)	1.42(0.23)
Language	86.8±14.3 ⁺⁺	86.3±15.6 ⁺⁺	94.6±10.9	94.9±13.0	43.50(<.001)	0.13(0.72)	0.61(0.44)
Attention	81.8±15.1	82.1±15.9	85.5±17.2	87.2±21.7	9.62(0.002)	0.17(0.68)	0.82(0.37)
Delayed memory	66.6±20.3 ^{*****}	77.5±20.7 ⁺⁺	85.7±15.0	90.0±14.9	98.65 (<.001)	21.19(<.001)	3.94(0.048)
Total RBANS scores	68.6±16.0 ^{***}	74.5±16.8 ⁺	79.1±12.8	82.3±16.0	50.16(<.001)	11.50(0.001)	0.39(0.53)

* indicates the comparison between males and females in patients or in healthy controls: * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

+ indicates the comparison between patient and healthy controls in males or females: + $p<0.01$, ++ $p<0.001$.

Table 4

Correlations between the repeatable battery for the assessment of neuropsychological status (RBANS) and the positive and negative syndrome scale (PANSS), duration of illness or antipsychotic dose in patients with schizophrenia

	Correlation With RBANS Score (r)					
	Immediate memory Index	Visuospatial/ constructional Index	Language Index	Attention Index	Delayed memory Index	Total RBANS scores
Male (n=122)						
Score on positive symptom scale	-0.01	0.01	-0.03	-0.09	-0.01	-0.03
Score on negative symptom scale	-0.34***	-0.31***	-0.45***	-0.29***	-0.36***	-0.40***
Score on general psychopathology scale	-0.23**	-0.11	-0.28**	-0.16	-0.26**	-0.24**
Total PANSS score	-0.28**	-0.20*	-0.36***	-0.25**	-0.29***	-0.32***
Duration of illness	-0.33***	-0.2	-0.13	-0.25**	-0.31***	-0.29***
Antipsychotic dose (CPZ equivalents)	0.03	-0.03	0.02	0.08	0.16	-0.22*
Female (n=78)						
Score on positive symptom scale	0.29*	0.30**	0.20	0.04	0.19	0.29*
Score on negative symptom scale	-0.22*	-0.26*	-0.45***	-0.22	-0.31**	-0.35**
Score on general psychopathology scale	0.23*	0.13	-0.09	-0.07	0.09	0.11
Total PANSS score	0.12	0.06	-0.17	-0.12	-0.03	0.00
Duration of illness	-0.12	-0.15	-0.25*	-0.20	-0.10	-0.18
Antipsychotic dose (CPZ equivalents)	0.16	0.20	0.15	0.17	0.19	0.23*

Note: chlorpromazine=CPZ. Pearson correlation analysis showed *p<0.05, **p<0.01, ***p<0.001.