Reprinted from the German Journal of Psychiatry · http://www.gjpsy.uni-goettingen.de · ISSN 1433-1055

Working Memory in Schizophrenia

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Abstract

Background: Working memory has been reported to be impaired in schizophrenia, but there are inconsistencies in the literature. Therefore, we undertook the current study with the objective of assessing both auditory and visuospatial working memory tasks in a sample of schizophrenia patients in comparison to normal controls, and its correlation with psychopathology.

Method: The sample comprised of 78 drug naive or drug free patients of either sex, aged between 18–45 years, fulfilling diagnosis of schizophrenia according to ICD-10 Diagnostic Criteria for Research, and 35 age, sex and education matched normal controls. SAPS and SANS were used to assess positive and negative symptoms in patients, respectively. To assess working memory, Letter-Number Sequencing and Spatial Span subtests of Wechsler Memory Scale, Third edition (WMS-III) were used.

Results: There were significantly lower scores in schizophrenia patients compared to normal controls in spatial span forward ($p<.001$, Cohen's $d = 2.51$), backward ($p<.001$, Cohen's $d = 2.62$) and total scores ($p<.001$, Cohen's $d = 2.78$) as well as letter-number sequencing scores ($p<.001$, Cohen's $d = 1.87$). In the patient group, there was significant negative correlation between SANS total score with spatial span forward ($\tau = -.227$, $p<.01$) and total scores ($\tau = -.164$, $p<.05$).

Conclusion: Our study suggests impairment of both visuospatial as well as auditory memory in patients of schizophrenia as compared to controls. Furthermore, visuospatial working memory correlated inversely with negative symptoms (German J Psychiatry 2010; 13 (3) 116–120).

Keywords: schizophrenia, working memory, negative symptoms

Received: 17.6.2010
Revised version: 8.7.2010
Published: 15.8.2010

Introduction

Attention and memory are the most frequently researched areas of cognitive impairment in patients with schizophrenia. Working memory, in particular, has emerged as an important domain of dysfunction (Lee & Park, 2005). Though neuropsychological studies have demonstrated deficits in several areas, working memory seems to be most severely affected (Saykin et al., 1991, 1994). Deficits in working memory are associated with the severity of negative symptoms as well as impairments in social and occupational functioning (Bowen et al., 1994; Corrigan et al., 1994). Broadly, two types of working memory paradigms have been investigated in schizophrenia (Perry et al., 2001). One involves transient, short-term memory that does not require manipulation of the stored information, whereas the other involves both maintenance and manipulation, a part of executive functioning. Schizophrenia patients often show more severe impairment on the second type (Barch, 2005). Working memory has two components, verbal and spatial, impairments of both having been reported in schizophrenia (Pantelis et al., 1997; Perry et al., 2001; Brown et al., 2007).

Although working memory deficits have been found in patients with schizophrenia in several studies, some researchers have also found no significant difference compared to normal controls. For example, Park and Holzman (1992) found that schizophrenia patients exhibited impaired visuospatial working memory performance but not impaired auditory working memory. To increase the complexity of simple digit span tasks, Gold et al. (1997) studied letter-number sequence task in schizophrenia patients to assess the capability to hold and manipulate information. They found deficits on the letter-number sequence task which suggest an impaired auditory working memory and also this impaired

letter-number sequence performance correlated significantly with Wisconsin Card Sorting Test perseverative responses, a measure of executive function. Hence, we undertook the current study with the objective of assessing both auditory and visuospatial working memory tasks in a sample of schizophrenia patients in comparison to normal controls, and its correlation with psychopathology.

Method

Participants

This was a cross-sectional, hospital-based study conducted in the Central Institute of Psychiatry, Ranchi, India. The study was approved by the ethical committee of our Institute. Sample consisted of 78 drug naive or drug free (at least 3 months) patients of either sex, aged between 18-45 years, fulfilling diagnosis of schizophrenia according to ICD-10 Diagnostic Criteria for Research (WHO, 1993) with illness duration less than two years and at least six years of formal education. Those with comorbid psychiatric disorder, substance abuse or dependence (except nicotine or caffeine), history of major medical or neurological disorders or history of electroconvulsive therapy in the past 6 months were excluded from the study. Normal control group consisted of 35 subjects who were age, sex and education matched with respect to schizophrenia group having General Health Questionnaire (GHQ-12; Goldberg & William, 1988) score of less than three and without any history of major medical or psychiatric disorder. Written informed consent was obtained from all the participants.

Table 1. Sample Characteristics

	Patients N=78 Mean (SD)	Normal N=35 Mean (SD)	Mann-Whitney U
Age	30.33 (6.78)	32.20 (7.53)	p = .243
Duration of illness in months	16.95 (6.34)	-	-
Age of onset	28.77 (6.84)	-	-
Age of first hospitalization	2.96 (9.15)	-	-
Number of hospitalization	0.13 (0.41)	-	-
SAPS total score	23.08 (9.48)	-	-
SANS total score	30.24 (13.36)	-	-
CDRS total score	2.69 (3.56)	-	-
	N (%)	**N (%)**	**Fisher's exact test (p)**
Sex			
Male	76 (97.4)	33 (94.3)	.586
Female	2 (2.6)	2 (5.7)	
Education			
Up to matric	43 (55.1)	19 (54.3)	
Intermediate	20 (25.6)	9 (25.7)	1
Graduate	15 (19.2)	7 (20.0)	
Domicile			
Urban	25 (32.1)	24 (68.6)	<.001
Rural	53 (67.9)	11 (31.4)	
Occupation			
Employed	34 (43.6)	30 (85.7)	<.001
Unemployed	44 (56.4)	5 (14.3)	
Marital status			
Single	28 (35.9)	9 (25.7)	.199
Married	50 (64.1)	26 (74.3)	

Note: *** p < .001 (2-tailed)

Tools

A semi-structured pro-forma specially designed for the study was used for recording socio-demographic and clinical details. A 34-item clinician administered Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984) and 25-item clinician administered Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) were used to assess positive and negative symptoms of schizophrenia, respectively. In both the scales, items are scored on a scale of 0 to 5 (0 = no abnormality and 5 = severe). To assess depression, a 9-items scale Calgary Depression Scale for Schizophrenia (Addington et al., 1990), specifically developed for the assessment of depression in schizophrenia was used. The 12-item version of General Health Questionnaire (GHQ-12; Goldberg & William, 1988) was used to screen normal controls. To assess working memory, Letter-Number Sequencing and Spatial Span subtests of Wechsler Memory Scale, Third edition (WMS-III; Wechsler, 1997) were used. Letter-Number Sequencing is a measure of auditory working memory in which a series of numbers and letters are presented in a random order and the examinee must reorganize the numbers into ascending order and the letters into alphabetical order. Total score ranges from 0-21 points. Spatial Span is the visual analogue of the digit span subtest which measures spatial working memory and consists of two parts, Spatial Span Forward and Spatial Span Backward. The score ranges from 0-32 points.

Procedure

Socio-demographic and clinical details were obtained from the subjects followed by rating on SANS, SAPS and CDRS to evaluate current psychopathology. Thereafter, tests of working memory were administered on all the subjects.

Statistical analysis

Statistical analysis was carried out using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). Normality of data was examined using histograms and Shapiro-Wilk test statistic. Mann-Whitney U test and Fisher's exact test were used to study the group differences in socio-demographic and clinical variables. Kendall's tau (τ), a non-parametric correlation, was used to assess bivariate relationship between working memory scores and clinical characteristics. Scatter plots were used to study the relationship between working memory and

Table 2: Comparison of working memory between schizophrenia patients and normal controls

	Patients N=78 Mean (SD)	Normal N=35 Mean (SD)	Mann-Whitney U
Spatial span forward	5.09 (1.57)	9.14 (1.65)	153.5***
Spatial span backward	3.09 (1.29)	7.06 (1.71)	148.5***
Spatial span total	8.21 (2.48)	16.20 (3.22)	134.5***
Letter-number sequencing	2.77 (1.14)	5.97 (2.13)	294.5***

Note: *** p < .001 (2-tailed)

clinical characteristics. The level of significance was kept at p<.05.

Results

Sample characteristics

The sample characteristics have been summarized in table 1. The mean age in patient group was 30.33 (SD 6.78) years and in controls was 32.20 (SD 7.53) years; there was no significant difference between them. Similarly, there was no significant difference between the two groups in terms of sex, education and marital status. However, there was significant difference in terms of domicile and occupation (p<.001). Mean age of onset of illness in the patient group was 28.77 (SD 6.84) years, whereas mean duration of illness was 16.95 (SD 6.34) months.

Working memory

Group comparison in working memory scores have been summarized in table 2. There were significantly lower scores in schizophrenia patients compared to normal controls in spatial span forward (p<.001, Cohen's d = 2.51), backward (p<.001, Cohen's d = 2.62) and total scores (p<.001, Cohen's d = 2.78) as well as letter-number sequencing scores (p<.001, Cohen's d = 1.87). Table 3 shows correlation between working memory and clinical variables. In the patient group, there was significant negative correlation between SANS total score with spatial span forward (τ = -.227, p<.01) and total scores (τ = -.164, p<.05) (figure 1). There was significant positive correlation between letter-number sequencing and age at first hospitalization (τ = .209, p<.05) as well as number of hospitalizations (τ = .208, p<.05). There were no correlations of working memory scores with SAPS or CDRS scores.

Table 3: Kendall's tau correlation between working memory with clinical variables

	Spatial span forward	Spatial span backward	Spatial span total	Letter-number sequencing
Age	-.054	-.073	-.106	.014
Duration of illness in months	.008	-.022	-.036	-.068
Age of onset	-.053	-.077	-.102	.008
Age of first hospitalization	.010	-.033	-.013	.209*
Number of hospitalization	.015	-.042	-.011	.208*
SAPS total score	-.063	-.053	-.066	-.010
SANS total score	-.227**	-.096	-.164*	-.072
CDRS total score	.032	.077	.060	.047

Note: * p < .05, ** p < .01 (2-tailed)

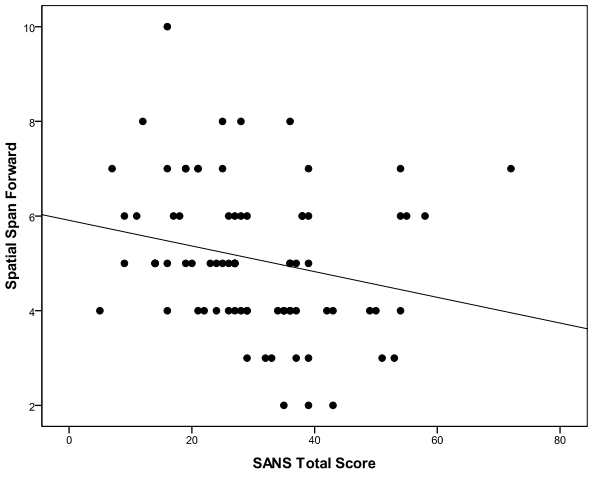

Fig 1: Scatterplot showing correlation of SANS total score with (a) spatial span forward and (b) spatial span total in patients with schizophrenia (N=78)

Discussion

The main findings from our study were impairment of both visuospatial as well as auditory memory. The effect sizes for the findings were large (Cohen, 1988). The re-

sults of this study support the hypothesis that schizophrenia patients have impaired performance on working memory measures when compared to a normal sample. In contrast to Park and Holzman (1992) who found impairment in visuospatial working memory with sparing of auditory working memory performance, our findings revealed impairment in both domains, thus refuting the *modality specific hypothesis* for working memory impairment in schizophrenia patients.

We found a significant negative correlation between negative symptoms as measured by SANS and spatial working memory in schizophrenia patients, though the effect size for the finding was small. The patients with greater severity of negative symptoms fared worse in spatial working memory tasks. The relationship of negative symptoms of schizophrenia with executive functioning deficits including working memory has been reported in several studies (Carter et al., 1996; Cameron et al., 2000; Palmer et al., 2000; Moritz et al., 2001). Furthermore, Carter et al. (1998) have reported association of functional hypofrontality with deficits in working memory. Also, there are evidences to suggest prominent role of frontal lobes in working memory tasks (D'Esposito, 2007) and frontal lobe abnormalities, specifically in dorsolateral prefrontal cortex, have been correlated with working memory task performance in schizophrenia patients (Honey and Fletcher, 2006; Kawada et al., 2009).

We found no correlation between positive symptoms and working memory tasks. This is in consonance with majority of studies which have found poor correlation between severity of positive symptoms of schizophrenia with executive dysfunction (Addington et al., 1997; Collins et al., 1997; Voruganti et al., 1997; Basso et al., 1998; Nieuwenstein et al., 2001). Verbal working memory did not correlate with either positive or negative symptoms. However, significant positive correlation with age at first hospitalization as well as number of hospitalizations appears paradoxical as both of these are indicators of greater illness severity.

Our study had adequate sample size to detect the difference between the groups. Limitations of our study include cross-sectional design and under-representation of females which limit generalizability of our findings across gender. Future studies should include neuroimaging modalities to take neuropsychological probes one step further in identifying neuroanatomical correlates of cognitive dysfunction in schizophrenia.

References

Addington J, Addington D, Garbarre L. Distractibility and Symptoms in Schizophrenia. J Psychiatry Neurosci 1997;22:180-184

Barch DM. The cognitive neuroscience of schizophrenia. Annu Rev Clin Psychol 2005;1:321-353

Basso MR, Nasrallah HA, Olson SC, Bornstein RA. Neuropsychological correlates of negative, disorganized and psychotic symptoms in schizophrenia. Schizophr Res 1998;31:99-111

Bowen L, Wallace CJ, Glynn SM, Nuechterlein KH. Schizophrenic individuals' cognitive functioning and performance in interpersonal interactions and skills training procedures. J Psychiatr Res 1994;28:289-301

Brown GG, Lohr J, Notestine R, Turner T, Gamst A, Eyler LT. Performance of schizophrenia and bipolar patients on verbal and figural working memory tasks. J Abnorm Psychol 2007;116:741-753

Cameron AM, Oram J, Geffen GM, Kavanagh DJ, McGrath JJ, Geffen LB. Working memory correlate of three symptom clusters in schizophrenia. Psychiatry Res 2002;110:49-61

Carter C, Robertson L, Nordahl T, Chaderjian M, Kraft L, O'Shora-Celaya L. Spatial working memory deficits and their relationship to negative symptoms in unmedicated schizophrenia patients. Biol Psychiatry 1996;40:930-932

Carter CS, Perlstein W, Ganguli R, Brar J, Mintun M, Cohen JD. Functional hypofrontality and working memory dysfunction in schizophrenia. Am J Psychiatry 1998;155:1285-1287

Cohen J. Statistical power analysis for the behavioral sciences. New Jersey: Lawrence Erlbaum; 1988

Collins AA, Remington GJ, Coulter K, Birkett K. Insight, neurocognitive function and symptom clusters in chronic schizophrenia. Schizophr Res 1997;27:37-44

Corrigan PW, Wallace CJ, Schade ML, Green MF. Learning medication self-management skills in schizophrenia: relationships with cognitive deficits and psychiatric symptoms. Behav Ther 1994;25:5-15

D'Esposito M. From cognitive to neural models of working memory. Philos Trans R Soc Lond B Biol Sci 2007;362:761-772

Gold JM, Carpenter C, Randolph C, Goldberg TE, Weinberger DR. Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. Arch Gen Psychiatry 1997;54:159-165

Honey GD, Fletcher PC. Investigating principles of human brain function underlying working memory: what insights from schizophrenia? Neuroscience 2006;139:59-71

Kawada R, Yoshizumi M, Hirao K, Fujiwara H, Miyata J, Shimizu M, et al. Brain volume and dysexecutive behavior in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2009;33:1255-1260

Lee J, Park S. Working memory impairments in schizophrenia: a meta-analysis. J Abnorm Psychol 2005;114:599-611

Moritz S, Andresen B, Jacobsen D, Mersmann K, Wilke U, Lambert M, et al. Neuropsychological correlates of schizophrenic syndrome in patients treated with atypical neuroleptics. Eur Psychiatry 2001;16:354-361

Nieuwenstein MR, Aleman A, de Haan EH. Relationship between symptoms dimensions and neurocognitive functioning in schizophrenia: a meta-analysis of WCST and CPT studies. J Psychiatr Res 2001;35:119-125

Palmer BW, Heaton R. Executive dysfunction in schizophrenia. In: Sharma T, Harvey P (eds) Cognition in schizophrenia. Impairments, importance and treatment strategies. New York: Oxford University Press; 2000: 51-72

Pantelis C, Barnes TR, Nelson HE, Tanner S, Weatherley L, Owen AM, et al. Frontalstriatal cognitive deficits in patients with chronic schizophrenia. Brain 1997;120:1823-1843

Park S, Holzman PS. Schizophrenics show spatial working memory deficits. Arch Gen Psychiatry 1992;49:975-982

Perry W, Heaton RK, Potterat E, Roebuck T, Minassian A, Braff DL. Working memory in schizophrenia: transient "online" storage versus executive functioning. Schizophr Bull 2001;27:157-176

Saykin AJ, Gur RC, Gur RE, Mozley PD, Mozley LH, Resnick SM, et al. Neuropsychological function in schizophrenia. Selective impairment in memory and learning. Arch Gen Psychiatry 1991;48:618-624

Saykin AJ, Shtasel DL, Gur RE, Kester DB, Mozley LH, Stafiniak P, et al. Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. Arch Gen Psychiatry 1994;51:124-131

Voruganti LN, Heslegrave RJ, Awad AG. Neurocognitive correlates of positive and negative symptoms in schizophrenia. Can J Psychiatry 1997;42:1066-1071

World Health Organization. The ICD-10 classification of mental and behavioural disorders - Diagnostic criteria for research. Geneva: World Health Organization; 1993