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Verbal learning in schizophrenia in remission, first-degree relatives, and correlation to symptoms

Abstract

Background: Cognitive impairments are fundamental in schizophrenia with verbal memory impairments commonly occurring not only in patients but also in unaffected genetically susceptible individuals. Deficits in verbal memory produce difficulty in problem-solving, emotional distress, and worsening of daily life skills resulting in a poor quality of life. **Objectives:** This study aims to evaluate the verbal memory in unaffected first-degree relatives of patients of schizophrenia in comparison to healthy controls as well as patients of schizophrenia in remission and to find correlation to symptom domains. **Methods:** It was a hospital-based, descriptive, cross-sectional case-control study. Three groups (n=40, each group) of patients, first-degree relatives, and controls were taken. Subjects were screened for mental retardation and remission was ascertained in the patient group by the Positive and Negative Syndrome Scale (PANSS). Rye's Auditory Verbal Learning (RAVL) test was used to assess verbal leaning. **Results:** Verbal memory impairments were significant both in patients and unaffected first-degree relatives. Further, these impairments showed a strong correlation to negative symptoms. **Conclusion:** Significant ($p<0.05$) verbal learning impairments were noted in patients and first-degree relatives which showed a correlation to negative symptoms.

Keywords: Retention. Recall. Cognitive Deficit. Psychosis. Memory.

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INTRODUCTION

Eugene Bleuler first described cognitive changes. Recent estimates suggest cognitive impairments to be present in up to 98% of the patients.[1] Clinical impairments arising as a result of cognitive deficits are noted in up to 80% of the patients and the remaining ones also fail to return to premorbid level of functioning.[2-4] The appearance and persistence of these deficits are unrelated to positive symptoms. They appear to predict the onset of psychosis. Deficits in verbal memory have been noted in healthy relatives also.[5-9]

Medial temporal lobe and prefrontal cortex mediate verbal learning. It is the ability to retain, store, and use information heard.[10] Verbal memory is one of the most affected cognitive domains in schizophrenia. It has been regarded at times as a predictor of antipsychotic response and a determinant of functional outcome.[11,12] Deficits in verbal memory produce difficulty in problem-solving, emotional distress, and worsening of daily life skills.[13-15] In schizophrenia, deficits in verbal memory appear before the symptoms start and persist even after symptoms have recovered.

Studies on patients of first-episode psychosis showed that verbal memory continued to deteriorate even on treatment though symptoms improve.[16] This suggests verbal memory to be more of a core with a trait-like dimension. Bilder and colleagues[17] showed a large number of first-episode patients to be having a performance of 1.5 standard deviation (SD) lower than controls. Patients of chronic schizophrenia performed similarly to patients of Alzheimer's, showing impairments in delayed recall as well as delayed recognition.[18,19]

Longitudinal studies on verbal memory had varying results. In a large outpatient-based study by Heaton and colleagues,[20] it was noted that visual and verbal memory remained stable at 1.5 and five-year follow-up. However, Gold and colleagues[21] had reported in a similar study that immediate recall improved with time, but deficient in delayed recall failed to improve. Verbal memory impairments were noted to correlate with positive symptoms.[22] Hoff and Kremen[2] followed-up patients annually from the first episode and found patients to be deteriorating progressively, with a performance one to two SD below normal.

Verbal memory impairments show an association with negative symptoms.[5] In a longitudinal study,[22] it was noted that deficits of verbal memory correlated more to symptoms at the onset of illness than after six months of treatment. Chronic patients did not show any benefit in verbal memory with treatment. This sets the need to explore the significance of verbal memory deficits in schizophrenia.

Aims and objectives

On reviewing the literature, the present study intends:

1. To access memory deficits even in stable patients of schizophrenia and first-degree relatives of patients of schizophrenia.
2. To estimate the extent of correlation of these deficits to various domains of symptoms.

MATERIAL AND METHODS

It was a descriptive cross-sectional, case-control study. The study was conducted at Nil Ratan Sircar Medical College and Hospital, Kolkata in India in 2019. Ethical clearance was provided by the institutional ethics clearance committee by letter No/NMC/3691. Samples were obtained by purposive sampling from the patients, their relatives, and informants of patients coming to the psychiatry department.

Sampling and definition

It was a purposive sampling where all cases who fulfilled inclusion and exclusion criteria were included. Inclusion criteria were subjects between 18-50 years, who were educated in English up to at least till tenth standard and consented to participate in the study. Exclusion criteria were subjects who had comorbid conditions such as drug abuse, except nicotine dependence, affective disorders, dementia, mental retardation, history of head injury and seizure within a one-year duration. The first group was stable patients in remission, the stable schizophrenics. First-degree relatives' group was parents, children, and siblings of those patients of schizophrenia who were admitted to the psychiatry ward or presenting to the outpatient department. Those who fulfilled inclusion and exclusion criteria but did not belong to either of the above groups were controls or third group.

Rating and assessment by tools

A specially prepared proforma was used to collect the patients' sociodemographic data which included age, gender, educational status, residential status, socioeconomic status, past history, family history, personal history, general physical examination, systemic examination, and mental status examination. The World Health Organization's tenth revision of the diagnostic criteria for research of the International Statistical Classification of Diseases and Related Health Problems (ICD-10 DCR)[23] was used to diagnose each patient. Mental retardation was ruled out by screening all subjects by Raven's Colored Progressive Matrices.[24] All subjects were screened by the Positive and Negative Syndrome Scale (PANSS)[25] for assessing the severity of illness in schizophrenia. The accepted criteria for remission as in literature was a PANSS score of less than three for all items in the last six months.[1] General Health Questionnaire-28 (GHQ-28)[26]was used for checking the presence of any psychiatric comorbidity.

Rey's Auditory Verbal Learning (RAVL) test[27] was used for the assessment of verbal learning. In this test, first, a list-A having 15 words are presented successively five times. After reading each time, the subject is asked to recall from memory in any order, though no hint is given. Next, a new list, list-B is presented and asked to recall immediately. This serves as interference list. Later, he has to recall list-A immediately for immediate recall and after a gap of 20 minutes, for delayed recall. Ultimately, a new list having new words mixed with those of list-A is presented and he is asked to identify words of list-A.

PANSS is a 30-item interval rating scale where each item can be rated up to seven. It rates separately positive, negative, and general symptom domains.[25]

Statistical analysis

The data was tabulated and descriptive values like mean and SD were calculated. Epi info7 and Microsoft Excel were used for analysis. Chi-square test was used for categorical variables and analysis of variance (ANOVA) for continuous variables. Pearson's coefficient of correlation was used to find a correlation to symptom domains.

RESULTS

There is no statistically significant difference existing among the groups with respect to age, educational status, occupation, and gender. A significant difference between groups was noted in the area of residence. Hence, groups were matched on age, gender, education, and occupation by design (Table 1).

Four set of scores were obtained (Table 2):
1. Immediate recall
2. Delayed recall
3. Delayed recognition (hits and errors)
4. Long-term retention percentage (LTRP)

Patients and first-degree relatives performed significantly worse than controls. Post-hoc (least significant difference [LDS]) showed first-degree relatives performed similar to patients in remission. However, in delayed recognition, patients performed worse than first-degree relatives. Symptom domains showed minimal symptoms as patients were in remission (Table 3). A strong negative correlation was found between negative symptoms with recall and retention (Table 4).

DISCUSSION

We aimed to study verbal memory in three groups, the remitted patients, first-degree relatives, and controls. The three groups were demographically matching in age and education. The version of RAVL test used is a test modified and standardised for Indian subjects.[27] It is designed to provide four sets of scores. It is a performance test where various tasks involving memory is allotted with fixed time and scoring criteria. Patients of schizophrenia even in remission showed significant impairments in verbal learning with respect to controls. Post-hoc LSD showed significant difference existing between groups. Impairments include deficits in immediate recall, delayed recall as well as long-term recall. This indicates that all stages of memory formation, i.e. registration, retention, and recall are affected. Further, this points to the fact that these deficits supersede the symptoms of the illness.[5] Our findings are similar to those noted by Bilder and colleagues,[17] in which a large number of patients in the post-psychotic phase in remission performed 1.5 SD below normal. Similar to previous studies, we observed that treatment could remit symptoms but not verbal memory deficits.[2,16]

Table 1: Sociodemographic variables

Variables		Group 1: patient (n=40)		Group 2: first-degree relative (n=40)		Group 3: control (n=40)		p
		n	%	n	%	n	%	
Sex (male)		22	55	24	60	21	53	0.01
Age (years)		30.88±8.24		31.27±8.87		29.26±7.91		0.5
Education	School	14	35	15	37	14	36	0.76
	High school	7	18	7	18	7	17	
	Graduate	8	21	9	23	9	23	
	Postgraduate	8	19	7	17	8	19	
	Professional	3	7	2	5	2	5	
Married	Yes	26	65	24	60	25	62.5	0.145
	No	14	35	16	40	15	37.5	
Occupation	Unemployed	17	42.5	14	35	9	22.5	0.28
	Unskilled	14	35	11	27.5	13	32.5	
	Skilled	9	22.5	15	37.5	18	45	
Residence	Rural	12	30	25	62.5	14	35	0.04
	Urban	28	70	15	37.5	26	65	
GHQ-28 score		6.03±1.14		2.00±0.81		1.87±0.74		<0.001

GHQ-28: General Health Questionnaire-28

Table 2: Performance in RAVL test

RAVL test	Patient n=40	First-degree relative n=50	Control n=50	F value	p
Immediate recall	9.97 (1.24)	10.41 (1.48)	11.98 (1.11)	28.65	<0.001
Delay recall	10.15 (1.05)	10.95 (1.72)	13.36 (1.58)	52.07	<0.001
RAVL hits	12.82 (1.34)	12.14 (2.56)	13.45 (1.16)	5.75	<0.001
RAVL error	6.44 (1.78)	6.32 (2.78)	3.94 (2.7)	13.56	<0.001
RAVL LTRP	90.83 (10.8)	91.64 (13.14)	97.79 (7.87)	5.44	0.01

RAVL: Rye's Auditory Verbal Learning; LTRP: Long-Term Retention Percentage

Table 3: Distribution of PANSS scores among patients of schizophrenia

PANSS domains	Minimum	Maximum	Mean	SD
Total	14	21	17.24	1.74
Positive	7	11	8.18	1.42
Negative	7	11	7.59	0.92
General	16	18	16.19	0.86

PANSS: The Positive and Negative Syndrome Scale, SD: Standard Deviation

Table 4: Pearson's co-efficient of correlation to symptoms

PANSS domains	Immediate recall	Delayed recall	RAVL error	RAVL LTRP
Negative	-0.63	-0.72	-0.10	-0.61
Positive	-0.34	-0.34	-0.12	-0.16
General	0.029	0.11	0.11	0.12

PANSS: The Positive and Negative Syndrome Scale, RAVL: Rye's Auditory Verbal Learning, LTRP: Long-Term Retention Percentage

Asymptomatic first-degree relatives have also been shown to harbour such impairments.[7] This raises the question that does verbal learning impairment possesses the potential of being a screening tool? Addington and Addington[28] compared the nature of verbal learning impairment in first-episode patients to those with a chronic course and found the deficits to be similar.

We intended to study the correlation of the extent of impairments to the symptom domains. Though positive and general symptoms did not show any correlation, negative symptoms showed a high inverse correlation to verbal learning. Addington and Addington,[28] in their study had also noted a similar finding. However, McDermid Vaz and Heinrichs[22] had noted positive symptoms to be showing a correlation to verbal memory deficits. In their study, patients of schizoaffective disorders were also included in cases. Hence, results may not be exactly comparable. Negative symptoms are the most difficult to treat and are the ones left over resulting in residual deficits. As treatment options for targeting negative symptoms are far less than positive ones, a suitable trait marker for early intervention may be useful for better disability limitations.

These facts taken together point to learning impairments as a trait marker present in the genetically susceptible population more often than the general population; hence, may be regarded as endophenotype.[13] It appears to be the

strongest predictor of functional outcome, causes emotional discomfort, and difficulty in problem-solving.[15]

Ultimately, these deficits limit the functional ability and skills needed for activities of daily living. People forget names of things they have been asked to fetch and show the inability to remember the sequence of events they are directed to perform. As a result, occupational and activities of daily living are affected. Screening for these verbal learning impairments could be a part of a routine assessment to aid in disability limitations in the future.

Strengths

1. Instruments standardised for the Indian population were used.
2. Groups were demographically matched by design.

Limitations

Being a hospital-based study, sample size remained a constraint.

Conclusion

Deficits in verbal learning persist in patients of schizophrenia even in remission. Genetically high-risk asymptomatic subjects also harbour such deficits, significantly more often than others. Further, deficits in verbal learning show a strong correlation to negative symptoms.

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AUTHOR CONTRIBUTIONS

SC: Principal investigator involved in every aspect including correspondence. OPS: Design of the work and revising it critically. SG: Acquisition, analysis, or interpretation of data.

REFERENCES

1. Keshavan MS, Diwadkar VA, Montrose DM, Stanley JA, Pettegrew JW. Premorbid characterization in schizophrenia: the Pittsburgh High-Risk Study. World Psychiatry. 2004;3:163-8.
2. Hoff AL, Kremen WS. Neuropsychology in schizophrenia: an update. Curr Opin Psych. 2003;1:149-55.
3. Palmer BW, Heaton RK, Paulsen JS, Kuck J, Braff D, Harris MJ, *et al*. Is it possible to be schizophrenic yet neuropsychologically normal? Neuropsychology. 1997;11:437-46.
4. Allen DN, Goldstein G, Warnick E. A consideration of neuropsychologically normal schizophrenia. J Int Neuropsychol Soc. 2003;9:56-63.
5. Hughes CI, Kumari V, Soni W, Das M, Binneman B, Drozd S, *et al*. Longitudinal study of symptoms and cognitive function in chronic schizophrenia. Schiz Res. 2003;59:137-46.
6. Toulopoulou T, Morris RG, Rabe-Hesketh S, Murray RM. Selectivity of verbal memory deficit in schizophrenic patients and their relatives. Am J Med Genet B Neuropsychiatr Genet. 2003;116B:1-7.
7. Green MF. Recent studies on the neurocognitive effects of second-generation antipsychotic medications. Curr Opin Psychiatry. 2002;15:25-9.
8. Toulopoulou T, Rabe-Hesketh S, King H, Murray RM, Morris RG. Episodic memory in schizophrenic patients and their relatives. Schizophr Res. 2003;63:261-71.
9. Cannon TD, Huttunen MO, Lonnqvist J, Tuulio-Henriksson A, Pirkola T, Glahn D, *et al*. The inheritance of neuropsychological dysfunction in twins discordant for schizophrenia. Am J Hum Gen. 2000;67:369-82.
10. Cirillo MA, Seidman LJ. Verbal declarative memory dysfunction in schizophrenia: from clinical assessment to genetics and brain mechanisms. Neuropsychol Rev. 2003;13:43-77.
11. Heinrichs RW, Zakzanis KK. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. Neuropsychology. 1998;12:426-45.
12. Aleman A, Hijman R, de Haan EH, Kahn RS. Memory impairment in schizophrenia: a meta-analysis. Am J Psychiatry. 1999;156:1358-66.
13. Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the 'right stuff'? Schizohr Bull. 2000;26:119-36.
14. Joober R, Rouleau GA, Lal S, Dixon M, O'Driscoll G, Palmour R, *et al*. Neuropsychological impairments in neuroleptic-responder verses – nonresponder schizophrenic patients and healthy volunteers. Schiz Res. 2000;53:229-38.
15. Lysaker PH, Bell MD, Greig TC, Bryson GJ. Emotional discomfort and impairments in verbal memory in schizophrenia. Psych Res. 2000;97:51-9.
16. Schuepbach D, Keshavan MS, Kmiec JA, Sweeney JA. Negative symptom resolution and improvements in specific cognitive deficits after acute treatment in first episode schizophrenia. Schiz Res. 2002;53:249-61.
17. Bilder RM, Volavka J, Czobor P, Malhotra AK, Kennedy JL, Ni X, *et al*. Neurocognitive correlates of the COMT Val(158) Met polymorphism in chronic schizophrenia. Biol Psychiatry. 2002;52:701-7.
18. McBride T, Moberg PJ, Arnold SE, Mozley LH, Mahr RN, Gibney M, *et al*. Neuropsychological functioning in elderly patients with schizophrenia and Alzheimer's disease. Schiz Res. 2002;55:217-27.
19. Putnam KM, Harvey PD. Memory performance of geriatric and nongeriatric chronic schizophrenic patients: a cross-sectional study. J Int Neuropsychol Soc. 1999;5:494-501.
20. Heaton RK, Gladsjo JA, Palmer BW, Kuck J, Marcotte TD, Jeste DV. Stability and course of neuropsychological deficits in schizophrenia. Arch Gen Psychiatry. 2001;58:24-32.
21. Gold S, Arndt S, Nopoulos P, O'Leary DS, Andreasen NC. Longitudinal study of cognitive function in first-episode and recent-onset schizophrenia. Am J Psychiatry. 1999;156:1342-8.
22. McDermid Vaz SA, Heinrichs RW. Schizophrenia and memory impairment: evidence for a neurocognitive subtype. Psychiatry Res. 2002;113:93-105.
23. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization; 1993.
24. Raven JC. Coloured progressive matrices sets A, Ab, B. Oxford: Oxford Psychologists Press; 1947.
25. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull. 1987;13:261-76.
26. Goldberg DP. Manual of the general health questionnaire. Windsor, England: NFER Publishing; 1978.
27. Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS neuropsychology battery-2004, manual. Bangalore: National Institute of Mental Health and Neurosciences; 2004.
28. Addington J, Addington D. Cognitive functioning in first episode schizophrenia. J Psych Neurosci. 2002;27:188-92.

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