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Verbal learning and memory and psychopathology in schizophrenia

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ABSTRACT

Background and aims: Verbal learning and memory (VLM) are the most impaired cognitive functions noted in schizophrenia. Though its association with negative symptoms is found consistently, only few have compared this relationship at a drug free/naïve state and on antipsychotic medications. Thus the aim of the study was to compare VLM functions in schizophrenia and normal controls and find its association between negative symptoms at drug free/naïve state and on antipsychotic medication.
Method: A sample of 78 initially drug naïve/free patients of schizophrenia of either sex, aged between 18 and 45 years, and 30 age, sex and education matched normal controls were assessed for VLM by Rey-Auditory-Verbal-Learning-Test (RAVLT). The schizophrenia group was assessed at baseline and at the end of six weeks treatment with RAVLT and for positive, negative and depressive symptoms.
Results: The schizophrenia group performed significantly poorly on VLM at both time points compared to normal controls, though significant improvement in the schizophrenia group was noted following six weeks treatment. Only negative symptoms inversely correlated with immediate memory span and verbal learning at baseline and in addition verbal memory at six weeks, while change in any of the dimensions of psychopathology (assessed in terms of positive, negative and depressive symptoms) over six weeks did not correlate with change in measures of cognitive functions.
Conclusion: For VLM deficits in schizophrenia, though correlated with negative symptoms, improvement with treatment could not be attributed to improvement in psychopathology.
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1. Background

Neurocognitive deficits are a core feature of schizophrenia. Verbal learning and memory (VLM) are one of the most impaired cognitive functions noted among all others (Toulopoulou and Murray, 2004). Evidence for VML deficits being consistent and quantitatively severe has come from reviews (Cirillo and Seidman, 2003; Heinrichs and Zakzanis, 1998) and meta-analysis (Aleman et al., 1999; Green, 1996). A profile analysis (using a comprehensive neuropsychological battery) of medication-naïve/free patients with schizophrenia showed that memory function was more severely impaired than other cognitive functions, such as attention, executive function, language, spatial abilities, or sensory and motor functions (Saykin et al., 1991, 1994). This deficit is persistent throughout the course of illness without being fully accounted for by duration of illness (Addington and Addington, 2002), changes in illness severity or medication effects. Relationship of psychopathology with VLM deficits shows significant association of negative symptoms (but small effect size) (Aleman et al., 1999) and none with positive symptoms (Addington and Addington, 2002). However, with improvement in symptoms Hughes et al. (2003) found this association was not maintained and concluded the lack of casual association of improvement of cognitive functions with symptom improvement. Contradictory findings have also been reported (Bilder et al., 2000; Vaz and Heinrichs, 2002). On reviewing the nature of memory deficits in schizophrenia, encoding/learning is found to be primarily impaired (Cirillo and Seidman, 2003) rather than an accelerated rate of forgetting (Gold et al., 2000). Yet some (Tracy et al., 2001) have argued the special case for verbal memory where retrieval processes are also disrupted compared to non-verbal memory. On the other hand meta-analysis (Aleman et al., 1999) has shown differential impairment between verbal and non-verbal material both in delayed recall and recognition memory, though this difference was not statistically significance. In the same analysis immediate and delayed verbal recall scores did not differ. Considering the intricacies related to encoding and retrieval processes in verbal memory functions and the contradictions in literature on VLM's relations with negative symptoms, the present

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study was undertaken. The objective of the study was to assess VLM in a sample of schizophrenia patients at two time points (one when drug free/naïve and the other after treatment for six weeks) in comparison to normal controls, and evaluate its correlation with psychopathology (assessed in terms of positive, negative and depressive symptoms). A six weeks post-treatment duration for evaluation was considered keeping in mind that most patients show clinical response at four weeks of continuous antipsychotic treatment. Moreover to prevent practice effect on repeating VLM tasks, six weeks time was considered adequate (McCaffrey et al., 2000).

2. Method

2.1. Participants

A six week hospital based follow-up study was conducted. The experimental sample comprised of 78 initially drug naïve or free (at least three months) patients of either sex, aged between 18 and 45 years, fulfilling diagnosis of schizophrenia according to ICD-10 Diagnostic Criteria for Research, 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 six months were excluded from the study. The normal control group consisted of 30 participants who were age, sex and education matched with respect to the schizophrenia group. Categorical/frequency matching was done by creating age and educational categories. Normal controls were defined as having General Health Questionnaire (GHQ)-12 (Goldberg and Williams, 1988) score of less than three and without any history of major medical or psychiatric disorders. The sampling was done purposively based on the above criteria and only those found cooperative for neuropsychological evaluation were recruited. Written informed consent was obtained from all the participants. The study was approved by the Ethical Committee of the Institute.

2.2. Tools

A semi-structured pro-forma 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 a 25-item clinician administered Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1981) were used to assess positive and negative symptoms of schizophrenia, respectively. In both the scales, items are scored on a scale of 0–5 (0 = no abnormality and 5 = severe). In view of the high prevalence of depressive symptoms in patients with schizophrenia (around 50%) (Buckley et al., 2009) and considering memory tasks to be influenced by depressive symptoms, an assessment for this was considered. To assess depression, a nine-items scale, the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1990), specifically developed for the assessment of depression in schizophrenia was used. The 12-item version of GHQ (Goldberg and Williams, 1988) was used to screen normal controls. To assess VLM, Rey Auditory Verbal Learning Test (RAVLT) was used. The patient group was assessed at two time points, once at baseline and again at the end of six weeks following treatment with antipsychotics. The RAVLT is adapted for different cultures by WHO (Maj et al., 1993), and is suitable for conditions in India. It particularly assesses immediate memory span, new learning, susceptibility to interference, and verbal memory. The test consists of presenting five successive trials (Trial 1–5) of a list of words, "List A" (every time in the same order), by reading aloud and a free recall after each trial. This is followed by presenting an interference list "B" of 15 unrelated words and free recall of list B. This is followed by a recall of list "A" shortly thereafter (Trial 6) and again after a delay of 20 min (Trial 7). Finally, a recognition test for list A is administered by reading aloud 30 words. The score on Trial 1 assesses the *immediate memory span*, sum of scores on Trial 1–5 forms *learning score*, sum of scores on Trial 6 and 7 and recognition trial forms the *memory score*.

2.3. Procedure

Socio-demographic and clinical details were obtained from the participants followed by rating on SANS, SAPS and CDSS to evaluate current psychopathology. Thereafter RAVLT was administered on all the participants. Individuals were treated at the discretion of the treating team. All the above evaluations were repeated after a period of six weeks treatment. Active measures were taken to ensure compliance to treatment.

2.4. Statistical analysis

Statistical analysis was carried out using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). Assessment of data distribution was done with histograms and Shapiro–Wilk test statistic and revealed a significant departure from normality for socio-demographic variables and also extreme skewness in RAVLT scores. Mann–Whitney *U* test and Fisher's exact test were used to study the group differences in socio-demographic variables. Paired t-test was used to evaluate improvement in psychopathology scores over time. Mann–Whitney *U* test and Wilcoxon signed ranks test were used to compare scores in the experimental group and control group and in the experimental group at baseline and at six weeks of follow-up respectively. Kendall's tau (τ), a non-parametric correlation, was used to assess bivariate relationship between RAVLT scores and clinical characteristics. The confidence interval was set at 95% and the level of significance was kept at $p < .05$.

3. Results

The sample characteristics have been summarized in Table 1. The mean age in the patient group was 30.32 (SD 6.79) years and in controls was 31.36 (SD 7.39) 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 28.76 (SD 6.83) years, whereas mean duration of illness was 16.94 (SD 6.33) months. Majority of the patients (94.9%) were treated with only atypical antipsychotics. And just under half of the patients (47.4%) were on less than 300 mg of chlorpromazine equivalent dosage of antipsychotics.

Table 2 shows the difference in psychopathology scores in the schizophrenia group at baseline and at six weeks and points towards significant improvement of symptoms in all dimensions with treatment. Table 2 also summarizes the comparison of RAVLT scores. The schizophrenia group performed significantly poorer on all measures both at baseline and at six weeks compared to normal controls. Significant improvement in the schizophrenia group was also noted following six weeks' treatment.

Table 3 shows correlation of various psychopathology scores with performance scores on RAVLT both at baseline and at six weeks assessment. Only negative symptoms correlated with measures of immediate memory span and verbal learning at baseline and in addition verbal memory at six weeks. Additional analysis was performed by first calculating improvement in various measures of psychopathology and VLM and then finding if any relationship exists between these improvements. Results

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