

ORIGINAL ARTICLE

**DEMOGRAPHIC AND CLINICAL FACTORS ASSOCIATED WITH
VERBAL MEMORY PERFORMANCE IN PATIENTS WITH
SCHIZOPHRENIA IN HOSPITAL UNIVERSITI SAINS MALAYSIA
(HUSM), MALAYSIA**

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Abstract

Objective: The present study aims to assess verbal memory performance in patients with schizophrenia attending HUSM and determine the relationship between the patients' verbal memory performance and their demographic/clinical factors. **Methods:** A cross sectional study of 114 patients with schizophrenia attending HUSM psychiatric services from December 2007 to May 2008 was conducted. The schizophrenia symptoms as well as verbal memory performance were assessed using the Brief Psychiatric Rating Scale, the Malay version of the Calgary Depression Scale (MVCDS), and the Malay version of the Auditory Verbal Learning Test (MVAVLT). The relationship between verbal memory performance and demographic/clinical symptoms was evaluated using Pearson Correlation. **Results:** Overall MVAVLT scores in all the trials were lowered in patients with schizophrenia compared to average healthy controls. There were significant relationships between occupational status and MVAVLT performance in Trial A1-A5 Total; between educational level and MVAVLT performance in Trial A1 and Trial A1-A5 Total and between severities of illness and MVAVLT performance in all indexes except Trial A1 after controlled for occupation and educational level. **Conclusions:** Patient with schizophrenia in HUSM performed significantly worse than healthy controls in verbal memory with or without interference. There were significant relationships between MVAVLT performance and patient's occupational status, educational level and severity of the illness but not depressive symptoms. *ASEAN Journal of Psychiatry, Vol.12(2): July – December 2011: XX XX.*

Keywords: schizophrenia; demographic; Malay version of the Auditory Verbal Learning Test; Brief Psychiatric Rating Scale; Malay version of the Calgary Depression Scale

Introduction

Schizophrenia is characterized by broad cognitive impairment, with varying degrees of deficit in all ability domains measured by standard clinical tests which include global and selective verbal memory, nonverbal memory and executive function [1]. Study by Green in 1996 emphasizes the significance of verbal memory for the functional outcome in schizophrenia [2] and was proposed to be one

of the main predictors of psychosocial functioning [3].

Paulsen et al. (1995) evaluated the potential clinical and demographic factors associated with learning and memory impairment in schizophrenia and found that patients with schizophrenia showed prominent retrieval deficit [4]. They also performed badly on all learning, recall and recognition memory measures and the most important clinical correlates of these impairments were earlier

age of onset, more negative symptoms, and greater anticholinergic medication dosage. Another study found that the patient's performance in the neuropsychological tests correlated with dosage of neuroleptic and anticholinergic medication [5]. They found that high neuroleptic and anticholinergic dosages were associated with poor verbal recognition memory. On the contrary, a meta-analysis conducted on 70 studies of memory in schizophrenia showed that the memory impairment is stable, wide ranging, and not substantially affected by potential moderating factors such as severity of psychopathology and duration of illness [6]. Thus, it is difficult to ascertain whether the observed memory dysfunctions in schizophrenia were related to variation in age of onset, educational level, effects of the illness or iatrogenic effects of pharmacotherapy.

Thus, the present study aims to (i) assess and obtain local data on verbal memory performance in patients with schizophrenia attending HUSM and (ii) determine the relationship between the patients' verbal memory performance and their demographic/clinical symptoms.

Methods

Subjects

This is a cross sectional study on 114 patients with schizophrenia. The subjects were conveniently selected from the outpatient clinic and psychiatric wards in Hospital Universiti Sains Malaysia (HUSM) within a six-month period (December 2007 till May 2008). They were cooperative and able to understand the Malay language. Patients were excluded if they scored 5 (moderately severe) or more in any of the Brief Psychiatric Rating Scale (BPRS) item, presence of a central nervous system disease, mental retardation or were not testable due to acute psychotic state or severe medical co-morbidity. The age limit of all subjects was set between 18 and 60 years, to enable legal consent and to minimize the effect of normal aging process on the cognitive performance. The study protocol was approved by the Research & Ethics Committee, Universiti Sains Malaysia. A single researcher trained in psychiatric interview and examination administered the test and interviewed all the subjects individually.

Assessments

The patients' verbal learning and memory performance were assessed using the validated Malay version of the Auditory Verbal Learning Test, MVAVLT [7]. The test was administered to all subjects by the same rater (second author) as described earlier [8]. The MVAVLT consists of two different lists (A and B) of 15 concrete nouns. Subjects were read list A five times (A1 to A5) at a rate of one item per second (tape recording was used to standardize the rate). Free verbal recall was tested immediately after each presentation. Then list B was presented followed by a free recall of list B. Thereafter, recall of list A (A6) was examined without prior presentation of list A. Recall of list A (A7) was repeated again after 20 minutes of rest without prior presentation of list A. Finally, subjects had to recognize the words from list A interspersed among semantically or phonetically related words in a third list comprised of 30 words. BPRS was used to measure positive symptoms, general psychopathology and affective symptoms in patients with schizophrenia. Sixteen symptom constructs were originally listed for rating on a seven-point scale (1 = not present, 7 = most severe), which document the intensity of symptoms in relatively independent areas. The rating is based upon observations made by the rater during a 15 to 30-minute interview (items which measure tension, emotional withdrawal, mannerisms and posturing, motor retardation and uncooperativeness), and subject verbal report (items which measure conceptual disorganization, unusual thought content, anxiety, guilt feelings, grandiosity, depressive mood, hostility, somatic concern, hallucinatory behaviour, suspiciousness and blunted affect). Subsequent additions to the scale were two additional items of excitement and disorientation.

The Malay version of The Calgary Depression Scale for schizophrenia (MVCDS) (translated by psychiatrist, Dr Riana Abdul Rahim) was used to assess the symptoms of major depressive disorder in patients with schizophrenia. The CDRS was first developed by Addington et al. (1990) and was specifically designed to assess co-morbid depressive symptoms in patients with

schizophrenia; its use in other patient populations has not been tested. The CDRS consists of nine items: depressed mood, hopelessness, self-deprecation, guilty ideas of reference, pathological guilt, depression worsening in the morning, early awakening, suicide, and observed depression. The items on the CDRS are all typical depressive symptoms and do not appear to overlap with the negative symptoms of schizophrenia (e.g., anhedonia is not included as a CDRS item).

Statistical Analysis

All analyses were conducted using SPSS version 18.0. The scores in the MVAVLT were taken as dependent variables. The patients' demographic and clinical characteristics were taken as independent variables. Statistical analysis started with descriptive statistics which included

frequency, percentage, mean, standard deviation and range accordingly for demographic characteristics, clinical characteristics and MVAVLT scores for each domain level. Relationships between MVAVLT performance and demographic as well as clinical characteristics were evaluated using Pearson Correlation. A *p* value of less than 0.05 was considered as significant.

Results

A total of 114 patients with schizophrenia, comprising of 68 males and 46 females, with a mean age of 34.6 (10.21) years were enrolled into the study. A majority of the patients were Malay (97.4%), single (64.9%), unemployed (51.8%) and received education up to secondary school (78.9%) as shown in Table 1.

Table 1. Demographic characteristics of schizophrenia patients attending HUSM

Demographic Variables	Group	N (%)	Mean (SD)
Age (years)	18 – 30	35 (30.7)	34.6 (10.21)
	30 – 40	47 (41.2)	
	41 – 60	32 (28.1)	
Gender	Male	68 (59.6)	
	Female	46 (40.4)	
Race	Malay	111 (97.4)	
	Chinese	1 (0.9)	
	Other	2 (1.8)	
Marital status	Single	74 (64.9)	
	Married	27 (23.7)	
	Divorced	13 (11.4)	
Occupation	Unemployed	59 (51.8)	
	Self employed	30 (26.3)	
	Government servant	17 (14.9)	
	Private sector	8 (7.0)	
Education level	Primary school	8 (7.0)	
	Secondary school	82 (71.9)	
	College / university	24 (21.1)	

A majority of patients had duration of illness for at least 5 years (69.3%) and were treated with atypical antipsychotics (58.8%) whereby 22.4% of them were on clozapine (Table 2). 33.3% of patients were on typical antipsychotics and the remaining patients (7.9%) received combination of typical depot injection and oral atypical antipsychotics. 22.8% of patients were on regular benzhexol, an anticholinergic drug, to counteract the extrapyramidal symptoms caused by the

typical antipsychotics (Table 2). A majority of them (63.2%) were compliance to the antipsychotics prescribed and attended regular clinic follow-up (62.3%). A majority of the patients (66.7%) had history of being admitted to the psychiatry ward at least twice. Concurrent medical illness was present in 8.8% of patients for which 7.0% of them were also on medication for their illness. 9.6% of the patients had previous history of substance abuse. All patients had mild to moderate

illness as measured by BPRS score. 34.2% of them had BPRS score at least 30 to 50, while the remaining (65.8%) scored less than 30.

Depression as defined by the MCVDRS score of 7 or more was present in 5.3% of patients.

Table 2. Clinical characteristics of patients with schizophrenia attending HUSM

Clinical variables	Characteristics	n (%)
Duration of illness (years)	< 2	15 (13.2)
	2 – < 5	20 (17.5)
	5 - < 10	24 (21.1)
	≥ 10	55 (48.2)
Types of antipsychotic	Typical	38 (33.3)
	Atypical /Clozapine	67 (58.8)/ 15 (22.4)
Use of anticholinergic	Both	9 (7.9)
	Yes /No	26 (22.8) /88 (77.2)
Follow up	Regular /Defaulter	71 (62.3)/ 43 (37.7)
Drug compliance	Yes /No	72 (63.2) /42 (36.8)
Concurrent medication	Yes /No	8 (7.0) /106 (93.0)
Number of hospitalization	< 2	38 (33.3)
	2 - < 6	50 (43.9)
	≥ 6	26 (22.8)
Concurrent medical illness	With/ Without	10 (8.8) /104 (91.2)
History of substance abuse	Yes/ No	11 (9.6) /103 (90.4)
BPRS score	< 30	75 (65.8)
	≥ 30 - 50	39 (34.2)
CDRS score	0 – 6 (no depression)	108 (94.7)
	≥ 7 (depression)	6 (5.3)

The mean MVAULT score were 5.0 (1.93) and 8.9 (2.57) out of 15 word lists for both Trial A1 and Trial A5 respectively (Table 3). The mean score for Trial A1-A5 Total was 35.6 (9.79) out of 75 word lists. As for Trial B, the mean score (3.7 (1.50)) was low when compared to Trial A1. These might be due to the difficulty in shifting attention to the new task after five learning trials. However, surprisingly the mean score for Trial A6 (7.5 (2.89)) was higher than Trial A1 even though

their memories had been interrupted by the new word list (list B). The mean score for delayed memory (Trial A7) was almost similar with the mean score of Trial A6 administered 20 minutes before. These showed that the schizophrenia patients still had the ability to sustain the previous learning information. The performance for the recognition task was also good with a mean score of 12.6 (2.60).

Table 3. Verbal memory and learning performance of patients with schizophrenia attending HUSM psychiatric services

MAVLT trials	Mean score (SD)	
	Schizophrenia patients n=114	Healthy controls ** n=15
A1 (Trial 1)	5.0 (1.93)	8.5 (2.20)
A5 (Trial 5)	8.9 (2.57)	12.2 (1.78)
Total Learning (A1+A2+A3+A4+A5)	35.6 (9.79)	53.2 (7.72)
B (Trial 6)	3.7 (1.50)	5.0 (1.60)

A6 (Trial 7)	7.5 (2.89)	11.0 (2.51)
A7 (Trial 8)	7.4 (2.71)	11.1 (2.49)
Recognition (Trial 9)	12.6 (2.60)	14.3 (0.88)

**Published data [7].

The verbal learning and memory performance was assessed using Malay version Auditory Verbal Learning Test (MVAULT).

Table 4. The relationship between MVAULT performance and demographic/clinical characteristics of patients with schizophrenia

	A1	A5	Total Learning	A6	A7	Recognition
Age	0.445	0.633	0.518	0.173	0.469	0.205
Gender	0.043*	0.410	0.210	0.090	0.193	0.681
Occupation	0.083	0.075	0.015*	0.377	0.571	0.302
Education level	0.013*	0.139	0.012*	0.335	0.382	0.056
Duration of Illness	0.204	0.699	0.714	0.293	0.754	0.479
Type of antipsychotic Use of	0.718	0.131	0.312	0.712	0.481	0.577
Anticholinergic	0.992	0.264	0.121	0.201	0.079	0.769
BPRS Score	0.020*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	0.001*
After controlled for education and occupation	0.046	< 0.001*	< 0.001*	< 0.001*	< 0.001*	0.001*
CDRS score	0.438	0.040*	0.193	0.361	0.153	0.913

* $p < 0.05$ was considered as statistically significant.

There were no significant relationships between age and MVAULT performance in all indexes measured (Table 4). There was a significant relationship between gender and mean score for Trial A1 ($p = 0.043$) but not in other trials. Males scored higher compared to females in Trial A1 and the mean difference between the two groups was 0.7 (95% CI = 0.02 to 1.46). Even though the other mean scores were not significant, the results consistently showed that males outperform females on most of the indexes on the MVAULT. Both educational level and employment status showed significant relationship with MVAULT performance. Patients who received college/university education scored higher compared to those who received primary/secondary education and the mean difference between the two groups was 1.1 (95% CI = 0.24 to 1.96) for Trial A1 and 5.6 (95% CI = 1.28 to 9.98) for Trial A1-A5 Total. Similarly, employed patients scored higher compared to unemployed patients in Trial A1-A5 Total and the mean difference between these two groups

was 4.4 (95% CI = 0.90 to 7.95) for Trial A1-A5 Total. These findings reflect that patient with schizophrenia from low educational background and unemployed had more memory symptoms that subsequently impaired their function. However, there were no significant relationship between MVAULT performance in all indexes measured and duration of illness, types of antipsychotic or use of anticholinergic medication. There were significant relationship between MVAULT performance in all indexes measured and BPRS score even after controlling for occupational status and educational level effects. The patients with higher total BPRS score (30 to 50) performed worse compared to those with lower BPRS score (<30) in all MVAULT indexes. In contrast, there was no significant relationship between MVAULT performance in all indexes measured and patient's emotional status as measured by CDRS, except for Trial A5.

Discussion

The present study found that performance of patients with schizophrenia was generally worse than healthy individuals [7] in measures of total learning, immediate memory, immediate memory after interruption using list B and delayed recall. Their performance on recognition tests was not severely impaired. This finding was consistent with previous studies [9, 10]. In addition, it was found that the deficits in recall were related to reduced use of organizational strategies to facilitate verbal encoding and retrieval [10]. The authors concluded that deficits in consistency of learning over several trials, as well as a strong relationship between semantic organizational strategies and reduced learning capacity, implicate prefrontal dysfunction as a contributor to verbal memory deficits in schizophrenia.

The present study provides information regarding the relationship between verbal memory dysfunction in schizophrenia with demographic characteristics. Most of the patient's demographic characteristics including age, gender, ethnicity, marital status, illness duration (years), number of hospitalization, follow up, drug compliance, use of anticholinergic drug and type of antipsychotics use were unrelated to verbal learning and memory performance except for patient's occupational status and educational level.

This study found no significant relationship between the MVAVLT performance and age and this is inconsistent with previous studies [11, 12]. A study by Wiens and colleagues in 1988 found a small but significant correlations between age and performance on Trials 3, 5 and 6 [11]. Another study reported significant age correlating with Trials 5, 6, 7 (delayed recall) and total learning in 600 subjects with seronegative homosexual and heterosexual males [12]. In the present study, there was no consistent score observed between the three age groups and the test performance did not decline with age.

In the present study, there were more male than female patients, 68 (59.6%) versus 46 (40.4%). This is a potential concern since women generally perform better than men on verbal tasks in particular verbal and recall tasks [13]. The present findings were contradictory to previous studies [14, 15].

Studies utilizing the California Verbal Learning Test (CVLT) specifically found that women tend to perform better than men on immediate recall and list learning recognition test [14]. The large difference in sample size between male and female patients with schizophrenia in this study could explain the different findings. However, studies have not been able to consistently replicate gender effects on RAVLT performance [15]. Thus, this appears to be a marginal effect that is of limited importance in interpreting RAVLT results.

There was significant relationship between memory (immediate memory and total learning) and educational level in the present study. This is in line with the findings by Query and Berger in 1980 [16]. That study found that education correlated significantly with recognition memory ($r = 0.41$) and learning ($r = 0.42$) [16]. However, low correlations of education with RAVLT score were observed in acute spinal cord injured patients wherein significant correlations were seen only for mean scores of Trials 4 and 5. The insignificant relationship between other MVAVLT scores and educational level in the present study could be explained by the small sample size and the broad classification of educational level whereby a few of the patients did not really complete secondary or primary school but were still included in the same group. The same confounds the college or university group in which a few of them did not complete their studies. Another strategy is to classify them according to duration of formal education received. However, it must be remembered that some of the patients who studied up to tertiary level had extended their study for several semesters only to fail the course at the end.

Significant relationship between memory and occupational status was only observed in Total Learning ($A1+A2+A3+A4+A5$). Even though there were no relationship in the other MVAVLT scores with the occupational status, the overall performances were better in the employed group. This finding is consistent with a review compiled by Green (1996) that emphasized the significance of verbal memory for the functional outcome in schizophrenia [2]. The classification of the occupational status should be more precise including the type of jobs and the duration of being

employed or unemployed. Some patients with schizophrenia may remain unemployed due to stigma or public perception of their inability to work rather than due to their cognitive impairment.

This study failed to identify a significant relationship between the type of antipsychotics used and MVAULT scores, consistent with previous study [1]. Another study, however, suggested that clozapine treatment was superior to typical antipsychotic in improving cognitive function in schizophrenia [17]. In this study, 58.8% of patients received atypical antipsychotics whereby almost a quarter of them received clozapine due to treatment-resistant schizophrenia. This subgroup of patients had a much more severe illness and probably had more memory symptoms prior to clozapine treatment thus resulting in lower MVAULT scores. The different dosage of antipsychotic used and the duration of treatment either in typical or atypical group could also contribute to the non-significant results since the impairment in memory in patients with schizophrenia frequently correlate with the high dose of typical antipsychotic used.

Anticholinergic medication has been associated with impaired memory function [18] and may antagonize the therapeutic effects of antipsychotic medication on positive symptoms in schizophrenia [19]. The present study, however, failed to identify a significant relationship between the use of anticholinergic medication with MVAULT scores. The regular administration of benhexol in 26 of 114 schizophrenia patients cannot explain group differences since no differences occurred between patients who were never or not regularly treated with benhexol. However, the pattern of results displayed in the present study showed better MVAULT scores in a group of patients who never or not regularly treated with benhexol. The data obtained regarding the use of benhexol in this study was very subjective whereby the information was gathered from the patients themselves and from the patients' medical records. The information regarding the dosage and duration of benhexol used are also useful. However, the usefulness of this approach is of limited value since many antipsychotics (e.g., chlorpromazine and quetiapine) possess significant intrinsic anticholinergic activity.

The present findings also did not show any relationship between duration of illness and MVAULT mean scores. These results indicate that the chronicity of the illness did not by itself determine memory function but other additional factors can also impair memory performance. These include adherence to medication, dosage and type of medication used and severity of relapses.

In line with previous studies, the present findings found significant relationship between severity of illness as measured by BPRS and MVAULT scores. The higher the total BPRS score, the worse performance in the MVAULT indexes. However, this study did not identify whether the patient's performance was related to specific symptomatology of illness. A study done by Moritz and colleagues in 2001 found that negative symptom was strongly correlated with memory dysfunction before and after controlling for distractibility [20].

The present finding failed to identify a significant relationship between depressive symptoms using CDRS and MVAULT scores except in Trial A5. This finding was in contrast to findings from other studies [20, 21, 22]. Query and Megran (1984) found that depression (as measured by the MMPI) accounted for reduced performance on Trial 1 [21] only. Hinkin et al. (1992) found that the Beck Depression Inventory (BDI) correlated only with Trial B in a sample of HIV patients [22]. Moritz et al. (2001) found that patients with depression and schizophrenia performed significantly worse than healthy controls in both short term and long term free recall as well as recognition test [20]. The possible explanation to the contrast in findings is the small sample size of the depressed group of schizophrenia patients as compared to non-depressed group in the present study. Some of the schizophrenia patients are very suggestible and tend to admit that they are having the symptoms. The other possible explanation is that the depression in schizophrenia might not be related to affective symptoms but may be related to somatic symptoms which were not measured in this study.

Limitations of this study include small sample size; unavailability of data on the verbal memory performance before and at the time of

disease onset as well as lack of control for external factors. The MVAVLT is ideally conducted in a quiet and comfortable room to minimize distractions and interruptions. However, it is difficult to ensure an ideal environment because this study was conducted in a clinic room during clinic session.

In conclusion, schizophrenia patients in the present study performed significantly worse than healthy controls in total learning, immediate memory with or without interference and delayed recall. There were significant relationships between MVAVLT performance and patient's occupational status as well as their educational level. This study was able to identify a significant relationship between MVAVLT performance and severity of illness but not depressive symptoms.

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