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Neuro-cognitive Performance in Patients with Schizophrenia: A Cross-sectional Study in a Psychiatric Clinic of a University Hospital

[1*]I Normala, [2]AR Abdul Hamid & [3]S Shamsul Azhar

[1] Department of Psychiatry, Faculty of Medicine and Health Sciences Universiti Putra Malaysia, Serdang, Selangor

[2] Department of Psychiatry, Faculty of Medicine, Universiti Kebangsaan Malaysia

[3] Department of Public Health, Faculty of Medicine, Universiti Kebangsaan Malaysia

ABSTRACT

Introduction: Poor neuro-cognitive performance in patients with schizophrenia has been described as a core symptom of the illness and is shown to be associated with poor psycho-social functioning. Management of schizophrenia has shifted its focus to treat this deficit apart from only emphasising on positive and negative symptoms, as it will subsequently improve patient functioning and outcome. **Objective:** The study aims to determine the proportion of neuro-cognitive impairment in patients with schizophrenia in a psychiatric clinic in Hospital Universiti Kebangsaan Malaysia and factors that are likely to be associated with the impairment. **Method:** A cross-sectional study design was conducted in this hospital-based study and subjects were randomly chosen from the psychiatric clinic. Rey Auditory Verbal Learning Test (RAVLT), Digit Forward and Backward (DF and DB), Trail Making Test (TMT) and Verbal Fluency Test (VF) were used to assess subjects' neuro-cognitive performance that measured their verbal memory and executive functioning of the brain. **Results:** The proportion of neuro-cognitive impairment is estimated at about 80% in patients with schizophrenia in this hospital-based study. A higher percentages of respondents had abnormal scores for RAVLT1, RAVLT5 and RAVLTB tests (75.6%, 68.3% and 82.9% respectively). The majority of respondents had normal scores for DF, VF tests (80.5% and 73.2% respectively), and about 51.2% of respondents had normal scores for DB test. For TMT, overall performance of respondents in Set A and B was poor. The mean duration of time taken to complete both sets was longer than that of a normal population based on age group: (age group: 18-39 years; TMT A 68.98 vs 40 seconds; TMT B 174.09 vs 90 seconds and age group: 40-49 years; TMT A 58.57 vs 45 seconds; TMT B 162.43 vs 100 seconds). There was a significant association between duration of illness and scores of RAVLT1 and between age of onset of illness and RAVLTB scores ($p<0.05$). There was no significant association between scores of all tests with the type of treatment received by respondents. **Conclusion:** The proportion of neuro-cognitive impairment in patients with schizophrenia is very high (80%) and has major implications on the current management of schizophrenia in which this core symptom should also be a focus of treatment. The significant association between clinical factors and neuro-cognitive impairment highlights the importance of modifying those factors in order to minimise the deficit in patients with schizophrenia.

Keywords: Executive function, neuro-cognitive impairment, schizophrenia, verbal memory

*Corresponding author: Dr Normala Ibrahim
Email: *nmala@medic.upm.edu.my*

INTRODUCTION

Neuro-cognitive impairment in patients with schizophrenia has been established as an independent core feature of the illness. It is not due to the effect of medication, institutionalisation or related to the presence of illness symptoms particularly negative features of schizophrenia. Kraeplin had first described it as *dementia praecox* and only in recent years has it been a focus of interest among researchers as the deficit predicts the psycho-social functioning outcome of patients with schizophrenia. Palmer *et al.* have shown that neuro-cognitive impairment is significant, affecting up to 75% of patients with schizophrenia[1] and among the stable outpatient schizophrenic population, only as few as 15% would be considered 'neuro-psychologically' normal.[2] It implicates 85% of neuro-cognitive impairment present in the least functionally impaired subgroup of patients.

There is a wide range of cognitive functions that are compromised in schizophrenia. These domains include attentional, executive functioning, verbal declarative memory and verbal fluency functions. Bilder *et al.* have shown that executive functioning and memory are commonly affected while others have revealed that executive function and verbal fluency have stronger deficits than memory impairment.[3]

Poor neuro-cognitive function in schizophrenia has been associated with a few clinical correlates of the illness itself. Among the established ones is the choice of pharmacological treatment that patients receive. The use of novel anti-psychotics has been proven to improve cognitive functioning of schizophrenic patients.[4] This preliminary finding has been supported by changes in brain functional activities using fMRI study in areas of prefrontal cortex.[5] Another correlate that is affected by poor neuro-cognitive function is performance in interpersonal and social abilities of schizophrenic patients. Lysaker *et al.* have proven that this deficit results in impairment in social integration.[6] Therefore, in clinical practice, it has several implications on the management of patients in allowing specific focus on the psycho-social and cognitive rehabilitation of patients to help improve their functional outcomes and quality of life.

There is lack of data locally on neuro-cognitive performance of schizophrenic patients in Malaysia. Zakaria compared performance of digit span and letter number sequencing tasks to assess verbal working memory in schizophrenic patients, their first degree relatives and normal subjects.[7] He reported that both patients and their relatives performed more poorly than normal subjects in the tasks. He also found that the scores of both tests were significantly affected by the subjects' level of education and occupational status, both of which are closely related in the local context.

In order to supplement more conclusive data on neuro-cognitive performance of schizophrenic patients for local use, the study aimed to estimate the proportion of neuro-cognitive impairment and determine factors associated with its presence in schizophrenic populations. As such, this research finding can be used as baseline data to improve the management of schizophrenic illness in Malaysia in terms of planning more favourable psycho-social treatment of patients.

METHODS

A cross-sectional design was used in this hospital-based study whereby 41 outpatients with schizophrenia were randomly selected from the patients' attendance list in a Psychiatric Clinic Hospital Universiti Kebangsaan Malaysia (HUKM) over a three-month period. The Postgraduate Research Committee of the Department of Psychiatry HUKM, after considering the associated ethical issues, granted permission to conduct the study.

The age limit of the participants was set between 18 to 60 years old, to enable legal consent, and to minimise the effect of normal aging process on neuro-cognitive performance. They were literate and able to understand the national language (Bahasa Malaysia) and English. The exclusion criteria for the study included overtly disturbed or aggressive patients, severe mental retardation or dementia, significant central nervous system diseases and history of head injury, comorbid psychiatric disorders and substance abuse or dependence, use of anti-cholinergic or benzodiazepine medication and those who have had a family history of psychiatric illness.

On selection, they were assessed using Mini International Neuropsychiatric Interview (MINI) diagnostic scale for DSM IV in order to generate a DSM IV diagnosis of schizophrenia. Following that, socio-demographic data was obtained and assessment for the symptomatology of the disorder was done using Brief Psychiatric Rating Scale (BPRS). The first author administered both assessments.

Subsequently, all subjects underwent a series of neuro-psychological tests to assess their neuro-cognitive performance. The tests used were Mini Mental State Examination (MMSE) in order to rule out any dementing illness, Rey Auditory Verbal Learning (RAVLT), Trail Making (TMT), Digit Span and Verbal Fluency tests. All tests were performed by the first author.

Statistical Package for Social Sciences (SPSS) was used to analyse the data and chi-square test was used in the analysis. *P* values of less than 0.05 were considered significant.

RESULTS

Demography of Respondents

Table 1 shows that the age range of 41 respondents interviewed is within 18 to 49 years old with a mean age of 32.07 with a standard deviation of +/- 8.7. Male respondents are in the majority and more than half of the respondents are employed. 58.5% of them have normal premorbid IQ.

Clinical Characteristics of Respondents

The mean age of onset of illness is 23.7 years old with a standard deviation of +/- 6.98 while the mean of duration of illness is 8.37 years with a standard deviation of +/- 7.29. All respondents have no active schizophrenic symptoms as reflected by the mean of BPRS total score (3.44 +/- 1.40 of standard deviation) (Table 2). Of the 41 respondents, 16 (39%) were prescribed with a combination of oral typical anti-psychotic and depot injection by their treating doctor, followed by oral atypical antipsychotic alone (29.3%), oral typical medication (17.1%) and a combination of oral atypical and depot injection (14.6%)(Table 1).

Table 1: Demographic characteristics and type of medication received by respondents

	Frequency	Percent
Age group		
18 to 39 years old	34	82.9
40 to 49 years old	7	17.1
Gender		
Male	26	63.4
Female	15	36.6
Employment		
Employed	23	56.1
Unemployed	18	43.9
Premorbid IQ		
Borderline	2	4.9
Dull normal	15	36.6
Normal	24	58.5
Medication		
Oral Atypical antipsychotic	12	29.3
Oral Typical antipsychotic	7	17.1
Oral Atypical + Depot	6	14.6
Oral Typical + Depot	16	39.0

Table 2: Clinical characteristics of respondents

	Mean +/- SD
Age of onset of illness (years old)	23.7+/- 6.98
Duration of illness (years)	8.37+/- 7.29
BPRS score	3.44+/- 1.40

RAVLT Tests Scores of Respondents

Figure 1 shows the mean score of RAVLT 1, 5 and B tests of respondents that reflect individual's verbal memory function as compared to the mean score generated from general population. Overall, there is poor performance of all RAVLT tests when the scores are categorised into normal and abnormal scores. High percentages of respondents have abnormal scores for all tests (RAVLT 1: 75.6%, RAVLT 5:68.3%, RAVLT B: 82.9%) (Figure 2).

Scores of Digit Span and Verbal Fluency Tests of Respondents

In general, performance in digit span and verbal fluency tests are not as compromised as RAVLT performance in all respondents. The mean scores for both tests reflect that they are

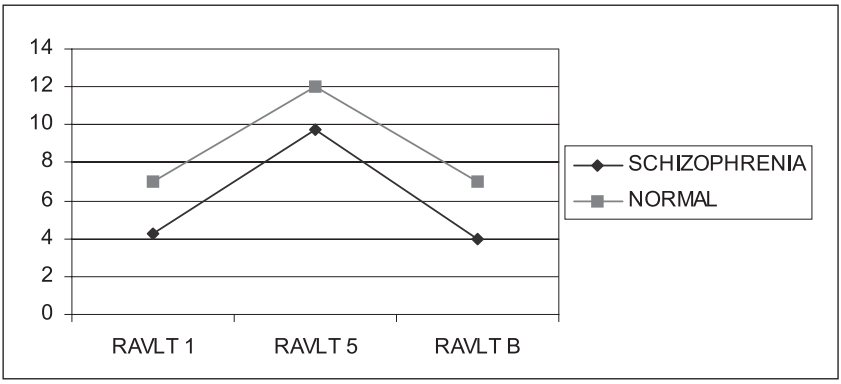

Figure 1. The mean score of Rey Auditory Verbal Learning Test (RAVLT) 1, 5 and B of respondents

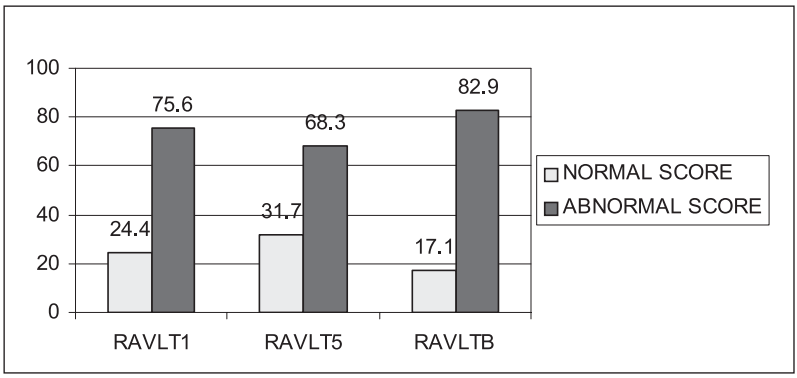

Figure 2. Percentage of respondents by dichotomous score of RAVLT 1,5 and B

as comparable as the ones scored by the general population. The majority of the respondents had normal scores for digit span and verbal fluency tests (DF: 80.5%, DB: 51.2%, VF: 73.2%) (Figure 3).

Scores of Trail Making Test of Respondents

Figures 4 and 5 show the mean duration of time taken by respondents to complete both TMT A and TMT B. Overall performance for both age groups was poor as respondents took a longer time to complete the task compared to the time taken by the general population. For the age group 18 - 39 years old, the respondents took a mean of 68.98 seconds to complete TMT A and 174.09 seconds to finish TMT B. The other age group took a mean of 58.57 seconds to complete TMT A and 162.43 seconds for TMT B.

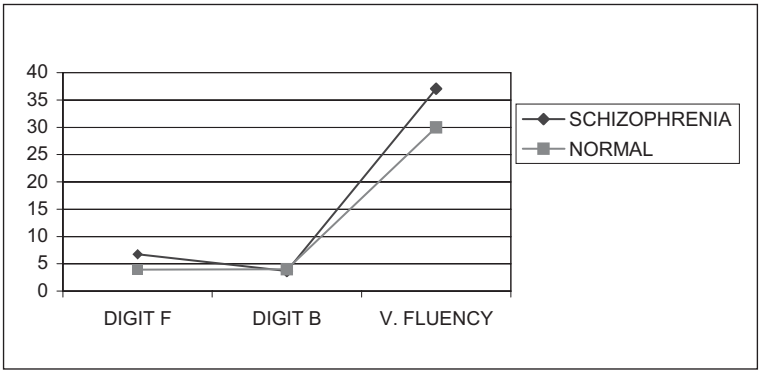

Figure 3. The mean score of Digit span and Verbal fluency tests of respondents

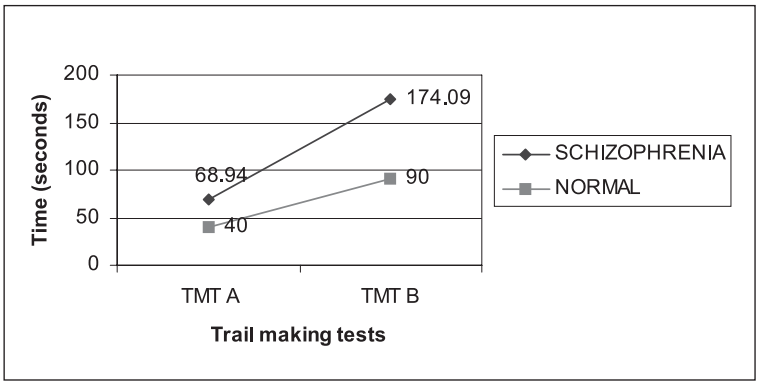

Figure 4. The mean score of Trail Making Tests A and B for age group 18-39 years old

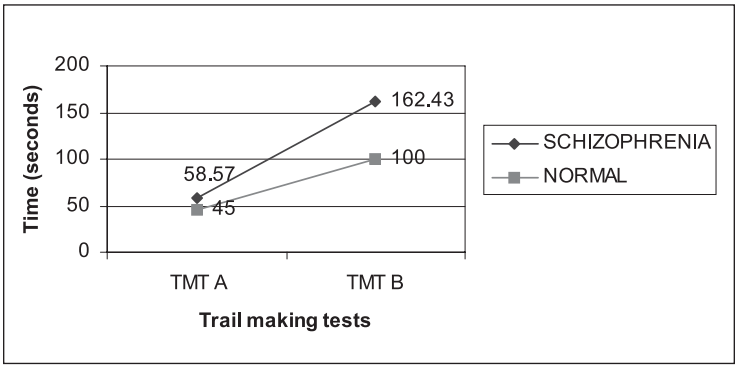

Figure 5. The mean score of Trail Making Tests A and B for age group 40 – 49 years old

Table 3. Association between clinical characteristics and RAVLT scores of respondents

	Score of RAVLT 1 N (%)		*P* value
	Normal	Abnormal	
Duration of illness (years)			
a. 0 to 5	2 (10.5)	17 (89.5)	
b. 6 to 10	5 (55.6)	4 (44.4)	0.049*
c. 11 to 20	3 (30.0)	7 (70.0)	
d. > 20	0 (0.0)	3 (100.0)	
	Score of RAVLT B N (%)		
	Normal	Abnormal	
Age of onset (years old)			
a. 15 to 29	5 (16.7)	25 (83.3)	
b. 30 to 39	0 (0.0)	8 (100.0)	0.032*
c. 40 and above	2 (66.7)	1 (33.3)	

Association between Demographic, Clinical Characteristics and Scores of Neuro-psychological Tests of Respondents

Table 3 shows the association between clinical characteristics of respondents' illness and their scores in RAVLT 1 and B tests. There is a significant association between duration of illness and scores of RAVLT 1 whereby a high percentage of those who had a longer duration of illness had poor scores in the test. There is also a significant association between the ages of illness onset with RAVLT B scores in that those who scored poorly in the test were also those who developed the illness at a younger age. There is no significant association between all scores of the tests with type of medication received by patients and other demographic or clinical characteristics of the respondents.

DISCUSSION

In this hospital-based study, it is estimated that about 80% of schizophrenic patients have neuro-cognition impairment as defined by the presence of one or more abnormal scores in any of the neuro-psychological assessments. The estimation of neuro-cognitive impairment in this study is high and is comparable to results shown in previous studies where there was significant impairment affecting up to 75 to 85% of patients with schizophrenia.[1-2]

In general, verbal memory, visuomotor tracking and mental set shifting components of executive functioning are much more affected in these patients as they scored poorly in RAVLT and TMT. RAVLT impairment indicates compromised verbal memory whereas TMT measures visuomotor tracking and mental set shifting are mainly associated with executive functioning. Scores of both tests in patients with schizophrenia differ from those generated

by the general population. They reflect specific impairment in cognitive functions which are mainly verbal memory and executive functioning. Many previous studies have had similar results in examining the pattern of neuro-cognitive impairment affected by illness.[3,8]

The study revealed that verbal fluency and attentional functions are not compromised as reflected by normal mean scores in both Verbal Fluency and Digit Span tests performed by patients with schizophrenia. The reason for the finding is that the majority of patients recruited had received a good education as reflected by their pre-morbid intelligence and they are within the younger age group. Both age and educational factors influence performance in Verbal Fluency and Digit Span tests. Therefore, the study is unable to replicate similar results shown by previous studies.[9] Although both tests measure memory and executive functioning, the finding denotes that possibly only certain components of both brain functions are affected by schizophrenic illness.

No demographic factors examined in this study showed any significant association with scores of neuro-psychological tests of patients. This finding is expected due to the small sample size. Any association between demographic factors and cognitive impairment may not carry much weight in the management of cognitive impairment of schizophrenia as factors such as age, gender and pre-morbid intelligence of patients are non-modifiable factors. Therefore, importance is focused on modifiable factors that can be manipulated so that further or existing neuro-cognitive impairment can be prevented or minimised.

Of all clinical factors examined in this study, duration of patients' illness and their age of illness onset have been found to be significantly associated with RAVLT 1 and B scores respectively. Both RAVLT 1 and B tests measure immediate memory component of verbal memory function. The study shows that patients across groups of different durations of illness have a high percentage of poor performance in immediate memory. It signifies that memory impairment is present in all patients with varied duration of illness. Therefore, we conclude the deficit is unrelated to duration of illness, and this is consistent with results from other studies.[10-11]

Another significant result in the study is that those who developed the illness at a younger age tend to have poor immediate memory compared to those who developed the illness later. This finding is not consistent with other studies where it is found that age of illness onset is not related to poor cognitive performance in schizophrenia.[10] Our results show that the 'forgetting' component is impaired but not the 'learning ability' of memory function. Gold *et al.* offered contrary results as they found 'impaired learning' and a normal rate of 'forgetting' while controlling the initial level of learning in patients with schizophrenia.[12] A possible explanation that could be offered for the different results would be that those who have an earlier onset of illness tend to be associated with a poor prognostic factor of the illness which is inclusive of neuro-cognitive deficit.

The use of novel anti-psychotics and psycho-social functioning of patients with schizophrenia have been extensively researched and previous studies[13-15] have found significant association with neuro-cognitive deficits. However, it is not evident in the present study as most of the recruited patients are employed and the majority receive typical anti-psychotic medications. Furthermore the sample size of the study was inadequate and its cross-sectional nature also would possibly hinder the emergence of such an association. A prospective design would be a better choice to bring out these associations.

CONCLUSION

The present study confirms the presence of neuro-cognitive impairment in patients with schizophrenia despite the limited sample size used. The estimated proportion of impairment is high and clinical factors found to be associated with it are duration of illness and age of illness onset. As such, these modifiable factors are vital in considering a more comprehensive psycho-social intervention which would include the rehabilitation of patients' cognitive function. Early detection of the illness should be emphasised so that early cognitive rehabilitation can be carried out in order to minimise or prevent further deterioration of cognitive function. This would over the long term help better predict the social functioning outcome of schizophrenic illness.

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