

ORIGINAL ARTICLE

VERBAL MEMORY TEST PERFORMANCE IN PATIENTS WITH BIPOLAR I DISORDER ATTENDING A PSYCHIATRIC CLINIC OF A UNIVERSITY HOSPITAL IN KUALA LUMPUR, MALAYSIA

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Abstract

Objective: The study aims to determine pattern of verbal memory and learning impairment and its associated factors among patients with bipolar I disorder in a psychiatric clinic of a university hospital. **Methods:** A case control study comparing verbal memory test performance in 40 patients with bipolar I disorder to that of 40 healthy normal subjects using Rey Auditory Verbal Learning Test (RAVLT). The association between demographic, clinical characteristics and poor verbal memory performance were examined. **Results:** Up to 92% of patients with bipolar I disorder have impaired short term working memory in this hospital-based study. They also recalled fewer words in all the RAVLT trials and had difficulties learning the word list in comparison to that of normal healthy individuals. Verbal memory and learning impairment are observed in bipolar illness in the absence of active mood symptoms while duration and severity of illness are not found to have any effect on verbal memory and learning. **Conclusion:** There is consistent verbal memory and learning problems in individuals with bipolar I disorder and their presence in the absence of mania, depression and mixed symptoms during the course of the illness suggests a trait related deficit. *ASEAN Journal of Psychiatry, Vol.10, No.2, July – Dec 2009: XX XX*

Keyword: Bipolar I disorder, verbal memory, learning, trait deficit

Introduction

Bipolar I disorder is a psychiatric diagnosis that is characterized by the

presence of recurrent manic, depressive or mixed episodes and they are usually separated by periods of apparent recovery. In community surveys of

industrialized countries, the lifetime risk for bipolar disorder is estimated between 0.3 to 1.5% while the lifetime prevalence of bipolar I disorder is approximately 1% [1-2]. However, the prevalence of bipolar spectrum disorders (bipolar I, bipolar II and cyclothymia) is much higher especially among patients with depression [3].

Neurocognitive impairment has been described in bipolar disorders in view of its resemblance to the disinhibition syndrome seen after frontal brain injury. Stratta et al. (1995) have reported that persistent cognitive impairment present in up to 32% of bipolar patients and case control studies by Clark et al. (2001) and Cavanagh et al. (2002) lend support to the ongoing consensus of this persistent syndrome in patients with bipolar disorder [4-6].

Most previous researches have observed that cognitive areas that seem to be more impaired in bipolar disorder are attention, learning, memory and frontal executive functions [7-8]. However, verbal episodic or declarative memory impairments are most consistently reported in bipolar patients in the euthymic phase of the illness [5,9]

Neuropsychological functioning has been postulated as a determinant of psychosocial and employment outcomes in bipolar disorder. Previous studies have shown that some neuropsychological measures especially those related to memory would be more strongly associated with psychosocial functioning rather than the clinical features of the illness. Between 30 to 50% of bipolar patients experience significant social disabilities may be

related to persistent neurocognitive impairment [10].

It was postulated that impairments in learning and memory mediate the illness process and functional outcome through an impact on adherence to treatment. They affected the patients' ability to remember directions for medication, importance of medication and the recollection of symptoms of side effects and so on. All these factors contribute significantly to the number of relapse of the illness that subsequently leads to further deterioration of the psychosocial functioning [11].

In local clinical setting, most psychosocial managements are emphasized more on patients with schizophrenia, as their social disabilities are more apparent than that of patients with bipolar disorder. There is lack of psychosocial rehabilitation program that is specifically tailored for patients with bipolar disorder in order to improve their social and occupational functioning. In order to fill in the gap, the present study aimed to determine the pattern of verbal memory and learning impairment in patients with bipolar I disorder and their associated factors. The data would have important implication in the planning of rehabilitation program for those patients specifically focusing on cognitive rehabilitation that in turn would help them to return to their optimal psychosocial functioning.

Methods

A case controlled design was used in the hospital-based study whereby 40 patients with bipolar I disorder diagnosis were randomly selected from the patients attendance list in Psychiatric Clinic

Universiti Kebangsaan Malaysia Medical Centre (UKMMC) (previously known as Hospital Universiti Kebangsaan Malaysia) within a six month period. The Ethic Research Committee of UKMMC granted permission to conduct the study after considering the associated ethical issues.

Forty subjects for control group were recruited from the hospital-based community who included healthy normal individuals working in UKMMC. They were unmatched control but the selected subjects for control would be most comparable to the case subjects in term of the age range and level of education. The age limit of the subjects was set between 18 to 60 years old, to enable legal consent and to minimize the effect of normal aging process on verbal memory test performance. They were literate and able to understand the national language (Bahasa Malaysia) and English.

The exclusion criteria for the case subjects of 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 and use of anticholinergic or benzodiazepine medication. As for the control group, an additional exclusion criterion would be those who have family history of psychiatric illness.

On selection, both case and control subjects were assessed using Mini International Neuropsychiatric Interview (MINI) diagnostic scale in order to generate DSM IV diagnosis of bipolar disorder and to rule out any psychiatric

disorders in the control group. Following that, sociodemographic data was obtained and assessment for the symptomatology of the disorder was done on case subjects using the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale (HAM-D). The first author administered all assessments.

Subsequently, all subjects underwent Rey Auditory Verbal Learning test (RAVLT) to assess their verbal memory and learning ability. The test provides a measure of immediate recall and evaluates learning over successive trials. Subjects are asked to recall a list of 15 words presented orally over 5 trials (RAVLT 1,2,3,4 and 5) with free recall after each trial. Following the fifth recall trial (RAVLT 5), an interference list consisting of 15 new words is presented (B). Recall of trial 1 (RAVLT 1) and trial B (RAVLT B) measure the short term (working) memory. The best learning score obtained is reflected in the score of trial 5 (RAVLT 5). The successive trials of RAVLT 1 to 5 assess the learning ability of subjects across trials. The test was performed by the first author.

Statistical Package for Social Sciences (SPSS) was used to analyse the data. Chi square, Independent t test and its non parametric equivalent were used in the analysis. *P* value of less than 0.05 was considered significant.

Results

Demography of respondents

Table 1 shows that the median age for the case group is 37.5 and a median of 27.0 for the control group. The control

group median age is younger than that of the case group and most respondents are within 18 to 39 years old where 55% of them are in the case group and 75% are in the control group. However, there is no significant difference for age in both groups after it was analysed using the Mann Whitney U test where the Z score = -1.349 and the p value = 0.177.

There is about 52.5% female in the case group and 47.5% represented the male gender. Majority of respondents in the control group are female (75%). The gender distribution shows significant difference between both case and control groups with the value of chi square = 4.38 and p value = 0.036 (Table 1).

In marital status distribution, more than half of the respondents in both case and control groups are married and the difference is not statistically significant with chi square = 0.82 and p value = 0.366. Majority of respondents in both groups are Malay employed and have normal intelligence. Distributions of race

and employment are statistically significant while there is no significant difference in intelligence between both groups (Table 1).

Clinical characteristics of respondents

The median age of onset of illness is 21 years old and the mean duration of illness is 10.95 years with a standard deviation of +/- 9.04. All respondents in the case groups have no active manic or depressive symptoms as reflected by the median of YMRS and HAMD scores (Table 2). The mean of total episode of relapse of the illness is 3.83 times.

In categories of the treatment group, 27.5% of respondents in the case group receive mood stabilizer alone whereby seven out of 11 of them are on anticonvulsant. More than 50% respondents are on a combination of mood stabilizer and antipsychotic with 17 of them are on atypical antipsychotic.

Table 1: Demographic characteristics of respondents

Variable	Case Med(IQR)	Control Med(IQR)	Mann Whitney U (z score)	p value
Age	37.5(20.0)	27.0(15.0)	-1.349	0.177
	Case n (%)	Control n (%)	χ² value	p value
Gender				
Male	19(47.5)	10(25.0)	4.38	0.036*
Female	21(52.5)	30(75.0)		
Marital status				
Married	21(52.5)	25(62.5)	0.82	0.366
Single	19(47.5)	15(37.5)		
Race				
Malay	30(75.0)	38(95.0)	10.275	0.006*
Chinese	9(22.5)	0(0.0)		
Others	1(2.5)	2(5.0)		
Premorbid IQ				
Borderline	2(5.0)	0(0.0)	4.514	0.105
Dull normal	6(15.0)	2(5.0)		
Normal	32(80.0)	38(95.0)		
Employment				
Employed	24(60.0)	40(100.0)	17.58	0.0001*
Unemployed	16(40.0)	0(0.0)		

Med= Median, IQR= Interquartile range

Table 2: Clinical characteristics of respondents in the case group

Variable	Med (IQR)
Age of onset of illness (years old)	21.0 (13.0)
Young Mania Rating Scale (YMRS) score	2.0 (4.0)
Hamilton Depression Rating Scale (HAMD) score	0.0 (0.0)
	Mean+/- SD
Duration of illness (years)	10.95+/- 9.04
Total episodes of relapse	3.83+/- 3.07
	n (%)
Medication	
Mood stabilizer (MS) only	11 (27.5)
MS + antipsychotic	22 (55.0)
MS + antidepressant	1 (2.5)
Antipsychotic only	6 (15.0)

Med= Median, IQR = Interquartile range, SD = Standard deviation

RAVLT Tests Scores of Respondents

Table 3 shows the median scores of RAVLT tests of respondents from both case and control groups. The scores reflect individual's verbal memory function. There is a significant

difference in performance of RAVLT between both groups when the analysis of Mann Whitney U was done. Subjects with bipolar disorder performed poorly in all subtests of RAVLT. The median scores were lower in bipolar subjects than that of normal healthy people.

Table 3: Median scores for RAVLT tests for case and control groups

Variable	Case Med(IQR)	Control Med(IQR)	Mann Whitney U (z score)	p value
RAVLT 1	5.0 (2.0)	7.0 (2.0)	- 4.161	0.0001*
RAVLT 2	7.0 (3.0)	11.0 (3.0)	- 5.223	0.0001*
RAVLT 3	9.0 (3.0)	13.0 (3.0)	- 5.390	0.0001*
RAVLT 4	10.0 (3.75)	14.0 (2.0)	- 6.120	0.0001*
RAVLT 5	11.0 (4.0)	14.0 (2.0)	- 5.473	0.0001*
RAVLT B	5.0 (2.0)	7.5 (3.0)	- 5.842	0.0001*
RAVLT 6	9.0 (4.75)	14.0 (2.0)	- 6.538	0.0001*

The scores of some of RAVLT subtests were subsequently dichotomized into normal and abnormal scores in order to analyze them using 2 by 2 tables and to determine the odds ratio for each of the association.

From table 4, majority of subjects with bipolar disorder obtained abnormal scores in both RAVLT 1 and B subtests. The scores differ significantly from that of normal subjects and it indicates that most of bipolar subjects have impaired immediate recall. The values of odds ratio (OR= 7.15 for RAVLT 1 and OR=22.90 for RAVLT B) suggest that bipolar subjects have about 7 to 22 times higher risk of having impairment in immediate recall than that of normal subjects.

For the best learning score, RAVLT 5 scores have significant difference between the two groups with about 57.5% of bipolar subjects obtained abnormal score. Bipolar patients learned

fewer words over the five learning trials in comparison to that of control respondents. The odds ratio value explains that those who have bipolar disorder are 53 times at higher risk to have impaired learning test in comparison to normal subjects.

In serial trials of RAVLT 1 to 5, less than 50% of the bipolar subjects showed impairment in this particular test. There are about 60% of them having normal scores and the difference is statistically significant. From the analysis, the odds ratio value indicates that the chance of subjects with bipolar disorder to develop impairment in successive learning is about 8 times higher than that of normal subjects.

Table 4: Distribution for dichotomized scores of RAVLT for case and control groups

Variable	Case n(%)	Control n(%)	χ^2 with Yate's correction	p value	OR(CI 95%)
RAVLT 1					
1) Abnormal	31 (77.5)	13 (32.5)	14.596	0.0001*	7.15(2.39-22.11)
2) Normal	9 (22.5)	27 (67.5)			
RAVLT 5					
1) Abnormal	23 (57.5)	1 (2.5)	26.250	0.0001*	52.76(6.55-1135.07)
2) Normal	17 (42.5)	39 (97.5)			
RAVLT B					
1) Abnormal	37 (92.5)	14 (35.0)	26.180	0.0001*	22.90(5.34-113.68)
2) Normal	3 (7.5)	26 (65.0)			
RAVLT 1 to 5 (successive learning)					
1) Abnormal	16 (40.0)	3 (7.5)	9.940	0.002*	8.22(1.94-40.06)
2) Normal	24 (60.0)	37 (92.5)			

OR = Odds ratio, CI= Confidence Interval

Association between demographic, clinical characteristics and RAVLT test scores of respondents

Demographic and clinical characteristics of the respondents that were examined in the study are shown in Table 1 and 2 respectively. They were analysed to look at the association with scores of RAVLT 1, B, 5 and serial trials of RAVLT 1 to 5. However, none of the demographic and clinical factors has shown significant association with the scores of RAVLT in both case and control groups.

Discussion

Finding from this study identified that bipolar patients performed poorly in verbal memory test as they recalled fewer words in all trials of RAVLT and had difficulties learning the RAVLT word list when compared with age matched control respondents. The percentage of bipolar patients that have impaired short-term working memory is high affecting up to 92% as reflected by the proportion of bipolar patients that has abnormal scores obtained in recall trials of RAVLT 1 and B. The results of the study are comparable to that of

previous case control studies where there was consistent poor performance in bipolar subjects using similar test and other equivalent verbal memory test [12-14]. In addition, bipolar patients did not differ from normal controls on measures of their pre morbid intelligence suggesting that verbal memory and learning difficulties are not attributable to general intellectual function before the illness developed.

The earlier studies have also shown that verbal memory impairment was present in stable and euthymic bipolar patients, which emphasize that compromised verbal memory in bipolar disorder is a trait dependent [13-14]. The present study replicates similar finding, as all bipolar patients recruited were free of active symptoms of mania or depression as indicated by the scores of YMRS and HAMD. It was found that short term working memory is much more affected than the successive learning ability in remitted bipolar patients. It suggests that verbal memory is impaired in patients with bipolar illness regardless of mood symptoms and may be related to the underlying pathophysiology of bipolar illness that warrants further investigation.

About sources of verbal memory impairment, two previous investigations have analysed further, whether or not the impairment identified was mediated by different verbal organizational strategies during learning [15-16] Both studies resulted in conflicting findings. Deckersbach et al. (2004) reported semantic clustering deficit as a mediating factor in bipolar memory impairment while Bearden et al. (2006) did not observe this but evidenced that underlying memory deficit is due to

encoding rather than retrieval of information. However, this study does not specifically designed to look into the underlying mechanism of memory deficit in bipolar illness. In addition to discrepancies of previous studies and lack of local data observing at sources of verbal memory deficit in bipolar disorder, it highlights the importance of studying this area in future to put more weight on existing evidences.

With respect to demographic and clinical characteristics of patients with bipolar disorder, none of the variables associated significantly with verbal memory impairment in bipolar respondents. In contrary to previous studies [17], we found no gender association with memory deficit in bipolar and control groups even there were significantly more female patients in the study. Ragland et al (2000) have suggested that female gender performed better in verbal memory test and suggests that it may relate to differences in underlying neurophysiology in different gender [18]. The most probable explanation for the discrepancy in this study is female respondents are in the younger age group and verbal memory tasks are greatly influenced by age and they are negatively correlated as shown by earlier studies [19]. Furthermore, any association between non-modifiable demographic factors such as gender and verbal memory impairment may not carry much weight in planning any cognitive rehabilitative interventions for bipolar patients. Therefore, focus is directed towards modifiable variables that could be manipulated so that further or existing impairment is prevented or minimized.

Consistent with Bearden et al 2006, this study did not find a significant effect of duration and severity of illness on verbal memory and learning performances in bipolar disorder. The finding contrasts with some previous studies and the reason being majority of the patients recruited in this study have less severe form of bipolar illness than those selected in the prior studies although their course of illness is chronic as reflected by the average numbers of relapse episodes and duration of illness [19]. Other possibility would be duration of illness and severity of illness are factors that have different measures of quantification in different studies that highlight the importance to have a standard measure to quantify those clinical factors in future.

The effect of psychotropic agents on neurocognition has been well researched and previous studies have shown that lithium and anticonvulsants do not have a clinically significant impact on cognitive function [20-21]. The present study also observed similar finding whereby there is no effect of psychotropic medications on verbal memory function. Bipolar patients in the study received a combination of mood stabilizers and antipsychotic. Majority of patients in the group were prescribed with atypical neuroleptic agents that has been shown to exhibit better side effect profile with regard to neurocognition and memory than typical antipsychotic [22]. Thus, it explains the insignificant association between psychotropic agents and verbal memory function in bipolar disorder.

A few issues need to be addressed in interpreting the findings in the study. Bipolar patients recruited were less educated and not well functioning than the control participants despite the similarity in age group and pre morbid intelligence. However, none of the factors has shown any significant effect on verbal memory performance. It suggests that those factors does not account for differences in verbal memory impairment between the two groups. Results obtained from verbal memory test performance may be subjected to halo effect, as the rater is not blinded to the subjects in both groups. The information obtained tends to fit in with the observer preconception. Therefore, the use of independent rater would be a better choice to overcome this shortcoming in future study.

In conclusion, the study is capable to discriminate poor verbal memory test performance found in bipolar disorder from normal healthy individuals. The finding concludes that the presence of verbal memory and learning deficit in bipolar disorder is universal despite cross-cultural difference between western and eastern populations. The study also suggests that impaired verbal memory and learning in bipolar illness is trait and not state related deficit as they present regardless of mood symptoms. The result of the study adds on to the existing evidence worldwide that verbal memory and learning function are impaired in bipolar disorder. As such, the data is important for local policy makers and rehabilitative specialists to design appropriate cognitive rehabilitation program that incorporates into existing psychosocial management for bipolar disorder.

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