PSYCHOLOGICAL MEDICINE

Clinical Insight in Schizophrenia Is Associated with Verbal Delayed Recall

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ABSRACT

Background: **Clinical insight is reliably associated with cognitive dysfunction in schizophrenia patients, with episodic memory as one of the most impaired forms of memory in this illness.**

Objectives: **This study aimed to examine clinical insight and its relationship with verbal learning among schizophrenia outpatient in Kelantan, Malaysia.**

Methods: **A total of 108 (mean age 33.7 years) stable schizophrenia outpatients were recruited. Clinical insight, psychopathology, and verbal learning were assessed using the Insight and Treatment Attitudes Questionnaire (ITAQ), Brief Psychiatric Rating Scale (BPRS), Auditory Verbal Learning Test (AVLT), respectively.**

Results: **In multiple linear regression final model, verbal delayed memory, duration of illness and primary educational status emerged as factors independently associated with clinical insight with 19.4% of the variation explained. No significant association was noted between clinical insight with other socio-demographic factors and schizophrenia psychopathology.**

Conclusions: **Clinical insight was independently associated with verbal delayed memory suggesting the important role of verbal memory, particularly delayed recall, in clinical insight. The association with duration of illness was explained by the study sample's relatively young age.**

KEY WORDS

clinical insight, insight into illness, delayed recall, episodic memory, verbal learning

INTRODUCTION

Poor clinical insight has profound prognostic and therapeutic consequences, and has been associated with low adherence to medication[1,2], greater frequency of hospitalizations and relapse[3], poor social and vocational functioning in schizophrenia patients[4]. Originally a dichotomous construct, it has evolved to multidimensional[5] with independent but overlapping domains such as unawareness of mental disorder, its symptoms, implications, and need for treatment[5,6]. Recent neuroimaging literature points to common as well as exclusive brain regions associated with insight dimensions[7].

Cognitive dysfunction[8,9], namely executive dysfunction, lower premorbid intelligence, memory, and to a lesser extent, impaired attention[10] is reliably associated with clinical insight. Memory impairments have been established as strong predictors of poor clinical and functional outcome in schizophrenia[11], with episodic memory as one of the most impaired forms of memory in this illness[12]. The inability to self-initiate effective memory strategies in the absence of direct prompts correlated with a failure to activate the left dorsolateral prefrontal cortex[13] represents a critical factor leading to deficient episodic memory in schizophrenia[14].

Nevertheless, patients are usually given psychoeducation to improve their clinical insight. The ability to remember health-related advice is dependent on patient's ability to listen, comprehend and retain information, collectively known as "verbal learning", Thus, this study aimed to examine clinical insight and its relationships with verbal learning among schizophrenia outpatient. The finding would add to the existing literature about the complex relationship between clinical insight and cognition, in particular memory. Since more than half of schizophrenia patients had poor medication adherence[15], the finding would be crucial in formulating effective strategies to address this issue.

METHODS

Participants and procedure

This research was approved by the HREC of Universiti Sains Malaysia and MREC of Health Ministry of Malaysia. The cross-sectional study was conducted over a period of 9 months in 2014 at Hospital Universiti Sains Malaysia (USM) and Hospital Raja Perempuan Zainab II (HRPZ-II) which are located in Kota Bharu, northeast of peninsular Malaysia.

The objectives and conduct of the study were briefly explained to

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Table 1. Socio-demographic and clinical characteristics

Variables	n (%)
Sex	
Male	63 (58.3)
Female	45 (41.7)
Race	
Malay	105 (97.2)
Chinese	1 (0.9)
Indian	-
Others	2 (1.9)
Marital Status	
Never married	74 (68.5)
Married	21 (19.4)
Divorced/separated	13 (12.0)
Employment Status	
Unemployed	59 (54.6)
Employed	49 (45.4)
Educational Status	
Primary	4 (3.7)
Secondary	73 (67.6)
Tertiary	31 (28.7)
Treatment Received	
Atypical antipsychotics	67 (62.0)
Typical antipsychotics	24 (22.2)
Both atypical and typical	17 (15.7)
Benzhexol Use	
Yes	14 (13.0)
No	94 (87.0)
	Mean(SD)
Age (yrs.)	33.67(10.11)
Duration of Illness (yrs.)	10.96 (7.71)
BPRS	23 (5)*
Verbal Learning	
Total learning	34.19 (10.61)
Delayed recall	7.0 (4)*
Recognition	14.0 (3)*
Insight data	
ITAQ	13.52 (4.16)

*Median (IQR) skewed distribution

Table 2. Associated factors of clinical insight by simple linear regression

Variables	b[a] (95%CI)	t[b] stat	p-value
Age	0.09(0.02,0.17)	2.400	0.018*
Gender	0.60(-1.02,2.21)	0.734	0.465
Race			
Malay	-0.84(-5.69,4.01)	-0.343	0.732
Chinese	6.54(-1.69,14.77)	1.576	0.118*
(Others)			
Marital Status			
Never married	-0.15(-1.86,1.57)	-0.167	0.868
Married	-0.70(2.71,1.31)	-0.693	0.490
(Divorced/Separated)			
Employment	1.33(-0.25,2.91)	1.668	0.098*
Educational Status			
Primary	3.88(-0.28,8.03)	1.849	0.067*
Secondary	-1.26(-2.95,0.42)	-1.484	0.141*
(Tertiary)			
Antipsychotics			
Atypical	-1.68(-3.29,-0.07)	-2.069	0.041*
Typical	1.80(-0.09,3.68)	1.890	0.062*
(Both)			
Benzhexol Use	1.42(-0.94,3.77)	1.191	0.236*
Duration of illness	0.15(0.05,0.25)	3.059	0.003*
BPRS	-0.32(-0.55,-0.08)	-2.665	0.009*
Verbal Learning			
Total learning	0.09(0.01,0.16)	2.348	0.021*
Delayed recall	0.41(0.14,0.69)	2.975	0.004*
Recognition	0.28(-0.07,0.64)	1.582	0.117*

[a]crude regression coefficient; [b]t statistic; *p < 0.25, included in the MLR

Table 3. Associated factors of clinical insight by multiple linear regression

Variables	b[a] (95%CI)	t[b] stat	p-value
Educational Status			
Primary	4.73(0.84,8.62)	2.409	0.018
Duration of illness	0.17(0.07,0.26)	3.426	< 0.001
Verbal Learning			
Delayed recall	0.37(0.11,0.63)	2.797	0.006

[a]adjusted regression coefficient; [b]t statistic; $R^2 = 0.194$.

No interaction and multicollinearity were found;

Forward multiple linear regression applied. Model assumptions were met.

the participants before obtaining the informed consent. The subject was then asked to fill in the self-rated questionnaire of BCIS. After this was completed, the information on socio-demographic and clinical data was obtained from both interview and clinical records. These were entered into the socio-demographic and clinical data form by the researcher. Following this, the verbal learning test was then administered using the Malay AVLT. Finally, the data collection was completed by using the BPRS to assess severity of psychopathology and the ITAQ to assess clinical insight during the interview.

Eligible schizophrenia patients attending the regular outpatient clinics were recruited for the study according to the following criteria: age (18-65 years), having diagnosis of schizophrenia as per Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR). Exclusion criteria included dementia, prior tramatic brain injury, relapse in the preceding 6 months, alcohol or drug dependence, debilitating medical or neurological illness, mental retardation or other major axis I disorder, and poor command of Malay language.

Measurements

Socio-demographic and clinical data of subjects were obtained through interview or from the medical records. Symptoms of schizophrenia were assessed using the Brief Psychiatric Rating Scale (BPRS) with scores ranging from 18 to 126. Higher scores indicate more severe symptoms[16]. The scale has high inter-rater reliability (0.62 to 0.87) as well as discriminant and concurrent validity[17].

Insight was assessed using the Insight and Treatment Attitudes Questionnaire (ITAQ) with scores ranging from 0 to 22, with higher scores indicating good clinical insight. This well-validated, structured interview[18], includes 11 questions assessing recognition of mental disorder and attitudes towards the need for medication, hospitalization, and follow-up care.

The patient's verbal learning and memory was assessed using the Malay version of the auditory verbal learning test (AVLT)[19]. It has a good factor validity (factor analysis of 0.66-0.98), test-retest reliability (0.24 to 0.84) and is sensitive in discriminating between normal and schizophrenia subjects.. Five acquisition trials, using List A, were given to each participant giving a total learning score (A1 + A2 + A3 + A4 + A5). Then, the participants were required to remember the items in List B (B1, interference trial). Following that List A must be repeated (A6, post interference, immediate recall memory). A gap of 20 minutes was given after A6 whereby at the end of this 20-minute gap, the participant was asked to recall List A again (A7, delayed memory recall). The final stage of the test involved recognising and identifying 15 List A words that were read out from a different list consisting of 30 words (List C)

which were semantically or phonetically related. In order to standardize the auditory input of List A, B and C, the researcher used a recorded audio as used in a previous study[20].

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 21 was used in the analyses. Mean (SD) was used for normally distributed continuous variables while median (IQR) was used to describe continuous variables of skewed distribution. Simple and multiple linear regression (MLR) analysis methods were employed to identify associated factors of clinical insight.

RESULTS

As shown in table 1, a total of 108 patients completed the questionnaires and analysed in this study. The mean age was 33.7 years old. Males and females comprised 58.3% (63) and 41.7% (45) of sample, respectively. The majority were Malays at 105 (97.2%). Most of them were never married (n = 74; 68.5%), unemployed (n = 59; 54.6%), secondary school educational status (n = 73; 67.6%), receiving atypical antipsychotics (n = 67; 62%) and not on benzhexol (n = 94; 87%). The mean duration of illness was 10.96 years (SD = 7.71). The BPRS median score of 23 (IQR = 5) reflected patient's relatively stable mental health, which was expected of schizophrenia outpatient. The verbal learning scores for total learning (mean = 34.19; SD = 4), delayed recall (median = 7; IQR = 4) and recognition (median = 14; IQR = 3) was consistent with working memor deficits, which is comparable to a previous study in similar setting[21].

The ITAQ mean scores was 13.52 with SD = 4.16. Table 2 represents the results obtained for clinical insight (ITAQ). The six variables significantly associated with clinical insight ($p < 0.05$) were age, atypical antipsychotic use, duration of illness, BPRS, total learning and delayed recall. On the basis of $p < 0.25$ with biological importance, a further seven variables including Chinese race ($p = 0.018$), employment status ($p = 0.098$), primary ($p = 0.067$) and secondary ($p = 0.141$) educational status, typical antipsychotic use ($p = 0.062$), benzhexol use ($p = 0.236$) and recognition scores ($p = 0.117$) were chosen to be included in the MLR for analysis.

From the various methods of MLR, the forward method produced the best final equation with three significant variables. Final equation for ITAQ = 8.97 + 0.17*(Duration of illness) + 0.37*(Delayed recall) + 4.73*(Primary educational status).This equation showed that there is a significant linear positive relationship between ITAQ score and duration of illness, delayed recall and those with primary educational status.

Therefore, in this model: (1) one year duration of illness corresponds to 0.17 scores higher in ITAQ; (2) one unit of delayed recall corresponds 0.37 unit scores higher in ITAQ; and (3) Those with primary educational status have 4.73 unit scores higher in ITAQ. According to the MLR model, 19.4% of the variation in the ITAQ score was explained by duration of illness, delayed recall and primary educational status ($R^2 = 0.194$).

DISCUSSION

In a previous study among offenders with schizophrenia, there was no significant association observed between clinical insight and general cognition measured by mini-mental state examination[22]. Nevertheless, verbal memory represents one of the most affected cognitive domains in schizophrenia. In this study, clinical insight was found to be independently associated with verbal delayed recall. During encoding, dorsolateral prefrontal cortex (DLPFC) activation was predictive of subsequent semantic clustering. Whereas, subregions of ventrolateral prefrontal cortex (VLPFC) were predictive of subsequent recall[23]. A recent neuroimaging study had found that patients with greater verbal memory impairments demonstrated significant cortical thinning in the left frontal lobe and the parahippocampal gyri[24]. These regions are known to be important in verbal memory performance. However, this study failed to find significant association with total learning or acquisition of information.

This study also found non-significant association between recognition memory and clinical insight. Probably this is related to schizophrenia patients intact ability to use semantic strategies to enhance their recognition memory performances, as compensatory mechanism to severe episodic retrieval impairment[25]. In a similar study[26], cognitive insight was not associated with verbal memory suggesting the ability to retain information to be more relevant to clinical rather than cognitive insight.

In this study, clinical insight was independently associated with duration of illness. This should be interpreted with caution as the relationship between clinical insight and duration of illness is not necessarily linear. Review of available literature suggests that the course of insight impairment follows a U-shaped curve, where insight impairment is severe during the first episode of psychosis, modestly improves over midlife, and declines again in late life[27]. In another study, insight impairment was more severe in later life ($\geq$ 60 years) than in earlier years and the relationships between impaired insight and cognition, particularly working memory, was stronger in later life than in earlier life[28]. As the mean age in this sample was 33.7 years, it was not surprising to note better insight with increasing duration of illness.

Lastly, clinical insight was independently associated with primary educational status which is in contrast to literature where insight is associated with number of years in education[29]. Good premorbid functioning including number of years in education and premorbid intelligence represent better cognition.

CONCLUSIONS

Clinical insight was independently associated with verbal delayed memory suggesting the important role of verbal memory, particularly delayed recall, in clinical insight. The association with duration of illness was explained by the the study sample's relatively young age. Lastly, the association with primary educational status was in contrast with the notion that number of years in education represents better cognition and predicts better insight.

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