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Relationship between insight and neurocognition in patients with bipolar I disorder in remission

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Abstract

The aim of this study was to examine the relationships between insight and neurocognition in a population of patients with bipolar I disorder who were in a remitted state. Using the Schedule of Assessment of Insight (SAI) and its expanded version, we evaluated 96 patients with bipolar I disorder in remission to determine their level of insight. We also evaluated their neurocognitive function included in the domains of executive function, attention, and memory. The associations between insight and neurocognitive function were examined by using the stepwise multiple regression analysis to control the confounding effects of sociodemographic and clinical factors. The results indicated that by controlling the confounding effects of other factors, executive function was positively associated with the SAI dimensions of awareness of illness and relabeling of phenomena, and the total expanded version of the SAI in remitted bipolar patients. The results of this study indicated that the relationships vary between different dimensions of insight and domains of neurocognitive function in remitted bipolar patients.
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1. Introduction

Insight of individuals with psychiatric disorders generally indicates an awareness of the psychiatric symptoms experienced, the presence of psychiatric disorders, and an awareness of the achieved effect of treatment [1,2]. Compared with schizophrenia, insight among patients with bipolar disorder is quite understudied and poorly understood empirically and conceptually [3]. As previous studies have revealed that a lack of insight is associated with bipolar patients' poor medical adherence [4] and poor psychosocial adjustment [5], further studies are necessary to examine correlates of insight in patients with bipolar disorder.

Neurocognitive dysfunction in bipolar disorder is increasingly being reported. Executive function, memory, and attention deficits are among the most commonly reported impairments in bipolar disorder [6-9]. The association of insight with neurocognition has become the focus of many research investigations on schizophrenia in the last few years [10]. However, very few studies have examined the relationship between insight and neurocognition in bipolar patients. Whereas Ghaemi and colleagues found that neither IQ nor memory was associated with insight in 16 manic patients [11], Varga and colleagues found that impaired insight was correlated to neurocognitive dysfunction in 18 bipolar symptomatic and 19 bipolar remitted patients [12]. Small sample size may partially account for the different results in these studies [13]. As insight changes across different mood stages [14,15], heterogeneous mood stages of subjects may also result in different results. Furthermore, although some studies have evaluated the association between insight and a variety of measures for neurocognition in bipolar patients, none have examined the effects of neurocognition that were grouped into domains or examined whether distinct domains of neurocognition have different effects on insight.

The aim of this study was to examine the relationships between insight and neurocognition in a population of patients with bipolar I disorder who were in a remitted state. We hypothesized that (1) the level of insight is positively

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associated with neurocognition in remitted bipolar patients and (2) the relationships vary between different dimensions of insight and domains of neurocognitive function.

2. Methods

2.1. Participants

From September 2002 to August 2004, 96 subjects with bipolar I disorder who were in a remitted state were enrolled from 2 university hospital psychiatric outpatient units. Two psychiatrists assessed all subjects systematically to confirm the diagnosis of bipolar I disorder based on the diagnostic schemes of the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* [16]. The exclusion criteria were subjects with comorbid mental retardation, obvious head injury, or substance use disorder. Psychopathology of subjects with bipolar I disorder was determined by using items 1 to 10 on the Young Mania Rating Scale (YMRS) [17] and the 24-item Hamilton Rating Scale for Depression (HAM-D) [18] except for the insight item. A *current state of remission* was defined by a YMRS score of ≤6 and a HAM-D score of ≤6 [14,19,20]. Lithium, valproic acid, and carbamazepine were the typical medications for the remitted subjects in this study. Only those who had repeated relapse of mood episodes even when regularly taking mood stabilizers will receive add-on atypical antipsychotics to prevent relapse in their remitted state. Among the 96 remitted bipolar subjects, 30 subjects (31.3%) who took atypical antipsychotic add-on mood stabilizers were judged as poor responders to mood stabilizer monotherapy. The protocol was approved by the Institutional Review Board of Kaohsiung Medical University. All patients provided written informed consent.

2.2. Measures

2.2.1. Schedule of Assessment of Insight

The Schedule of Assessment of Insight (SAI) measures 3 separate dimensions of insight: treatment compliance (0-4), recognition of illness (0-6), and relabeling of phenomena (0-4) (2). An expanded version of this scale, SAI-E [21], was also used and includes items on awareness of change in mental functioning, need for treatment, and psychosocial consequences of the illness. The full score of the SAI-E is 24. The Chinese version of the SAI has been used to examine the insight of patients with bipolar disorder and schizophrenia in previous studies [22,23]. Higher SAI and SAI-E scores indicate greater insight.

2.2.2. Neurocognitive functioning

A series of neurocognitive evaluations was undertaken. These tests consisted of the Wisconsin Card Sorting Test (WCST) [24], the third edition of the Wechsler Adult Intelligence Scale (WAIS-III) [25], the third edition of the Wechsler Memory Scale (WMS-III) [26], the Continuous Performance Task (CPT) [27], the Controlled Oral Word Association Test, [28] and the Line Cancellation Test [29].

Table 1
Domains of neurocognitive function

Domain	Test	Mean (SD)	Range
Executive function	WCST: the ratio of perseverative errors to the no. of trials administered	18.5 (11.3)	3.9-68.0
	CPT: no. of error responses	3.2 (4.0)	0-22
	WMS-III: working memory index	87.5 (14.7)	60-127
	WAIS-III: similarity	9.1 (2.8)	1-15
	WAIS-III: digit symbol	6.8 (2.8)	1-13
	Controlled Oral Word Association Test	38.9 (9.0)	21-65
Attention	Line Cancellation Test: total score	89.1 (1.6)	82-90
	CPT: no. of correct responses	27.1 (5.3)	2-31
	CPT: no. of omission errors	2.9 (4.1)	0-23
Memory	WMS-III: auditory immediate index	89.3 (17.4)	47-120
	WMS-III: visual immediate index	80.8 (16.8)	45-142
	WMS-III: auditory delayed index	91.3 (17.0)	46-124
	WMS-III: visual delayed index	79.0 (15.6)	47-132

Selected measures from individual tests were grouped into 3 cognitive domains based on findings from previous research [30,31]. Table 1 displays the neurocognitive function tests included in the domains of executive function, attention, and memory.

2.3. Procedures and statistical analysis

All subjects provided written informed consent. Two psychiatrists performed the semistructured interviews to determine insight of all subjects on the SAI and SAI-E, and psychopathology on the YMRS and HAM-D. A neuropsychologist performed a series of neuropsychological tests on all subjects without knowledge of their corresponding insight or clinical characteristics. A research assistant collected subjects' sociodemographic characteristics, duration of illness information, and numbers of previous manic and depressive episodes from the subjects and their chart records. The kinds of medications used for treatment were also recorded from the chart records.

Composite scores for each neurocognitive domain were calculated by converting the subjects' raw scores to standardized z scores. The z scores were then summed in each domain to provide a single score. A higher score indicated better neurocognitive function. Confirmatory factor analysis (CFA) was conducted to examine factor structure of the neurocognitive function tests. The χ^2 and other goodness-of-fit indices were used to assess the model fit of the neurocognitive function domains [32], and a nonsignificant χ^2 was interpreted as an indication of good model fit. Four additional fit indices were also used to assess model fit: comparative fit index (CFI), nonnormed fit index (NNFI), root mean square error of approximation (RMSEA), and standardized root mean residual (SRMR) [33]. The following were considered to be an indication of a well-fitting model: CFI >0.95, NNFI >0.95, RMSEA <0.08, and SRMR <0.08 [33-35]. Cronbach α was used to determine the internal consistency of each neurocognitive function domain [36].

Table 2
Sociodemographic and clinical characteristics and insight in bipolar subjects

	Mean (SD)	Range	n (%)
Sociodemographic characteristics			
Age (y)	40.8 (12.7)	16-75	
Education (y)	11.8 (3.4)	1-20	
Sex: male			50 (52.1)
Clinical characteristics			
YMRS score	0.7 (1.7)	0-6	
HAM-D score	0.8 (1.9)	0-6	
Duration of illness (mo)	149.0 (126.6)	1-516	
No. of previous mood episodes	5.1 (4.8)	1-20	
Have psychotic pictures			38 (39.6)
Poor response to mood stabilizers			30 (31.3)
Insight on the SAI			
Treatment compliance	2.9 (1.2)	0-4	
Awareness of illness	3.2 (2.0)	0-6	
Relabeling of phenomena	2.3 (1.4)	0-4	
SAI-E score	14.0 (7.4)	0-24	

The associations between insight, neurocognitive function, and sociodemographic and clinical characteristics were examined using the 2-step procedure of variable selection [37]. In the first step, univariate regression analyses were used to examine the association between insight and each factor. The significant factors were further selected and included in the stepwise multiple regression analysis to examine their association with insight. An α value of .05 was used to indicate significance for all statistical tests.

3. Results

The neurocognitive function test scores included in the domains of executive function, attention, and memory are shown in Table 1. The χ^2 for the hypothetic CFA model of neurocognitive function domains was 407.044 ($P > .05$). The values of NNFI, CFI, RMSEA, and SRMR were 0.936, 0.950, 0.080, and 0.079, respectively. The results indicate that the hypothetic factor CFA model fitted the data well. The value of Cronbach α for 3 neurocognitive function domains was 0.700 for executive function, 0.723 for attention, and 0.927 for memory, indicating satisfactory internal consistency.

Sociodemographic and clinical characteristics, and insight are shown in Table 2. The low mean present scores on the YMRS and HAM-D indicated that all bipolar subjects were in a state of remission. The associations between insight, neurocognitive function, and sociodemographic and clinical characteristics in the univariate analyses are shown in Table 3. The results indicated that executive function, memory, and education level were positively associated with the SAI dimensions of awareness of illness and relabeling of phenomena, and the SAI-E in remitted bipolar subjects. Furthermore, poor response to mood stabilizers in their courses of treatment was negatively associated with the SAI dimension of relabeling of phenomena and the SAI-E. However, the SAI dimension of treatment compliance was only negatively associated with poor response to mood stabilizers but not with any domain of neurocognitive function. Attention was not associated with any dimension of insight.

The significant factors described above were further included in the stepwise multiple regression analyses. The results indicated that by controlling confounding effects of other factors, executive function was still positively associated with the SAI dimensions of awareness of illness and relabeling of phenomena, and the SAI-E (Table 4).

4. Discussion

The principal finding of this study is that executive function is positively correlated with total SAI-E score. Further analyses found that executive function is positively

Table 3
The associations between insight and neurocognitive function and sociodemographic and clinical characteristics in univariate regression analyses

	Treatment compliance		Awareness of illness		Relabeling of phenomena		SAI-E score	
	β	t	β	t	β	t	β	t
Neurocognitive function								
Executive function	.172	1.688	.277	2.791**	.308	3.140**	.267	2.684**
Memory	.163	1.600	.228	2.273*	.221	2.198*	.219	2.174*
Attention	.040	0.387	.148	1.452	.104	1.018	.136	1.328
Sociodemographic characteristics								
Age	.123	1.199	−.115	−1.117	−.060	−0.583	−.037	−0.359
Education	.169	1.660	.214	2.128*	.225	2.240*	.205	2.027*
Sex: male	.133	1.297	.117	1.140	.064	0.617	.101	0.984
Duration of illness	.170	1.674	.135	1.324	.111	1.079	.123	1.201
No. of previous mood episodes	.114	1.114	.094	0.915	.047	0.453	.059	0.563
Have psychotic pictures	−.162	−1.589	−.069	−0.672	−.134	−1.312	−.124	−1.210
Poor response to mood stabilizers	−.226	−2.249*	−.160	−1.574	−.251	−2.517*	−.217	−2.153*

* $P < .05$.
** $P < .01$.

Table 4
Variables associated with insight examined by using multiple regression analyses

	Treatment compliance		Awareness of illness		Relabeling of phenomena		SAI-E score	
	β	t	β	t	β	t	β	t
Executive function	–	–	.277	2.791 **	.273	2.792 **	.267	2.684 **
Poor response to mood stabilizers	−.226	−2.249 *	–	–	−.205	−2.092 *	–	–

* $P < .05$.
** $P < .01$.

correlated with awareness of illness and relabeling of phenomena but not insight into treatment in the remitted bipolar patients. In Markova and Berrios's clinical model of insight [38], to detect formless experience, to register it against templates of past experience, and to judge it as unusual experience are basic processes of insight elaboration. Based on this hypothesis, executive function may influence the formation of insight in 2 pathways. First, a deficit of self-assessment and feedback into altering responses to changed situations may be important in the apparent unawareness of illness and symptoms in individuals with psychosis [39,40]. For example, individuals with poor insight would fail to alter their responses in the light of negative feedback on the WCST. Second, the inability to hold symptom information in working memory while comparing it with past experiences may make it difficult to recognize that a symptom is aberrant [41].

From the results of this study, there should be different strategies of ameliorating poor insight for bipolar patients with poor executive function. Lysaker et al (1998) proposed that if poor insight results from impairments in flexibility of abstract thought, then simple educative measures or guided success experiences may not be effective. Instead, the development of cognitive rehabilitation interventions that target such impairments in executive function may hold greatest promise for lasting change [42].

Memory impairment is a core symptom of many psychotic disorders. Keefe (1998) proposed that the effect of disrupted memory for perceptual events may dilute the original perceptual event, which creates similarities in the phenomenal experiences of memories of actual experiences and self-generated imagined events [43]. Furthermore, memory deficits could result in an individual's inability to retrieve supporting information about the event whose source is under consideration. However, memory was positively associated with awareness of illness and relabeling of phenomena only in the univariate but not in the multiple regression analyses.

Interest in the relationship between poor insight and attention deficit was initiated because of the finding that brain-damaged patients with attention deficit cannot discriminate the percept that arises from context and expectancy from that which reflects physical changes [44]. It was suggested that deficits in the distribution of attentional resources could result in impaired insight in psychotic patients [45]. The results of this study further support the observation that insight is not associated with attention deficit in bipolar patients.

Our study also found that unlike the awareness of illness and phenomena, insight into treatment was not correlated with neurocognition in this study, which further supports the observation that varieties of insight dimensions have different relationships with neurocognitive functions [39]. This result also suggests that insight in bipolar disorder should not be considered a single concept of a psychopathology.

Some limitations of this study should be addressed. The study sample consisted of a population of remitted bipolar patients with a long duration of illness. Furthermore, they were recruited from medical units. The study results may not be generalized to all patients with bipolar disorder.

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