

Experience of Subjective Symptoms in Euthymic Patients with Bipolar Disorder

Bipolar patients often experience subjective symptoms even if they do not have active psychotic symptoms in their euthymic state. Most studies about subjective symptoms are conducted in schizophrenia, and there are few studies involving bipolar patients. We examined the nature of the subjective symptoms of bipolar patients in their euthymic state, and we also compared it to that of schizophrenia and normal control. Thirty bipolar patients, 25 patients with schizophrenia, and 21 normal control subjects were included. Subjective symptoms were assessed using the Korean version of the Frankfurter Beschwerde Fragebogen (K-FBF) and the Symptom Check List 90-R (SCL90-R). Euthymic state was confirmed by assessing objective psychopathology with the Positive and Negative Syndrome scale of Schizophrenia (PANSS), the Young Mania Rating Scale (YMRS), and the Montgomery Asberg Depression Rating Scale (MADRS). K-FBF score was significantly higher in bipolar patients than in normal controls, but similar to that in schizophrenia patients ($F=5.86$, $p=0.004$, $R^2=2033.6$). In contrast, SCL90-R scores did not differ significantly among the three groups. Euthymic bipolar patients experience subjective symptoms that are more confined to cognitive domain. This finding supports the hypothesis that subtle cognitive impairments persists in euthymic bipolar patients.

Key Words : Bipolar Disorder; Euthymic State; Subjective Experience

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INTRODUCTION

Bipolar patients often experience subtle cognitive impairment (1-4) and functional disturbances during their euthymic states (5, 6). These subjective experiences may be related to distorted cognitive functions in these patients (7). The subjective experience of cognitive impairment may result from problems in central executive functions (8) or may be related to attentional style associated with stress (9). Such cognitive impairments consequently imply a breakdown in supervising attention systems. Because cognitive ability is critical in interpersonal relationships and social skills, the persistence of functional disturbances among euthymic bipolar patients may therefore be explained by cognitive impairment.

Most studies of subjective experiences have been conducted in patients with schizophrenia (10, 11). It is generally accepted that cognitive dysfunction persists in the remitted schizophrenics (2, 7, 12). In contrast, we do not have definite evidence of persistent cognitive dysfunction in euthymic patients with bipolar disorder (13-15). More recently, however, the number of studies on the persistence of cognitive and perceptual distortion in bipolar patients has increased (15-17).

To date, little attention has been paid to subjective cognitive impairment in bipolar disorder. To our knowledge, there

are few studies to compare subjective experience of patients with bipolar disorder with the patients with schizophrenia, and the results were inconsistent (3, 4, 12).

Subjective experiences are evaluated with questionnaires, which have shown only a moderate correlation with objective performance. Since subjective experiences may be distinct from objective pathology (18, 19), it is necessary to evaluate subjective experiences and objective symptoms separately. Representative tools available to evaluate subjective experiences are the Frankfurter Beschwerde Fragebogen (FBF) (20), the Bonn Scale of the Assessment of Basic Disturbances in Schizophrenia (BSABS) (11) and the Symptom Check List 90-R (SCL90-R) (21, 22). The FBF is used primarily to evaluate cognitive disturbances (20, 23), whereas the SCL90-R is used to evaluate a broader range of subjective psychiatric complaints (21).

The aims of this study were as follows: first, we tried to determine if euthymic bipolar patients experience subjective symptom that is distinguishable from the normal controls. Second, we tried to know if their subjective experiences are comparable to those of schizophrenics. Third, we also tried to determine whether these subjective experiences are affected primarily by cognitive impairment or by the perception of discomfort secondary to mood and psychotic symptoms.

MATERIALS AND METHODS

Subjects

Subjects with bipolar disorder and schizophrenia were recruited at the psychiatric department of a tertiary referral center with an inpatient ward for acute psychiatric patients between May and September 2004. Consecutively admitted patients who were diagnosed as bipolar I disorder or schizophrenia by Diagnostic and Statistical Manual for psychiatric disorder-IV criteria (24) were included. Total 72 subjects met the inclusion criteria (38 bipolar and 34 schizophrenia).

Of the 72 subjects who met the inclusion criteria, all gave informed consent. To avoid diagnostic uncertainties related to the spectrum of schizophrenia, patients who had psychotic periods without mood symptoms or mood incongruent psychotic symptoms were excluded (2 bipolar patients). We also excluded patients who failed to complete the questionnaires (1 schizophrenia and 2 bipolar patients), who had a history of organic mental disorder (1 bipolar and 3 schizophrenia patients), or who were currently abusing drugs or alcohol (3 bipolar and 4 schizophrenia patients). Thus, the patient sample consisted of 30 patients with bipolar disorder and 25 patients with schizophrenia.

Normal controls were recruited by advertisement. We interviewed 26 individuals. We investigated their demographic data, medical and psychiatric history. We excluded individuals with any medical or psychiatric illness that might affect cognitive function. We applied the same exclusion criteria as applied to the patient groups, leaving 21 normal control subjects.

Assessment

For patients with bipolar disorder and schizophrenia, data on illness characteristics, including the number of episodes, duration of illness, and family history, were compiled from patient interviews and medical records. In patients of whom we could not determine the age of onset, we used the age at first admission.

One of the authors conducted the clinical assessment. Objective psychopathology was assessed using the Positive and Negative Syndrome Scale of Schizophrenia (PANSS) (25-27), the Young Mania Rating Scale (YMRS) (28), and the Montgomery Asberg Depression Rating Scale (MADRS) (29). Euthymia was defined as a YMRS total score ≤ 12 (30) and a MADRS cutoff value ≤ 9 (31). Every bipolar patient was in an euthymic state. The PANSS total score of every schizophrenia patient was less than 60, and the mean of any three subscales of the PANSS (i.e. the PANSS positive, negative, and general scales) was not greater than 3 (mild).

Subjective cognitive impairments were assessed using the Korean version of the Frankfurt Beschwerde Fragebogen (K-FBF) (32) and the SCL90-R (22). The K-FBF and SCL90-R

are self-reporting scales. The K-FBF consists of 103 items and 10 phenomenological areas. Ten phenomenological areas are specific anxiety, selective attention, deterioration of discrimination, psychomotor disorder, perceptual disorder, cognitive floating, blocking symptoms, language disorder, automatic behavior disorder, and coping responses. Each item consists of a 6-point response scale, from 'strongly disagree' (1) to 'strongly agree' (5). As mentioned before, an abnormality assessed by the K-FBF is known to reflect cognitive dysfunction. We obtained total scores of K-FBF, which is standardized by sex and age in each of the three groups. The SCL90-R consists of 9 dimensions and 90 items. Nine dimensions are 'somatization', 'obsessive-compulsive', 'interpersonal sensitivity', 'depression', 'anxiety', 'depression', 'hostility', 'phobic anxiety', 'paranoid ideation', and 'psychoticism'. Each item consists of 5-point response scale, from 'not at all' to 'very severe'. Since it contains comprehensive psychiatric symptoms, it is useful for assessing overall subjective dysfunction. Standardized total score of SCL90-R that is called the 'global score index' was obtained in each of the three groups.

Statistical analysis

Analysis of variance (ANOVA) and the Kruskal-Wallis test were used to examine the differences among the three groups, and post hoc analysis was performed by the Duncan method. Independent t-test, Mann-Whitney U test, and Fisher's exact test were used to examine the difference between schizophrenia and bipolar disorder groups. All statistical analyses were performed using SPSS version 11.0 for Windows.

RESULTS

Demographic data and clinical characteristics

Table 1 shows the demographic characteristics of the bipolar disorder, schizophrenia, and normal control groups. There were no significant differences in the distribution of sex ($\chi^2=0.819$, $df=2$, $p=0.664$), age ($F=0.189$, $df=2$, $p=0.828$), and education years ($F=2.953$, $df=2$, $p=0.058$) among the three groups. There were significant differences in the employment ($\chi^2=25.02$, $df=2$, $p<0.001$), distribution of socioeconomic status ($\chi^2=11.66$, $df=4$, $p<0.020$), and marital status ($\chi^2=60.32$, $df=6$, $p<0.001$) among the three groups. There was no significant differences in employment ($\chi^2=0.262$, $df=1$, $p=0.609$), socioeconomic status ($\chi^2=7.087$, $df=2$, $p=0.069$) and marital status ($\chi^2=0.794$, $df=3$, $p=0.672$) between the bipolar disorder group and schizophrenia group. However, the bipolar disorder group showed a significantly lower rate of employment ($\chi^2=23.03$, $df=1$, $p<0.001$) than the normal control group. There were also significant differences in marital status ($\chi^2=34.33$, $df=3$, $p<0.001$) and socioeconomic status ($\chi^2=10.99$, $df=2$, $p=0.004$) between the bipolar dis-

order group and the schizophrenia group.

There was no significant difference in the number of previous episode ($t=-0.622$, $df=53$, $p=0.537$), age at onset ($t=-1.101$, $df=53$, $p=0.276$), duration of illness ($t=-1.831$, $df=53$, $p=0.073$), hospitalized period ($t=-0.915$, $df=2$, $p=0.640$), YMRS ($t=-1.473$, $df=53$, $p=0.147$), and PANSS positive symptom score ($t=1.556$, $df=2$, $p=0.126$) between the bipolar disorder group and the normal control group.

The bipolar disorder group showed significantly lower MADRS ($t=2.557$, $df=2$, $p=0.013$) and PANSS total ($t=6.494$, $df=53$, $p<0.001$), negative symptom ($t=-5.254$, $df=2$, $p<0.001$), and general symptom score ($t=5.301$, $df=2$, $p<0.001$) than the schizophrenia group (Table 2). There were no other significant differences between the bipolar disorder and schizophrenia groups.

Subjective experiences in the three groups

The K-FBF score differed significantly among the three

groups (Table 3) by ANOVA. The K-FBF standardized total score was significantly higher among bipolar patients than among normal controls, but was similar to the score of schizophrenia patients ($F=5.86$, $p=0.004$, $R^2=2033.6$). In contrast, the standardized total score on the SCL90-R did not differ significantly among the three groups ($F=3.102$, $p=0.051$, $R^2=246.776$).

All the phenomenological domain of K-FBF showed significant difference among the three groups (Table 4). The scores were significantly higher in the bipolar group than in the normal control group, and they were similar between the bipolar group and schizophrenia group.

Most dimension scores of SCL90-R did not show a significant difference among the three groups except depression, anxiety, phobic anxiety, and paranoid ideation (Table 5). Depression, anxiety, phobic anxiety, and paranoid ideation subscale scores of the bipolar group were similar to those of the normal control group, and they were lower than those of the schizophrenia group.

Table 1. Demographic characteristics of the two patient groups and the control group

Characteristics	Bipolar disorder (n=30)	Schizophrenia (n=25)	Normal (n=21)	χ^2/F	p
Sex					
Female (%)	12 (40.0)	13 (52.0)	10 (47.6)	0.819	0.664
Male (%)	18 (60.0)	12 (48.0)	11 (52.4)		
Age, yr (mean \pm SD)	35.0 \pm 11.0	34.0 \pm 8.7	33.57 \pm 4.1	0.189	0.828
Employed (%)	10 (33.3)	10 (40.0)	21 (100)	25.02	<0.001
Education, yr (mean \pm SD)	12.7 \pm 3.3	13.0 \pm 3.1	14.62 \pm 1.8	2.953	0.058
Marital status				60.32	<0.001
Single (%)	12 (40.0)	18 (72.0)	0 (0)		
Married (%)	11 (36.7)	6 (24.0)	21 (100)		
Divorced (%)	5 (16.7)	0 (0)	0 (0)		
Separated (%)	0 (0)	0 (0)	0 (0)		
Other (%)	2 (6.7)	1 (4.0)	0 (0)		
Socioeconomic status				12.27	0.009
Upper (%)	8 (26.7)	4 (16.0)	0 (0)		
Middle (%)	18 (60)	17 (68.0)	20 (100)		
Lower (%)	4 (13.3)	4 (16.0)	0 (0)		

Table 2. Clinical characteristics of the bipolar and schizophrenic groups

Characteristics	Bipolar disorder (n=30)	Schizophrenia (n=25)	t	df	p
Number of previous episodes	3.16 \pm 2.41	3.63 \pm 3.10	-0.622	53	0.537
Age at onset, yr (mean \pm SD)	25.8 \pm 9.2	23.4 \pm 6.8	-1.101	53	0.276
Duration of illness, months (mean \pm SD)	93.5 \pm 110.8	46.2 \pm 72.0	-1.831	53	0.073
Hospitalized period, months (mean \pm SD)	3.8 \pm 3.4	5.8 \pm 11.4	0.915	53	0.64
YMRS	5.3 \pm 4.6	3.6 \pm 4.1	-1.473	53	0.147
MADRS	1.9 \pm 2.4	4.1 \pm 3.9	2.557	53	0.013
PANSS positive symptoms	8.8 \pm 2.0	10.0 \pm 3.3	1.556	53	0.126
PANSS negative symptoms	8.4 \pm 2.1	13.2 \pm 4.5	5.254	53	<0.001
PANSS general symptoms	17.5 \pm 2.1	22.4 \pm 4.5	5.301	53	<0.001
PANSS total score	34.7 \pm 4.6	45.4 \pm 7.5	6.494	53	<0.001

YMRS, Young Mania Rating scale score; MADRS, Montgomery Asberg Depression Rating Scale score; PANSS, Positive And Negative Syndrome Scale.

Correlation of subjective experiences and objective psychopathology

There were no significant correlations between K-FBF total score and PANSS total score ($r=0.184$, $p=0.331$), YMRS total score ($r=0.328$, $p=0.077$), and MADRS total score ($r=0.246$, $p=0.191$). Standardized total score (global score index) of the SCL90-R also showed no significant positive correlations with PANSS total score ($r=0.333$, $p=0.072$) and YMRS total score ($r=0.341$, $p=0.066$). The SCL90-R, however, was significantly correlated with MADRS total scores ($r=0.512$, $p=0.004$).

DISCUSSION

We have shown here that subjective symptoms measured by K-FBF still exist in the euthymic bipolar patients. It implies the possibility that pathological processes of bipolar disorder progress silently even in the euthymic state. Current routine psychiatric assessments, however, are focused on objective psychopathology. We recommend to include items to evaluate subjective experiences as psychopathological assessment tools for bipolar patients.

In this study, mood states of all subjects were euthymic and objective psychopathology was not correlated to subjective symptoms measured by the K-FBF. Thus, subjective symptoms measured by K-FBF might not be secondary to psychosis or mood symptoms. This finding further supports that the subjective experience of bipolar patients is a distinct pathology from objective pathology.

Table 3. Subjective experiences among the three groups

Group	Bipolar disorder (n=30)	Schizophrenia (n=25)	Normal (n=21)	p
K-FBF	32.27 ± 17.69	37.04 ± 24.81	18.71 ± 8.63	0.004
SCL90-R	41.63 ± 8.96	46.32 ± 11.71	40.19 ± 3.09	0.051

K-FBF, Korean version of Frankfurter Beschwerde Fragebogen; SCL90-R, Symptom Check List 90-R.

Table 5. Comparison of subscale scores of SCL90-R among the three groups

	Bipolar disorder	Schizophrenia	Normal	F	p
Somatization	41.03 ± 5.25	44.84 ± 11.74	42.95 ± 4.33	1.613	0.206
Obsessive-compulsive	41.87 ± 11.00	46.28 ± 13.00	40.67 ± 3.41	1.974	0.146
Interpersonal sensitivity	43.00 ± 10.41	47.44 ± 11.40	41.95 ± 4.86	2.232	0.115
Depression	42.47 ± 9.23	47.85 ± 10.63	42.38 ± 4.02	3.254	0.044
Anxiety	42.90 ± 8.15	47.32 ± 11.54	40.62 ± 2.82	3.774	0.028
Hostility	43.37 ± 5.44	45.20 ± 8.68	43.62 ± 4.19	0.617	0.542
Phobic anxiety	45.13 ± 7.21	51.24 ± 14.37	42.29 ± 2.03		0.006
Paranoid ideation	43.67 ± 7.32	50.921 ± 2.94	41.95 ± 4.71		0.002
Psychoticism	44.07 ± 8.58	48.12 ± 9.42	42.81 ± 3.47		0.056

SCL90-R, Symptom Check List 90-R.

Subscale scores are presented as mean ± SD.

It is likely that the subjective experiences in bipolar patients are mainly caused by cognitive impairment. In contrast to the K-FBF score, which differed significantly between bipolar patients and controls, SCL90-R did not show a significant difference. The K-FBF mainly measures cognitive impairment in information processing (20), whereas the SCL90-R also measures various other physiological symptoms and complaints than the cognitive domain (21). Thus, the SCL90-R evaluates overall subjective dysfunction without specific restriction to the cognitive domain.

The degree of subjective cognitive impairments, as measured by the K-FBF, was comparable in bipolar patients and schizophrenics. Similar to schizophrenics, bipolar patients may be cognitively impaired. At present, however, we can not say for certain whether this common psychopathology is due to

Table 4. Comparison of ten phenomenological subscale of K-FBF among the three groups

	Bipolar disorder	Schizophrenia	Normal	F	p
Specific anxiety	3.20 ± 2.28	3.60 ± 2.74	1.90 ± 1.09	3.637	0.031
Selective attention	3.27 ± 2.23	3.84 ± 2.90	1.67 ± 0.92	5.758	0.005
Deterioration of discrimination	3.40 ± 1.96	4.04 ± 2.76	2.00 ± 0.89	5.771	0.005
Psychomotor disorder	3.67 ± 1.99	3.56 ± 2.52	2.14 ± 0.79	4.342	0.017
Perceptual disorder	3.13 ± 2.24	3.28 ± 2.62	1.71 ± 0.15	3.667	0.030
Cognitive floating	2.97 ± 1.88	4.15 ± 2.93	2.05 ± 0.12	5.682	0.006
Blocking symptoms	3.03 ± 1.83	3.68 ± 2.63	1.86 ± 0.15	4.869	0.010
Language disorder	3.10 ± 1.90	3.68 ± 2.66	2.10 ± 0.38	3.398	0.039
Automatic behavior disorder	3.07 ± 1.86	3.96 ± 3.08	1.52 ± 0.75	7.407	0.001
Coping responses	3.43 ± 2.25	4.04 ± 2.75	4.04 ± 2.75	6.605	0.002

Subscale scores are presented as mean ± SD.

a common etiology or phenomenological overlapping between two diseases.

We did not measure the influence of subjective experiences of bipolar patients on daily interpersonal and social activities in this study. However, we can be fairly certain that subjective experiences in euthymic bipolar patients is not routinely assessed and treated. Subjective experience is clinically neglected. Further research about their influence on the social and occupational functions is necessary. Attainment of a euthymic state may not be sufficient; rather, the remission of subjective experiences should be the target of treatment.

The present study has several limitations. First, the number of subjects was small and our patient groups may not be representative of the overall population of patients with bipolar disorder and schizophrenia. Second, medications that might have affected the patient's cognitive ability were not controlled. Third, we measured only subjective cognitive impairment, not the level of cognitive impairment objectively. Further studies including the assessment of objective cognitive impairment will be needed. Fourth, this study did not provide practical implications of subjective symptoms. Thus, additional research is necessary to confirm the relationship between subjective symptoms and difficulties in daily lives of individuals with bipolar disorder.

REFERENCES

- Cooke RG, Robb JC, Young LT, Joffe RT. *Well-being and functioning in patients with bipolar disorder assessed using the MOS 20-ITEM short form (SF-20)*. *J Affect Disord* 1996; 39: 93-7.
- Peralta V, Cuesta MJ. *Subjective experiences in psychotic disorders: diagnostic value and clinical correlates*. *Compr Psychiatry* 1998; 39: 11-5.
- Ricca V, Galassi F, La Malfa G, Mannucci E, Barciulli E, Cabras PL. *Assessment of basic symptoms in schizophrenia, schizoaffective and bipolar disorders*. *Psychopathology* 1997; 30: 53-8.
- Arduini L, Kalyvoka A, Stratta P, Gianfelice D, Rinaldi O, Rossi A. *Subjective experiences in schizophrenia and bipolar disorders*. *Eur Arch Psychiatry Clin Neurosci* 2002; 252: 24-7.
- Dion GL, Tohen M, Anthony WA, Waternaux CS. *Symptoms and functioning of patients with bipolar disorder six months after hospitalization*. *Hosp Community Psychiatry* 1988; 39: 652-7.
- Coryell W, Scheftner W, Keller M, Endicott J, Maser J, Klerman GL. *The enduring psychosocial consequences of mania and depression*. *Am J Psychiatry* 1993; 150: 720-7.
- Peralta V, Cuesta MJ. *Subjective experiences in schizophrenia: a critical review*. *Compr Psychiatry* 1994; 35: 198-204.
- Martin M, Jones G. *Distribution of attention in cognitive failure*. *Hum Learn* 1983; 2: 221-6.
- Broadbent DE, Broadbent MH, Jones JL. *Performance correlates of self-reported cognitive failure and of obsessiveness*. *Br J Clin Psychol* 1986; 25: 285-99.
- Huber G. *The concept of substrate-close basic symptoms and its significance for the theory and therapy of schizophrenic diseases*. *Nervenarzt* 1983; 54: 23-32.
- Gross G, Huber G. *Bonner Skala für die Beurteilung von Basis Symptomen*. Berlin, Springer, 1987
- Parnas J, Handest P, Saebye D, Jansson L. *Anomalies of subjective experience in schizophrenia and psychotic bipolar illness*. *Acta Psychiatr Scand* 2003; 108: 126-33.
- Weygandt W. *Über die mischzustände des manisch-depressiven irreseins*. Munich, Verlag von JF Lehmann 1899.
- Ferrier IN, Stanton BR, Kelly TP, Scott J. *Neuropsychological function in euthymic patients with bipolar disorder*. *Br J Psychiatry* 1999; 175: 246-51.
- Ferrier IN, Thompson JM. *Cognitive impairment in bipolar affective disorder: implications for the bipolar diathesis*. *Br J Psychiatry* 2002; 180: 293-5.
- Clark L, Iversen SD, Goodwin GM. *Sustained attention deficit in bipolar disorder*. *Br J Psychiatry* 2002; 180: 313-9.
- Cavanagh JT, Van Beck M, Muir W, Blackwood DH. *Case-control study of neurocognitive function in euthymic patients with bipolar disorder: an association with mania*. *Br J Psychiatry* 2002; 180: 320-6.
- Hermann D. *Know the memory: the use of questionnaires to assess and study memory*. *Psychol Bull* 1982; 92: 434-52.
- van den Bosch RJ, Rombouts RP, van Asma MJ. *Subjective cognitive dysfunction in schizophrenic and depressed patients*. *Compr Psychiatry* 1993; 34: 130-6.
- Süllwold L, Huber G. *Basic schizophrenic disorders*. *Monogr Gesamtgeb Psychiatr Psychiatry Ser* 1986; 42: 1-177.
- Derogatis LR, Cleary PA. *Factorial invariance across gender for the primary symptom dimensions of the SCL-90*. *Br J Soc Clin Psychol* 1977; 16: 347-56.
- Kim KI, Kim JH. *Korean manual of symptom check list-90-revision*. Seoul, ChungAng Aptitude Press 1984.
- Moritz S, Perro C, Woodward TS, Krausz M. *Subjective cognitive dysfunction in first-episode patients predicts symptomatic outcome: a replication*. *Psychopathology* 2002; 35: 367-8.
- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. Washington, D.C., American Psychiatric Association. 1994.
- Kay SR, Fiszbein A, Opler LA. *The positive and negative syndrome scale (PANSS) for schizophrenia*. *Schizophr Bull* 1987; 13: 261-76.
- Kay SR, Opler LA, Lindenmayer JP. *Reliability and validity of the positive and negative syndrome scale for schizophrenics*. *Psychiatry Res* 1988; 23: 99-110.
- Kay SR, Opler LA, Lindenmayer JP. *The Positive and Negative Syndrome Scale (PANSS): rationale and standardisation*. *Br J Psychiatry* 1989; 7: 59-67.
- Young RC, Biggs JT, Ziegler VE, Meyer DA. *A rating scale for mania: reliability, validity and sensitivity*. *Br J Psychiatry* 1978; 133: 429-35.
- Montgomery SA, Asberg M. *A new depression scale designed to be sensitive to change*. *Br J Psychiatry* 1979; 134: 382-9.
- Tohen M, Jacobs TG, Grundy SL, McElroy SL, Banov MC, Janicak PG, Sanger T, Risser R, Zhang F, Toma V, Francis J, Tollefson GD,

- Breier A. *Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-controlled study. The Olanzapine HGGW Study Group. Arch Gen Psychiatry* 2000; 57: 841-9.
31. Zimmerman M, Posternak MA, Chelminski I. *Defining remission on the Montgomery-Asberg depression rating scale. J Clin Psychiatry* 2004; 65: 163-8.
32. Kim JK, Chang HI, Yum TH, Song JY, Yoon DJ, Jeong WS, Oh DJ. *A Standardization Study of Kyung Hee-Frankfurter Beschwerde Fragebogen. Korean J Psychopathol* 1993; 2: 61-90.