



Effects of Behavioral Activation/Inhibition Systems as Predictors of Substance Abuse in Bipolar Patients

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Abstract

Background: Recently, more evidence has been presented regarding the role of behavioral activation/inhibition systems as predictors of substance use disorders. In fact, these systems are regarded as potentially important factors in the development of this complex psychiatric problem.

Objectives: This study aimed to determine how behavioral activation/inhibition systems, namely behavioral activation, behavioral inhibition, and fight-flight freezing systems, affect substance abuse in bipolar patients.

Methods: A total of 79 patients with bipolar disorder were selected among hospitalized patients in the psychiatric ward of Kamkar-Arabnia Hospital in Qom, Iran. The participants completed the Gray-Wilson personality questionnaire, Hamilton Rating Scale for Depression, Mood Disorder Questionnaire, and a sociodemographic questionnaire.

Results: Behavioral activation and behavioral inhibition systems emerged as significant predictors of substance abuse in bipolar patients ($\chi^2 = 52.511$; $df = 3$; $P < 0.0005$). Gender and type of bipolar disorder (I or II) showed no significant association with the scores of behavioral activation, behavioral inhibition, or fight-flight freezing systems. Also, the behavioral inhibition system scores could predict manic mood ($\chi^2 = 7.067$; $df = 3$; $P < 0.070$).

Conclusions: The findings of the current study provide further evidence regarding the role of behavioral activation and inhibition systems as predictors of substance abuse in bipolar patients.

Keywords: Addiction, Behavioral Activation/Inhibition Systems, Bipolar Disorder, Substance Abuse

1. Background

Bipolar disorder, as a common psychiatric problem, is associated with the high risk of suicide and suicidal behaviors (1-3). The cooccurrence of substance abuse with bipolar disorder is related to the complexity of clinical symptoms, disease trajectory and severity, poor treatment compliance, and high recurrence (4-7). Some studies suggest that substance use and bipolar disorders have common risk factors (8-10).

To explain the psychopathology of bipolar and substance use disorders, a large number of studies have applied Gray's reinforcement sensitivity theory (RST) (11). Gray suggested three systems for RST, including the behavioral approach system (BAS), behavioral inhibition system (BIS), and fight-flight system (12-14). BAS deals with conditioned and unconditioned appetitive stimuli and is activated in response to reward or termination of punishment with a positive response and approach (15, 16).

BIS is related to conditioned aversive stimuli and withdrawal/avoidance behaviors. The fight-flight system, recently revised as fight-flight-freezing system (FFFS) (14), deals with unconditional aversive stimuli and motivates avoidant or escape behaviors in response to aversive stimuli. Substantial evidence suggests that dysregulation of the Gray's system is related to the psychopathology of mental disorders, such as general anxiety, obsessive-compulsive disorder (17), bipolar disorder (18, 19), and substance use disorder (16).

BAS is one of the prominent psychological models of bipolar disorder (10, 20, 21). BAS dysregulation is hypothesized to play a major role in this type of disorder (20). It has been suggested that in bipolar disorders, the hypersensitivity of BAS leads to mania/hypomania symptoms, such as hyperactivity, increased goal-directed behaviors, increased energy, euphoric moods, and irritability (20-22). On the other hand, decreased activation of BAS can produce de-

pressive symptoms, such as lack of energy, low mood, anhedonia, and passivity (20, 21, 23, 24). Also, it is hypothesized that dysregulation of both BAS and BIS contributes to bipolar disorder.

According to the mentioned model of bipolar disorder, mania symptoms are related to high BAS and low BIS activation, while depressive symptoms are associated with high BIS and low BAS activation (25). The hypersensitivity of BAS and consequently the increased reward sensitivity are assumed to play a major role in addictive behaviors, including substance abuse and addiction among bipolar patients (10, 17). Similarly, recent findings have supported this model, which assumes that BAS hypersensitivity contributes to addiction and substance use disorders (16).

2. Objectives

The current study aimed to investigate the effects of BAS and BIS as predictors of substance abuse in bipolar patients, considering the importance of recognizing factors which can influence this disorder.

3. Materials and Methods

In this study, we aimed to determine which systems (i.e., BAS, BIS, and FFFS) can predict the type of bipolar disorder, hypomania, mania, and depressive episodes in bipolar patients. In addition, we studied whether the sensitivity of these systems could mediate the cooccurrence of bipolar and substance use disorders.

3.1. Patients

The study population included 79 inpatients (42 males, 37 females; mean age, 34.41 ± 8.99 years; range, 18 - 65 years), who were diagnosed with bipolar disorder type I or II, based on the diagnostic and statistical manual of mental disorders-fifth edition (DSM-V) criteria in a diagnostic interview. All patients were recruited from the psychiatric ward of Kamkar-Arabnia Hospital in Qom, Iran. During three months, 79 patients with bipolar disorder were selected via convenience sampling.

Substance abuse data were collected using a demographic questionnaire and medical records. According to the collected information, bipolar patients with drug abuse at admission were separated from other bipolar patients. For evaluation of depressive and manic/hypomanic moods, the Hamilton rating scale for depression (HRSD by Hamilton) (26, 27) and mood disorder questionnaire (MDQ by Hirschfeld) (28) were used. In addition, each participant completed the Gray-Wilson personality questionnaire (GWPQ) (29, 30) for evaluation of behavioral systems.

The participants also completed a sociodemographic questionnaire.

The exclusion criteria were as follows: (1) acute phase of disease, (2) poor psychological status affecting the subject's responses to questions, (3) bipolar disorder with psychotic features or other psychotic disorders, (4) dementia, epilepsy, or chronic diseases, and (5) inadequate skills for reading or comprehending the questionnaires. Data of the addictive group (n, 34) were as follows: gender (male), 79.4; age (mean \pm SD), 36.76 ± 8.2 years; education (mean \pm SD), 10 ± 2 years; marital status (single, married, and divorced), 23.5, 55.9, and 20.6; history of hospitalization (yes), 80.1; and type of bipolar disorder (type I), 61.8. The corresponding data in the normal group (n, 45) were as follows: 33.3 people; 32.64 ± 9.19 years; 12 ± 3 years; 46.7, 40.0, and 13.3 people; 40.9; and 28.9, respectively.

3.2. Data Collection Tools

The validity of HRSD was reported to range from 0.65 to 0.90, measuring depression severity (31). The interrater reliability was reported to be very high for the total HRSD score (0.80 - 0.98) (32). In a previous study, the sensitivity and specificity of this tool were 78.1% and 74.6%, respectively (33). The validity of the Persian version of this instrument was reported to range from 0.39 to 0.55 with respect to the dysfunctional attitudes scale and beck depression inventory (34).

In addition, the results showed that MDQ had relatively good sensitivity (0.73) and specificity (0.90) in an outpatient psychiatric sample (28). In this regard, a recent study reported an internal consistency coefficient of 0.25 for MDQ (35). In a previous study on an Iranian sample, a cut-off value of five, sensitivity of 0.63, specificity of 0.71, and test-retest reliability of 0.91 were reported for MDQ (36).

GWPQ (11, 12) is used to assess six typical rodent reactions to reinforcement: BAS (approach and active avoidance), BIS (passive avoidance and extinction), and FFS (fight and flight). In a study by Wilson and colleagues (30), this scale showed acceptable internal consistency (alpha coefficient, 0.6 - 0.7). Also, a strong relationship was found between fight and approach reactions and between flight and passive avoidance. Based on the findings, the internal consistency of the Persian version was 0.71 for BAS, 0.64 for BIS, and 0.59 for FFS (37).

The logistic regression model was used to determine if it is possible to predict the group of subjects according to quantitative variables. In this study, we used this model to predict the group of subjects in terms of addiction, based on the components of BIS, BAS, and FFFS. Statistical analysis was performed in SPSS version 21.

4. Results

A logistic regression analysis was performed with the state of addiction as the dependent variable and three components of BIS, BAS, and FFFS as the predictive variables. In general, 79 participants were included in the analysis. As presented in Table 1, the model was reliably significant ($\chi^2 = 52.511$; $df = 3$; $P < 0.0005$). The analysis showed that this model could explain 0.486 - 0.652 of variance in addiction.

The classification details showed that correct prediction was 91.1% for being non-addicted and 76.5% for being addicted; generally, 84.8% of predictions were correct (Table 2).

Also, BIS and BAS could significantly predict addiction, which shows that only these two components of the behavioral activation-inhibition system are valid for prediction in the model. Every unit of increase in the BIS component resulted in a 1.296 increment in the probability of not being addicted. Conversely, every unit of increase in the BAS component resulted in a 0.661 reduction in the probability of not being addicted. In other words, an increase in BIS and BAS reduced and increased the probability of addiction, respectively.

In the second analysis, the patient's mood at the time of assessment and depressive/manic moods (regardless of the type of bipolar disorder) were used as dependent variables, while components of the behavioral activation-inhibition system were entered as predictive variables. As indicated in Table 3, the model was only marginally significant ($\chi^2 = 7.067$; $df = 3$; $P < 0.070$). The analysis showed that this model could explain 0.086 to 0.114 of variance in having a depressive or manic mood at the time of evaluation.

The results of the analysis showed that the correct prediction percentage was 81.4% for being depressed and 47.2% for being manic; generally, 65.8% of predictions were correct (Table 4). Also, the analysis showed that only BIS could significantly predict depressive or manic mood, which shows that only this component of the behavioral activation-inhibition system is valid for prediction in the model. Every unit of increase in the BIS component resulted in a 0.895 reduction in the probability of depressive mood. In other words, an increase in BIS reduced the probability of depressive mood and increased the probability of manic mood.

Moreover, the logistic regression analysis was performed for predicting the type of bipolar disorder (type I or II). Gender was considered as the dependent variable, while the behavioral activation-inhibition system was regarded as the predictive variable; the results were insignificant. Therefore, patients with different types of mood disorders, regardless of their gender, could not be identified

in terms of the behavioral activation-inhibition system.

5. Discussion

The results indicated that the behavioral activation-inhibition system could differentiate between addicted and non-addicted patients with bipolar disorder. Addiction was distinguishable with an increase in BAS and a reduction in BIS. Previous studies have shown that bipolar patients often engage in impulsive and high-risk behaviors, including substance abuse (38). Several studies have also investigated the role of BAS/BIS in bipolar disorder, documenting a strong association between these systems and substance abuse (10, 17).

Our findings showed that in bipolar patients, BAS sensitivity could significantly predict addiction. Consistent with our finding, the results of several studies have indicated that BAS hypersensitivity plays a major role in substance abuse of bipolar patients (10, 16, 17, 39). In addition, it has been suggested that high activity and sensitivity of BAS are associated with substance use disorders (16). As some researchers have suggested (10), hypersensitivity of BAS can lead to the cooccurrence of bipolar disorder with substance abuse.

It is believed that some personality traits, such as impulsiveness (40, 41) and novelty seeking (42, 43), are among the most important factors related to both bipolar and substance use disorders. On the other hand, some studies have found that these personality traits are associated with the activation-inhibition system (19, 44). It seems that personality traits, such as high impulsivity and novelty seeking, act as mediators between BAS hypersensitivity and substance abuse in these patients.

The present study indicated that reduction of BIS was related to the increased risk of substance abuse in bipolar patients. This finding implicates that an increase in BAS activity and simultaneous reduction of BIS activity can lead to substance abuse (an impulsive behavior) in bipolar patients. Reduction of BIS activity has been suggested to reduce responses to frightful and conditioned stimuli and result in impulsive, novelty-seeking, and sensation-seeking behaviors.

Additionally, the results indicated that the high activity of BIS could predict manic moods in bipolar patients considering their mood at the time of assessment (depressive versus manic mood episodes), while previous research reports that high activity of BAS is related to mania and hypomania symptoms (20-22). The heterogeneity of samples, cooccurrence of substance abuse and bipolar disorder, and comorbidities (concurrency of bipolar disorder with other disorders) can be the causes of this inconsistency.

Table 1. The Omnibus Tests of Model Coefficients and Model Summary

| | Chi-Square | df | P Value | -2-Log Likelihood | Cox & Snell R-Square | Nagelkerke R-Square |
|---------------|------------|----|---------|-------------------|----------------------|---------------------|
| Step 1 | | | | 55.470 | 0.486 | 0.652 |
| Step | 52.511 | 3 | 0.000 | | | |
| Block | 52.511 | 3 | 0.000 | | | |
| Model | 52.511 | 3 | 0.000 | | | |

Table 2. The Classification of Variables in the Equation^a

| Observed | Predicted | | | B | SE | Wald | df | P Value | Exp (B) | |
|---------------------------|-----------------------|------|------|-------------------------|--------|-------|--------|---------|---------|---------|
| | Subjects ^b | | | | | | | | | |
| | A | B | C | | | | | | | |
| Step 1 | | | | Step 1 ^c BIS | 0.259 | 0.100 | 6.745 | 1 | 0.009 | 1.296 |
| Depressive mood | 8 | 76.5 | | BAS | -0.414 | 0.098 | 17.833 | 1 | 0.000 | 0.661 |
| Manic mood | 26 | 41 | 91.1 | FFFS | -0.024 | 0.087 | 0.076 | 1 | 0.782 | 0.976 |
| Overall percentage | 4 | | 84.8 | Constant | 6.703 | 2.679 | 6.263 | 1 | 0.012 | 815,027 |

^a The cut-off value is 0.500.

^b A: addicted; B: non-addicted; C: percentage of correct predictions.

^c Variable (s) were entered in step 1 (BIS, BAS, and FFFS).

Table 3. The Omnibus Tests of Model Coefficients and Model Summary

| | Chi-Square | df | P Value | -2-log likelihood | Cox & Snell R-Square | Nagelkerke R-Square |
|---------------|------------|----|---------|-------------------|----------------------|---------------------|
| Step 1 | | | | 101.829 | 0.086 | 0.114 |
| Step | 7.067 | 3 | 0.070 | | | |
| Block | 7.067 | 3 | 0.070 | | | |
| Model | 7.067 | 3 | 0.070 | | | |

Table 4. Classification of Variables in the Equation^a

| Observed | Predicted | | | B | SE | Wald | df | P Value | Exp (B) | |
|---------------------------|-----------------------|----|------|-------------------------|--------|-------|-------|---------|---------|-------|
| | Subjects ^b | | | | | | | | | |
| | A | B | C | | | | | | | |
| Step 1^c | | | | Step 1 ^c BIS | -0.111 | 0.052 | 4.504 | 1 | 0.034 | 0.895 |
| Depressive mood | 35 | 8 | 81.4 | BAS | 0.058 | 0.048 | 1.440 | 1 | 0.230 | 1.060 |
| Manic mood | 19 | 17 | 47.2 | FFFS | 0.054 | 0.053 | 1.041 | 1 | 0.308 | 1.055 |
| Overall percentage | | | 65.8 | Constant | 0.528 | 1.407 | 0.141 | 1 | 0.707 | 1.696 |

^a The cut-off value is 0.500.

^b A: addicted; B: non-addicted; C: percentage of correct predictions.

^c Variable (s) were entered in step 1 (BIS, BAS, and FFFS).

There was no significant association between the type of bipolar disorder (I and II) and behavioral activation-inhibition system. In this study, the behavioral activation-inhibition system was unable to predict the type of bipolar disorder. This finding is inconsistent with another previous study (19), which reported that BAS scores were significantly higher in patients with type I bipolar disorder, compared to those with type II disorder. It seems that type of disorder is not affected by the type of behavioral activation-inhibition system; in other words, regardless of the type of disorder, dysregulation of the behavioral activation-inhibition system serves as a risk factor for all types of bipolar spectrum disorders.

In both types of bipolar disorder, I and II, an increase occurs in BAS, as confirmed in the current study. However, if the difference in the severity of bipolar disorders (I and II) is significant, the score of BAS will be higher in type I patients, compared to patients with type II bipolar disorder. Therefore, differences in the severity of signs and symptoms between patients with type I and II bipolar disorders should be considered when comparing samples according to the type of disorder.

No significant association was found between the gender of patients and BAS or BIS activity; in other words, gender could not predict BAS or BIS activity. Therefore, personal neurobiological variables may play a more impor-

tant role in BAS and BIS activities of bipolar patients in comparison with gender. The unavailability of outpatients for participation in this study may be considered as one of its limitations, which should be taken into account in future studies.

5.1. Conclusion

The results of this study provided further evidence regarding the role of BAS and BIS as predictors of substance abuse in bipolar patients. In addition to the explanatory models of bipolar disorder and substance abuse, these results can be used for specific physical and psychological interventions, which are designed to help patients with these disorders.

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Footnotes

Authors' Contribution: The first author wrote the primary draft of the manuscript. The second author participated in designing the research project and helped to draft the manuscript. The third author performed the statistical analysis and revised the manuscript. The fourth author collected the clinical data. All authors read and approved the final manuscript.

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