# Impulsivity in tramadol dependence and bipolar I disorder patients: a comparative study

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## **Background**

Tramadol has become widespread in Egypt. Impulsivity is recognized as a factor in the initiation and maintenance of substance use disorders. Moreover, bipolar disorder (BD) is commonly associated with impulsivity. Impulsivity seems to be relatively independent of mood state and is higher in individuals with past history of substance use. So, comparing impulsivity in BD and tramadol dependence is needed to determine if there is any difference. Impulsivity was evaluated by the Barratt Impulsiveness Scale in 30 male patients with BD in partial remission without any comorbid substance use disorder and age-matched 30 male patients with tramadol dependence in partial remission. Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID1), addiction severity index, Young Mania Rating Scale, and Eysenck's Personality Questionnaire were used.

#### Results

There was no difference among BD and tramadol dependence groups of patients on subscales attentional and motor impulsivity measures. However, the male tramadol dependence patient group scored higher than the male BD patient group for total and nonplanning impulsivity scores.

#### Conclusion

This study found that BD and tramadol dependence patients were similar on attention and motor impulsivity subscales but on the total score and nonplanning subscale, patients with tramadol dependence are more impulsive than patients with BD. Increased tendency to criminal behavior is associated with the increase in total and motor scores of Barratt Impulsiveness Scale in tramadol dependence patients as well as with the total scores of Young Mania Rating Scale in BD patients. Moreover, the severity of mania is correlated with the attentional domain of impulsivity.

## Keywords:

bipolar disorder, impulsivity, tramadol dependence

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## **Background**

The propensity to act on an impulse without hesitation or concern for the consequences is known as impulsivity. Impulsive decisions are often ill-conceived, abrupt, and may result in unfavorable outcomes (Burnett Heyes *et al.*, 2012).

Impulsivity is categorized into two parts: trait impulsivity, which is a constant aspect of impulsivity through episodes of the disorder, and state impulsivity, which varies depending on the state of the disorder (Celikeloglu *et al.*, 2015).

Despite the fact that impulsivity is not a psychiatric diagnosis, it seems to be an indication that is more common with some mental disorders such as personality disorder, bipolar disorder (BD), impulse-control disorder, and substance use (Ozten *et al.*, 2015).

BD is a common mental illness with an overall lifetime prevalence of about 1% in the general population (Müller-Oerlinghausen *et al.*, 2002).

Patients with BD display increased impulsivity not only during a manic state but also during an euthymic state (Strakowski *et al.*, 2010).

In bipolar and related disorders, impulsivity has both state-dependent and trait-dependent components. The trait-dependent component, reflected in personality measures such as the BIS (Barratt Impulsiveness Scale) may be related to relatively stable biological

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measures of impulsivity such as the level of serotonergic function (Manuck et al., 1998).

The state-dependent component, reflected by increased commission errors in a challenging version of the Continuous Performance Test (the Immediate and Delayed Memory Tasks) (IMT-DMT), seems to correlate with severity of manic but not of depressive symptoms (Swann et al., 2001).

The link between impulsivity and drug abuse has been extensively researched. A consistent relationship has been found in cross-sectional studies (Johnson et al., 2003) and prospective studies measuring substance use from early adolescence (Tarter et al., 2004).

A number of research groups have suggested that impulsivity is not a homogeneous construct, but rather consists of at least two related dimensions (Reynolds et al., 2006). The first of these dimensions (reward drive) relates to the motivating factors that are most instrumental in the decision to use substances, and influence the continued use of substances. The second dimension, implicated in drug use (rash impulsiveness), is the decreased ability to cease the drug-taking behavior once an approach response has started, despite future negative consequences of that behavior (Dawe et al., 2004).

The abuse of tramadol has widely expanded Egypt since 2008 leading to increasing addiction treatment center admissions due to its use (Abolmaged et al., 2013). Tramadol is the second most common abused drug in Egypt after cannabis (Sabry et al., 2015). It is also implicated in 18.7% of road accident deaths in Egypt, which has one of the highest rates of trafficrelated mortality worldwide (Fawzy et al., 2010).

Therefore, the aim of this study was to assess impulsivity in patients with BD and patients with tramadol dependence and to compare impulsivity of patients with BD and patients with tramadol dependence.

# Methods

# **Participants**

This study was a comparative, cross-sectional study. The Scientific and Ethics committees of the Department of Psychiatry, Faculty of Medicine, Cairo University has approved the study. A written informed consent was taken from patients after discussing with them the aim of the study. A convenient sample of 60 male patients aged 18-45 years was recruited from Psychiatry and Addiction Treatment Hospital of Cairo University, Faculty of Medicine (Kasr Al-Ainy) over a period of 6 months. The sample consists of 30 patients fulfilling the DSM IV criteria of tramadol dependence as the main addictive substance in early partial remission in whom none of the criteria for tramadol use disorder have been met for at least 3 months but for less than 12 months (with the exception of craving, or a strong desire or urge to use tramadol, may be met).

Thirty patients fulfilling DSM IV criteria of bipolar I disorder, most recent episode manic in partial remission, these patients are being in remission for at least 1 month from the last episode and this was determined clinically and by a Young Mania Rating Scale (YMRS) of 7 or less at the end point, with no core item of the YMRS (i.e. irritability, speech, and disruptive aggressive behavior) having a score greater than two patients with comorbid psychiatric disorder (dual diagnosis), organic brain conditions, and clinically below average intelligence quotient (IQ) were excluded from the study.

## **Tools**

**Patients** subjected to Kasr Al-Ainy semistructured interview and the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID) (First et al., 2002) to establish the diagnoses of bipolar I disorder and tramadol dependence. Tramadol dependence patients were subjected to the Addiction Severity Index (ASI) (McLellan et al., 1992), Arabic version (Qasem et al., 2003). The YMRS (Young et al., 1978) was administrated to the bipolar I disorder group of patients. Both groups of patients were subjected to the Barratt impulsiviness scale-11 (Patton et al., 1995) and Eysenck's Personality Questionnaire (EPQ) (Eysenck and Eysenck, 1975) translated to Arabic by Ahmed Mohamed Abdel Khalek in 1983 (Abdel Khalek and Eysenck, 1983).

Psychometric tools used in the study:

Structured clinical interview for DSM-IV-TR axis I disorders (SCID I)

The structured clinical interview for DSM-IV-TR axis I disorders (SCID I) is a clinician-administered, semistructured interview for use with psychiatric patients or with nonpatient community subjects who are undergoing evaluation for psychopathology. The SCID I was developed to provide coverage of psychiatric diagnosis according to DSM-IV. It is designed to be more efficient and simpler to use compared with the existing instruments consequently requires less time training and administration.

Structured clinical interview for DSM-IV-TR axis II disorders (SCID II) is a semistructured interview of 108 questions arranged according to diagnosis, yielding both categorical diagnoses and dimensional scores for each of DSM-IV personality disorders.

## **EPQ**

It is used to assess neuroticism, psychoticism, introversion &z.urule; extroversion, criminality, and lie scale.

The questionnaire is formed of 90 questions to be answered by yes or no. Each one of the five dimensions has certain questions and each question takes a score and then the total score for each dimension is calculated.

## Barratt impulsiveness scale-11

BIS-11 is the most commonly administrated selfreport measure for the assessment of impulsivity in both research and clinical settings. It was translated into Arabic and then back translated to English to check the translation in Kasr Al-Ainy Psychiatry Department. Over the last 50 years, the BIS-11 has significantly influenced the way that impulsivity is conceptualized in psychology and psychiatry.

The BIS, version 11 (BIS-11) is a 30-item self-report questionnaire designed to assess general impulsiveness.

It is proposed that impulsiveness is composed of three subtraits:

Attentional impulsiveness is defined as an inability to focus attention or concentrate (eight items): 5,6,9,11,20,24,26,28.

Motor impulsiveness is defined as acting without thinking (11 items): 2,3,4,16,17,19,21,22,23,25,30.

Nonplanning impulsiveness is defined as a lack of 'futuring' or forethought (11 items): 1,7,8,10,12, 13,14,15,18,27,29.

ASI is a semistructured interview for substance abuse assessment and treatment planning. The ASI is designed to gather valuable information about areas of a client's life that may contribute to their substanceabuse problems. It is designed to address seven potential problem areas in substance-abusing patients: medical status, employment and support,

drug use, alcohol use, legal status, family/social status, and psychiatric status.

#### **YMRS**

The YMRS is one of the most frequently utilized rating scales to assess manic symptoms. The scale has 11 items and is based on the patient's subjective report of his clinical condition over the previous 48 h. Additional information is based on clinical observations made during the course of the clinical interview.

There are four items that are graded on a 0—8 scale (irritability, speech, thought content, and disruptive/ aggressive behavior), while the remaining seven items are graded on a 0-4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients.

The YMRS is a rating scale used to evaluate manic symptoms at baseline and over time in individuals with mania.

The scale takes 15–30 min to complete.

#### Statistical analysis

All data were computed and conducted the SPSS (Statistical Package for Social Sciences version 16) (SPSS Inc., Chicago, USA) software for statistical analysis. Descriptive statistics were used illustrating the mean and SD of quantitative data. The variables were analyzed using the suitable tests for comparison (e.g. t-test, analysis of variance,  $\chi^2$  as indicated as well as the suitable measures of association (Pearson's correlation and regression).

# Results

The two groups included in the study were matched regarding age, education, and marital status. The demographic characteristics of the study participants are illustrated in Table 1.

As regards clinical data, the comparison between both groups revealed that 23.3% of the BD group of patients had a history of suicidal attempts versus 13.3% of the tramadol dependence group of patients with no difference statistically significant (P=0.506).Furthermore, it was found that 86.7% of tramadoldependent patients (group I) had no personality disorder versus 93.3% of bipolar I disorder patients. Borderline personality disorder was 3.3% of tramadoldependent patients as well as bipolar I disorder patients

Also, 6.7% of tramadol-dependent patients and 3.3% of bipolar I disorder patients group had antisocial personality disorder. In addition, histrionic personality disorder was found in 3.3% of tramadol-dependent patients and in none of bipolar group of patients. This comparison between both groups show statistically significant difference as *P*=0.714.

As regards psychometric data, there was a statistically significant difference between both groups as regards the presence of impulsivity, on non-planning scale and total scores showing P-values of 0.003 and 0.005, respectively, as shown in Table 2.

Moreover, the comparison between both groups showed no statistically significant difference across the different domains of the EPQ: psychoticism scale, neuroticism scale, criminality scale, lie scale, extroversion scale. P-values are 0.808, 0.280, 0.161, 0.093, and 0.880, respectively.

It was found that age of the patients showed statistically significant positive correlation (P=0.033) with motor impulsivity domain of BIS as well as with ASI occupational and legal subscales (P=0.019, 0.030, respectively).

Concerning the group of tramadol addiction statistically significant patients, positive correlation between the legal state and total score of BIS (P=0,031) as well as between the legal state and motor subscale of BIS was detected (P=0.013). In addition, our study showed that increase in total score of BIS is associated with more severe psychiatric problems (P=0.040). Moreover, the increase in the severity of family troubles was associated with increased scores of motor subscale of BIS (P=0.043). Furthermore, a statistically significant positive correlation (*P*=0.005, 0.008) was revealed between the motor domain and total score of BIS, respectively, and criminality subscale of EPQ as shown in Fig. 1.

Concerning the BD group of patients, our study showed that increased scores of YMRS is associated with the increase in the attentional subscale of BIS (*P*=0.034). Moreover, a statistically significant positive correlation (P=0.018) was revealed between the YMRS scores and criminality subscale of EPQ as shown in Figure 2.

Table 1 Demographic characteristics of the participants of the two groups (patients with tramadol dependence, patients with

	Tramadol dependence $[n \ (\%)]$	Bipolar disorder [n (%)]	P value	
Age (mean±SD)	28.83±5.36	28.83±5.49		
Education				
Primary	8 (26.7)	5 (16.7)	0.224	
Preparatory	7 (23.3)	4 (13.3)		
Secondary	9 (30)	17 (56.7)		
Higher education	6 (20.0)	4 (13.3)		
Occupation				
Not working	15 (50.0)	7 (23.3)	0.039	
Noskilled	7 (23.3)	16 (53.3)		
Skilled	8 (26.7)	7 (23.3)		
Marital status				
Single	15 (50)	11 (36.7)	0.416	
Married	13 (43.3)	18 (60)		
Divorced	2 (6.7)	1 (3.3)		

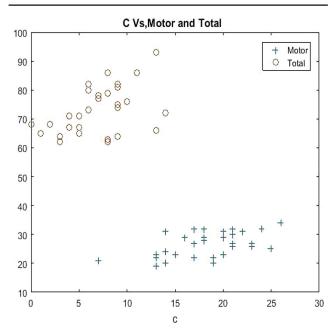
Table 2 Impulsivity in the patients with tramadol dependence, patients with bipolar disorder on using Barratt impulsiveness scale

BIS	Group	N	Mean	SD	Р
Attentional domain	Tramadol Dependence	30	18.2333	2.48698	0.103
	Bipolar I Disorder	30	16.9000	3.63271	
Motor domain	Tramadol Dependence	30	26.5667	4.35243	0.203
	Bipolar I Disorder	30	25.0000	5.05146	
Nonplanning domain	Tramadol Dependence	30	28.4000	4.16554	0.003
	Bipolar I Disorder	30	24.9667	4.34292	
Total score	Tramadol Dependence	30	73.2000	8.20177	0.005
	Bipolar I Disorder	30	66.8667	8.64923	

 $P \le 0.05$  is significant.

As regards the correlation between age of the patient and impulsivity, this study found that age has a statistically significant positive correlation (P=0.033) with motor impulsivity domain of BIS in tramadol-dependent patients; this is illustrated in Figure 3, where no statistically significant correlation was found between age of the patient and impulsivity domains in BD group of patients.

Figure 1



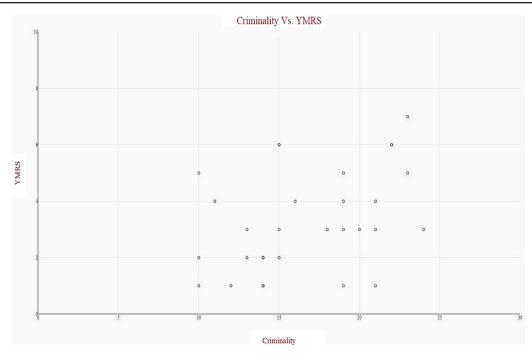
Correlation of criminality and motor domain and total score of Barratt Impulsiveness Scale in the tramadol-dependent group.

## **Discussion**

This study results found that total impulsivity, attention subscale, motor and non-planning scores are high on BIS in both groups. There is statistically significant difference between both groups in total impulsivity score and nonplanning subscale of BIS. Group 1 (the tramadol-dependent patients) showed statistically significant higher scores on nonplanning subscale and total score of BIS more than group 2 (bipolar 1 disorder patients). Elevated levels of impulsivity is thought to be core and pervasive feature of both BD and substance use disorders. More impulsive individuals with BD may be more susceptible to substance abuse or substance abuse itself could cause impulsivity to be increased in general, so BD and substance abuse would be associated independently with increased impulsivity (Dawes et al., 1997; Lejoyeux et al., 1999).

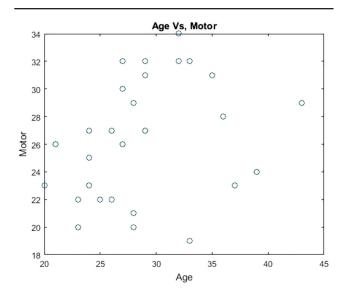
Previous studies had investigated the difference of impulsivity between isolated BD and SUD. It was found that isolated BD and SUD both have increased total impulsivity, subscale attention; and motor impulsivity did not differ which is consistent with our results. However, on the nonplanning subscale, BD patients are more impulsive than substance use disorder patients which is opposite of the result obtained in this study. Nonplanning impulsivity was higher in BP than in substance use disorder. This refers to BD patients having special features when they are compared with SUD about impulsivity: lack of sense of future (Ozten et al., 2015).

Figure 2



Correlation of criminality and Young Mania Rating Scale scores in bipolar I disorder group.

Figure 3



Correlation of age and motor impulsivity domain of Barratt Impulsiveness Scale in tramadol-dependent group.

In this study, the bipolar sample was in partial remission and by clinical assessment the sample did not show any significant symptoms of manic episode but the period of remission has been less than 2 months. Findings in this work confirm prior results of higher levels of impulsivity even when patients are euthymic (Peluso et al., 2007; Swann et al., 2008). These findings indicate that the impulsivity found among bipolar patients may be independent of mood state.

There was statistically significant positive correlation between the legal state and total score and motor subscale of BIS. This means that increased total score and motor subscale score are associated with increased severity of legal state. This is consistent with Rodríguez-Cintas et al. (2016), who found that cocaine-opioid dependent patients had higher scores in drugs and legal subscores of ASI, a finding that could be related to the enhancing effect of both substances. There was statistically significant positive correlation between the family status and motor subscale of BIS. This means that increase in the severity of family troubles is associated with increased scores of motor subscale. These findings are consistent with a review done on substance dependence consequences, which states that substance abuse is more than a health issue; it is a significant moral, social, and economic dilemma with widespread implications (WHO, 2014).

In this study, there was a positive correlation between criminality and total and motor subscales of impulsivity in tramadol-dependent patients. Studies have shown that the most common crimes committed by addicts involve stealing money or jewelry first from the family members. Due to cultural stigma many families may find reporting thefts by a family member difficult, which may explain why 80% of the studied group sample had no or mild legal problems. Participants, who had legal problems whether mild, moderate or severe, varied between dealing drugs, assault, driving under influence, embezzlement, financial schemes, and robberies. In a study by Easton et al. (2000), it was found that drug abuse and treatment nonadherence were linked to acts of violence and against property. They also discovered that criminal inclinations are linked to a person's willingness to modify their substance usage behaviors. There was statistically significant positive correlation between psychiatry state and the total score of BIS. This means that increased total score of BIS is associated with more severe psychiatric problems. A previous Egyptian study has found that the psychiatric dimension was the most considerate problem in tramadol dependent patients according to the ASI (Mohamed et al., 2015).

Psychiatric manifestations co-occurring with substance dependence were found to be as the long-term effects of neurobiological adaptations and opioid system dysregulation caused by long-term drug use. These effects are the result of long-term activation of the m receptor opiate drugs, which causes neurochemical changes in opioid receptor-bearing neurons (Kieffer and Evans, 2002).

There was statistically significant positive correlation between the YMRS scores and attentional subscale of BIS. This means that increased scores of YMRS is associated with an increase of attentional impulsivity. This is in line with Swann et al. (2007), who found that increasing Mania rating scale score was associated with more frequent and more rapid impulsive responses on the IMT, reflecting the tendency to make rapid, There unplanned responses. was statistically significant positive correlation between the YMRS and criminality subscale of EPQ. This means that increased scores of YMMS is associated with increased criminal behavior. This is consistent with a study by Swann et al. (2011), who found that selfreported criminal history was related to a recurrent course of illness with predominately manic episodes, and also participants reporting histories of convictions had a recurrent course of illness with predominately manic episodes, with increased probability of substance use disorders and suicide attempts. Furthermore, a large community-based study found predominately manic course tripled the prevalence of conviction history (Graz et al., 2009) and a crime registry study found that those individuals who had been released from a mental health facility for an affective condition, their proclivity for mania was linked to later conviction (Soyka and Zingg, 2010).

#### Limitations

The sample size of this study was limited, so the results of this study cannot be generalized. Moreover, the use of medications could potentially be a limitation as mood stabilizers are used in managing impulsivity. Moreover, the correlation of onset of illness and duration of illness with impulsivity was investigated in this study Finally, no female patients were included in the study due to the limited number of female substance users seeking psychiatric help. This is due to the cultural concepts related to stigma in Arabian communities toward substance use in females.

## Conclusion

The tramadol-dependent patients showed statistically significant higher scores on nonplanning subscale and total score of BIS than bipolar 1 disorder patients. Increased tendency to criminal behavior is associated with the increase in total and motor scores of BIS in tramadol-dependent patients as well as with the total scores of YMRS in the bipolar group of patients. Furthermore, the severity of mania is correlated with the attentional domain of impulsivity.

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#### **Conflicts of interest**

There are no conflicts of interest.

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