Impulsivity, aggression and suicidal behavior in unipolar and bipolar disorders

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ARTICLE INFO

Article history:
Received 6 April 2011
Received in revised form 25 May 2011
Accepted 26 May 2011
Available online 1 July 2011

Keywords: Impulsivity
Aggression
Suicidal behavior
Bipolar disorder
Mood disorders

ABSTRACT

Background: Predictors of suicidal behaviors (SB) in bipolar (BD) and major depressive disorder (MDD) patients are poorly understood. It has been recognized that behavioral dysregulation characterizes SB with traits of impulsivity and aggression being particularly salient. However, little is known about how these traits are segregated among mood disorder patients with and without a history of suicide attempt (SA).

Methods: This article aims to compare impulsivity and aggression between 143 controls, 138 BD and 186 MDD subjects with or without a history of SA.

Results: BD and MDD patients showed higher impulsivity scores (BIS-10=57.9 vs. 44.7, \( p<0.0001 \)) and more severe lifetime aggression than controls (Lifetime History of Aggression=7.3 vs. 3.9, \( p<0.0001 \)). Whereas impulsivity helped to distinguish MDD subjects without a history of SA from those with such a history, this was not the case in BD subjects where no difference in impulsive traits was observed between BD without and with history of SA (57.2 vs. 63.2 for BIS-10; \( p=0.259 \)). Impulsive and aggressive traits were strongly correlated in suicide attempters (independently of the diagnosis) but not in non-suicide attempters.

Limitations: Dimensional traits were not characterized at different stages of illness.

Conclusions: Impulsivity, as a single trait, may be a reliable suicide risk marker in MDD but not in BD patients, and its strong correlation with aggressive traits seems specifically related to SB. Our study therefore suggests that the specific dimension of impulsive aggression should be systematically assessed in mood disorder patients to address properly their suicidal risk.

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1. Introduction

Affective disorders are commonly associated with a high rate of suicide attempts (SA) and completion. Lifetime prevalence of suicidal behavior (SB) is particularly elevated in bipolar disorder (BD) patients and was generally found to be higher than in major depressive disorder (MDD) subjects (Rihmer and Kiss, 2002). For instance, it has been estimated that the rate of suicide attempts in MDD and BD patients is two to six times higher respectively than in the general population (Tondo et al., 2007). However, not all patients suffering from BD or MDD actually attempt suicide. Additional factors must therefore play a role in increasing the suicide risk in these clinical populations.

Numerous studies have strongly suggested that impulsivity represents such a risk factor, either independently or in
association with aggressive and/or anxious traits (Apter et al., 1993; Brodsky et al., 2001; Dumais et al., 2005; Horesh et al., 1999; Oquendo et al., 2000). Accordingly, impulsivity should be more pronounced in mood disorder patients who have made one or more SA than in those patients who never displayed any kind of SB (Carpiniello et al., 2011; Swann et al., 2009). This relationship must also be somehow independent of the nature of the underlying disorder. The situation is nevertheless complicated by the fact that impulsive behavior is commonly associated with BD (Swann et al., 2009) and with borderline personality disorder (BPD), a condition characterized by recurrent depressive episodes and repeated SA (Leichsenring et al., 2011).

From this perspective, the present study aims to compare impulsive and aggressive traits in controls and in patients with either BD or MDD and segregated according to their history of SA. We expected patients suffering from affective disorders to display higher impulsivity than controls. We also hypothesized that subjects with a history of SB would have higher impulsivity levels compared to those who never attempted suicide and wondered if impulsive characteristics would be as pronounced in MDD as in BD suicide attempters. In other words, do BD patients show higher impulsivity than MDD patients and do BD patients with a history of SA have the highest scores? We finally investigated the possibility that the correlation between impulsive and aggressive traits could be a better marker for suicide risk than either trait alone.

2. Methods

2.1. Subjects

The control and clinical samples included in the study were recruited within the framework of ongoing psychiatric genetic studies on affective disorders and SB. One hundred and forty-three controls were recruited from the Blood Donor Center of the University Hospitals of Geneva (Switzerland) and 138 BD and 186 MDD were recruited following hospitalization in the psychiatric units of the University Hospitals of Geneva. All subjects completed various self-report questionnaires, including French versions of the Barrat Impulsivity Scale (BIS-10) and of the Brown and Goodwin assessment of Lifetime History of Aggression (LHA). The BIS-10 is a psychometric measure of impulsivity with a multidimensional structure, generally separated into three components: motor (behavior), attentional (cognitive) and non-planning (Bayle et al., 2000; Patton et al., 1995). The LHA is a nine-item interview assessing lifetime aggressive behaviors in adolescence and adulthood (Brown et al., 1979). The absence or presence of any past or current psychiatric disorder was assessed with the French version of the Diagnostic Interview for Genetic Studies (DIGS) (Preissing et al., 1999). The presence of a comorbid borderline personality disorder (BPD) was taken into account and clinically diagnosed according to the DSM-IV criteria and clinical notes. To avoid biasing assessments with the acute depressive or manic states that led to the hospitalization, MDD and BD subjects were assessed a few days before hospital discharge in the euthymic state.

The study protocol was approved by the ethics committee of the University Hospital of Geneva and subjects were recruited after informed written consent was obtained.

2.2. Statistical analysis

Linear regression with adjustment for age and gender was used to investigate differences in BIS-10 and LHA scores between controls and cases and between mood disorder patients with or without SA. The simple correlation matrix or covariance matrix was used to investigate the correlation of LHA and BIS-10 within the different diagnostic categories. As BIS-10 and corresponding subscales as well as LHA were non-normally distributed, they were square-root transformed. All analyses were done in STATA v.10.

3. Results

3.1. Sample

Table 1 shows the clinical and demographic characteristics of control, MDD and BD subjects. BD subjects were significantly younger than controls (beta (b) = −4.71; p = 0.001; 95% CI from −7.52 to −1.88). There were significantly more males among the controls than among the BD and MDD subjects. It is noteworthy that 42 MDD (36%) and 17 BD (25%) patients with a history of SA had a comorbid BPD. There was significantly more subjects with comorbid BPD in MDD patients (N = 44; 23.7%) than in BD patients (N = 20; 14.5%) (X2 = 4.2; p = 0.041) — Of note almost all subjects with comorbid BPD had a history of SA (N = 59 on 64 [92.2%]; p < 0.0001).

3.2. BIS-10

Female gender and younger age were both significantly associated with higher BIS-10 total scores in the whole population (b = 0.39; p = 0.001; 95% CI from 0.16 to 0.62 and b = −0.03; p < 0.0001; 95% CI from −0.04 to −0.02 respectively). The same pattern was observed for each of the BIS-10 subscales, with the exception of the effect of gender on non-planning score, which was not significant (Supplementary Fig. S1).

After adjustment for age and gender, controls scored significantly lower for BIS-10 total score than affective disorder subjects (44.7 [SD = 12.9] vs. 57.9 [SD = 18.6]; b = 0.77; p < 0.0001; 95% CI from 0.54 to 1) and than MDD and BD subjects separately (b = 0.71; p < 0.0001; 95% CI from 0.46 to 0.97 and b = 0.9; p < 0.0001; 95% CI from 0.62 to 1.17 respectively) (Table 1). This difference was also significant for each BIS-10 subscale (Table 1).

Interestingly, MDD subjects with a history of SA scored significantly higher for BIS-10 total score than MDD subjects without past SA (50.7 [SD = 17.6] vs. 58.8 [SD = 17.6]; b = 0.40; p = 0.031; 95% CI from 0.04 to 0.77) (Fig. 1A). This difference was mainly accounted for by the attentional subscale score (b = 0.33; p = 0.011; 95% CI from 0.07 to 0.59) (Supplementary Fig. S2). By contrast, there was no significant difference either on BIS-10 total score or on any subscale score between BD subjects without and with a past
SA (57.2 [SD = 17.3] vs. 63.2 [SD = 20.7] for BIS-10 total score; b = 0.24; p = 0.259; 95% CI from −0.19 to 0.68).

It is worth noting that MDD subjects without a past SA scored significantly higher than controls for BIS-10 total score (44.7 [SD = 12.9] vs. 50.7 [SD = 17.6]; b = 0.38; p = 0.016; 95% CI from 0.07 to 0.69).

Finally, MDD and BD patients with comorbid BPD had higher BIS-10 total scores than those patients without such comorbidity (62.9 [SD = 16.9] vs. 56.5 [SD = 18.8]), but the difference was not statistically significant (b = 2.62; p = 0.317; 95% CI from −2.52 to 7.77).

After adjustment on comorbid BPD, the observed association showing higher BIS-10 total scores in MDD subjects with a history of SA compared to those without such a history was no more significant (b = 0.35; p = 0.079; 95% CI from −0.05 to 0.74); however the association with the attentional subscale score was still significant (b = 0.30; p = 0.029; 95% CI from 0.03 to 0.59).

There was no significant interaction between history of SA and diagnoses (MDD or BD) on BIS-10 total scores (b = −0.19; p = 0.513; 95% CI from −0.75 to 0.38).

### 3.3. LHA

Being younger was significantly associated with higher LHA scores (b = −0.02; p = 0.007; 95% CI from −0.03 to

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**Table 1**

Demographic and clinical characteristics of controls, MDD and BD subjects.

<table>
<thead>
<tr>
<th></th>
<th>Controls (N=143)</th>
<th>MDD (N=186)</th>
<th>BD (N=138)</th>
<th>MDD vs. controls</th>
<th>BD vs. controls</th>
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<tbody>
<tr>
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<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
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<td>43.2</td>
<td>11.4</td>
<td>41.1</td>
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<td>55.7</td>
<td>17.9</td>
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<td>19.2</td>
<td>7.3</td>
<td>20.7</td>
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<td>15.9</td>
<td>7.8</td>
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<td>20.7</td>
<td>7.2</td>
<td>21.2</td>
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<td>4.6</td>
<td>6.1</td>
<td>6.4</td>
<td>8.2</td>
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</table>

<table>
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<th>MDD/SA+</th>
<th>BD/SA−</th>
<th>BD/SA+</th>
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<td>105</td>
<td>56.5</td>
<td>74</td>
</tr>
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<td>117</td>
<td>62.9</td>
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<td>Axis II: BPD</td>
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<td>0</td>
<td>44</td>
<td>23.7</td>
<td>20</td>
</tr>
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</table>

* Available LHA scores: controls (N=110), MDD (N=120) and BD (N=68).

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**Fig. 1.** BIS-10 total score (A) and LHA score (B) for controls, MDD/SA− (MDD patients without a history of suicide attempt), BD/SA− (BD patients without a history of suicide attempt), MDD/SA+ (MDD patients with a history of suicide attempt) and BD/SA+ (BD patients with a history of suicide attempt).
−0.005). After adjustment for age and gender, controls scored significantly lower on LHA than affective disorder subjects (3.9 [SD = 4.6] vs. 7.3 [6.9]; b = 0.75; p < 0.0001; 95% CI from 0.42 to 1.07) and than MDD and BD subjects separately (b = 0.75; p = 0.001; 95% CI from 0.33 to 1.17 and b = 1.13; p < 0.0001; 95% CI from 0.71 to 1.56) (Table 1).

There was no significant difference in LHA score between MDD subjects with and without a history of SA or between BD subjects with and without such a history.

BD subjects scored significantly higher than MDD on LHA (b = 0.50; p = 0.012; 95% CI from 0.11 to 0.90) (Table 1). This difference was mainly accounted for by significantly lower LHA score in MDD patients without a history of SA compared to all BD subjects (b = 0.75; p = 0.002; 95% CI from 0.29 to 1.22) (Fig. 1B). The difference was highly significant when MDD patients without a history of SA were compared to BD subjects without a history of SA (b = 0.73; p = 0.008; 95% CI from 0.20 to 1.26).

There was no significant interaction between history of SA and diagnoses (MDD or BD) on LHA scores (b = −0.39; p = 0.333; 95% CI from −1.21 to 0.41).

3.4. BIS-10/LHA

The strongest correlations between BIS-10 total score and LHA score were observed for MDD subjects with a history of SA (0.42, p = 0.001) and BD subjects with history of SA (0.40, p = 0.098) (Fig. 2 and Table 2). There was no correlation (or only a very weak correlation) for controls (−0.03), MDD without a history of SA (0.29) and BD without a history of SA (0.10).

4. Discussion

In this study, BD and MDD patients had significantly higher BIS-10 total scores and subscores than controls who had never suffered any affective disorder. Nevertheless, whereas the trait impulsivity was almost as high in BD subjects without SA as in BD subjects with SA, MDD patients with a history of SA scored significantly higher on BIS-10 than MDD patients without SA.

BD and MDD patients also displayed more frequent and severe lifetime aggressive behaviors than control subjects, but there was no difference between suicide attempters and non-attempters in both clinical populations. Suicide attempters, however, whether suffering from a bipolar or unipolar disorder, showed a strong correlation between impulsive and aggressive traits.

The trait impulsivity has already been associated with BD or MDD as such, regardless of the state of illness. Indeed, Swann et al. (2003) reported higher BIS scores in BD patients compared to controls and found no difference between euthymic and manic subjects. Recently, elevated BIS scores were reported in depressed BD and MDD patients compared to controls, but impulsivity appeared to be less independent of mood state in MDD than in BD subjects (Peluso et al., 2007). These data suggest a general pattern of increased impulsivity in mood disorders, with a different picture between BD and MDD patients at the level of the underlying dimensions (motor, non-planning, attentional).

The link between impulsivity and SB appears to be complex therefore and possibly dependent on the underlying psychiatric disorder. In our study, there was no significant difference in BIS scores for BD subjects with or without SA,
whereas MDD patients with a history of SA scored significantly higher than MDD subjects without SA. Thus impulsivity may not be a reliable predictor of suicide risk in BD and MDD patients, at least when evaluated as a single trait. This is concordant with recent studies suggesting that impulsivity alone may not be the only predictor of SB (Carli et al., 2010) and that aggression should be part of the construct associated with SB (Mann et al., 2009).

Indeed, in a small sample of BD subjects, Oquendo et al. (2000) found higher lifetime aggression in attempters than in non-attempters, but no difference in lifetime impulsivity as assessed by BIS, whereas Michaelis et al. (2004) reported higher levels of overall hostility and a trend toward higher impulsivity in BD attempters compared to BD non-attempters. A similar trend toward higher BIS scores in BD attempters than in non-attempters has been reported by Swann et al. (2005), while in a laboratory measure of behavioral performance – the immediate memory task – BD subjects with a history of SA displayed more impulsive errors than BD patients without SA. Furthermore, this tendency toward rapid, unplanned responses was stronger in BD subjects with a history of severe SA.

Impulsivity has been more often reported to increase the risk of SB in mood disorder patients when associated with aggressive traits. Soloff et al. (2000) showed that impulsive aggression increases the risk of SB in patients with either BD or MDD. Likewise, Oquendo et al. (2004) reported that impulsive and aggressive traits, besides other clinical factors, contribute to predicting future SB in depressed BD and MDD subjects. In a study on adolescents, suicidal BD patients were significantly more impulsive than non-suicidal BD, whereas there was no significant difference in impulsivity in MDD suicidal vs. non-suicidal adolescents. Moreover, impulsivity and aggression correlated significantly and positively with

### Table 2

Correlation matrix showing the correlation between and significance of (italic) BIS-10 total score, BIS-10 subscales and LHA. Significant correlations between LHA and BIS-10 scores are highlighted in bold.

<table>
<thead>
<tr>
<th></th>
<th>BIS-10 tot</th>
<th>Attentional</th>
<th>Non-planning</th>
<th>Motor</th>
<th>LHA</th>
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<tr>
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<tr>
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<td>−0.0044</td>
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</tr>
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<td>BIS-10 tot</td>
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<td></td>
<td></td>
<td></td>
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suicidal behavior in BD, but not in MDD subjects (Horesh et al., 2003). Impulsive and aggressive behaviors have also been associated with suicide completion, although this relation was not independent of cluster B personality disorder and alcohol abuse (Dumais et al., 2005).

Despite a recent investigation suggesting that aggressiveness, but not impulsiveness or hostility, could distinguish suicide attempters from non-attempters with major depression (Keilp et al., 2006), the association of impulsive and aggressive traits seems to be more specifically related to SB than either trait alone (Turecki, 2005). The results obtained in this study tend to strengthen such a view, although we should underscore some limitations of the study. Impulsive and aggressive traits were not characterized at different stages of a patient’s illness, alcohol and substance abuse/dependence were not taken into account and the suicidal MDD sample was highly co-morbid with BPD, which could have biased the severity of impulsive and aggressive traits in this sample. The question then arises of the generalization of these results to non-comorbid MDD SAs. Nevertheless MMD subjects with a history of SA still showed higher BIS-10 total scores at least for the attentional subscale compared to MDD subjects without a history of SA and this after adjustment on comorbid BPD. This suggests that the observed association is independent of this comorbidity.

Interestingly, our results, which showed no difference between BD and controls in impulsivity, could be linked to biological markers of SB. While there is a remarkably consistent association between low concentrations of CSF 5-hydroxyindoleacetic acid (5-HIAA) and SB in MDD, this is not the case in BD (Agren, 1980; Asberg, 1997). Given that impulsivity has been linked to a low level of 5-HIAA (Kruesi et al., 1990), these findings possibly suggest that the major role played by psychological factors such as impulsivity in suicide attempt or suicide in MDD does not provide sufficient explanation for suicide attempt or suicide in BD given the already high level of impulsivity in these subjects.

Impulsive and aggressive traits may be considered distal precursors of SB, developmentally shaped by the interaction of environmental adverse events (childhood trauma) and genetic factors. They are, however, relatively heterogeneous constructs underlying complex cognitive and behavioral dispositions, whose diverse components deserve further investigation for their possible implication in SB, whether in BD or in MDD subjects. Together with related personality traits such as anger dyscontrol, they may represent intermediate phenotypes underlying the familial transmission of vulnerability to SB (Baud, 2005; McGirr and Turecki, 2007). Their clinical assessment should be an important step in evaluating the risk of suicide in mood disordered patients.

Role of funding source
This study was supported by the SNF grant #320030-112084.

Conflict of interest
Authors have no conflicts of interest.

Appendix A. Supplementary data
Supplementary data to this article can be found online at doi:10.1016/j.jad.2011.05.048.

References