A review of panic and suicide in bipolar disorder: Does comorbidity increase risk?

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Abstract

Introduction: Bipolar mood disorder carries a serious suicide risk. Panic disorder, which also confers an independent risk of suicide and psychiatric comorbidity, in general has been found to amplify suicidality in mood-disordered patients. This article assesses the available literature on how panic and suicide relate to each other in bipolar mood-disordered patients.

Methods: We conducted a search on Medline and PsycINFO using the keywords “anxiety”, “attempted suicide”, “completed suicide”, “mortality”, “self-harm” in combination with “bipolar”, “manic depression” and “panic”. Twenty-four articles were included in the evaluation.

Results: 14 papers support increased risk, 9 papers do not support increased risk, and 3 papers are inconclusive.

Conclusions: The presence of comorbid panic disorder in individuals with bipolar disorder may confer an increased risk of suicide risk. Some papers’ reviewed have conflicting conclusions but the majority of papers support an increased risk. This is consistent with a recent (2008) literature review supporting increased risk of suicide in bipolar patients with comorbid anxiety disorders. Future research should study specific bipolar subgroups, focus on anxiety and panic symptoms rather than diagnosis, and look at the role of specific pharmacological treatment in patients with comorbid mood and anxiety disorders.

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Keywords: Anxiety; Attempted suicide; Completed suicide; Mortality; Self-harm; Bipolar; Manic depression; Panic

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1. Introduction

Bipolar and panic disorders are common and serious psychiatric conditions, each of which confers increased risk of suicide attempt or completion. According to one study, bipolar mood disorder (BD) carries an 18.9% risk of suicide attempt with numerous factors proposed as contributors (Goodwin and Jameson, 1990). Panic disorder (PD) also has been reported to pose an independent risk of suicide (Weissman et al., 1989, Sareen et al., 2005). Psychiatric comorbidity has been found to amplify suicidality in mood-disordered patients (Goodwin and Hoven, 2002; Nemeroff 2002; MacKinnon et al., 1998; Frank et al., 2002; Freeman et al., 2002; Savino et al., 1993; Chen and Dilsaver, 1995) and comorbidity of mood and anxiety disorders is considered to be the rule rather than the exception (Nemeroff, 2002). However, few investigations have looked specifically at the role of panic in this regard. Given the possibility that patients who meet criteria for bipolar disorder and panic disorder may represent a clinical subgroup presenting a particularly high suicide risk (MacKinnon et al., 2005), we have reviewed available literature that present data relating to this issue.

2. Methods

Our review evaluates suicide in bipolar disorder populations across all age groups who present with comorbid panic symptoms. We conducted a literature search on Medline and PsycINFO dating between 1950 and August 2007 employing the following keywords: comorbidity, completed suicide, attempted suicide, mortality, and self-harm in combination with bipolar disorder, manic depression and panic disorder. We excluded all articles whose primary focus was on: alcohol/substance abuse, schizophrenia, schizoaffective disorder, personality disorders, unipolar depression, trauma, physical/sexual abuse, medical disorders, insomnia, primary care, insight, and pharmacology. Twenty-four original research articles were included in the evaluation and are summarized as follows: support an increased risk of suicide, do not support an increased risk of suicide, or are inconclusive. Subtypes of bipolar disorder evaluated include: bipolar disorder NOS, bipolar-I depression and mania, bipolar-II depression and hypomania, bipolar disorder with mixed states, bipolar disorder with rapid mood switching, and bipolar disorder with psychosis. Some papers are included in more than one section as they use bipolar samples from more than one subgroup. In addition, all papers specify rates of panic disorder within the bipolar subgroup, but in some papers only anxiety symptoms are measured in relation to suicide. As anxiety and panic symptoms can serve as a proxy for panic disorder, these papers are also included in the review.

3. Results

The following papers support an increased risk of suicide in people with comorbid bipolar and panic disorders. Study information is listed in Table 1.

3.1. Bipolar NOS

The bipolar NOS group consists of bipolar illness that does not fit into the other subtypes of bipolar disorder. One large ($N=229$) prospective study (Clayton, 1993) of patients with bipolar disorder concluded that anxiety symptoms (psychic anxiety, worry, and panic attacks) are predictive of short term or “early” (within one year of initial assessment) suicide risk in patients with major affective disorders (including “manic-depressive illness”). Clayton comments that most subjects did not meet criteria for panic disorder, but does not comment on the number that did. Furthermore, she emphasizes that anxiety symptoms, rather than diagnosis, are predictive of suicidal behavior.

Several retrospective studies have specifically examined the effect of panic disorder on suicide in patients with bipolar disorder NOS. Two studies (Simon et al., 2004, 2007) used 475 and 120 subjects, respectively,
from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). The more recent study demonstrates that lifetime anxiety disorders, including panic disorder, are associated with current and lifetime suicidal ideation as measure by the Beck Scale for Suicidal Ideation and the Suicide Behaviors Questionnaire. It also reports increased suicide attempts in this group; subjects with comorbid panic disorder were more than twice as likely to attempt suicide. The earlier study cites rates of comorbid panic and bipolar disorder ranging from 10.6–62.5%. It reports a prevalence of current panic disorder of 8% and lifetime panic disorder of 17.3%. Moreover, subjects with comorbid panic disorder + agoraphobia (current and lifetime) had statistically significant shorter durations of euthymic mood compared to subjects without panic disorder. Bipolar subjects with comorbid panic disorder-agoraphobia (current only) also had statistically significant shorter durations of euthymic mood compared to subjects without panic disorder. The authors suggest that early anxiety may be a precursor or prodrome to bipolar disorder and that they may share a genetic / biological commonality.

A study (Young et al., 1993) of 81 patients with bipolar disorder I and II (combined for analysis) examined whether anxiety symptoms in bipolar disorder have an impact on suicidal behavior. Using six items from the SADS-LV, patients were divided into High and Low Anxiety Groups. Those in the High Anxiety Group (including PD) had increased suicide attempts; Suicide attempts OR=2.1; suicide ideation OR=4.3. The authors suggest that early anxiety may be a precursor or prodrome to bipolar disorder and that they may share a genetic / biological commonality.

Chen and Dilsaver (1996) report the comorbidity of panic disorder among bipolar and unipolar subjects (N=168) as 20.8% and 10%, respectively. They compared lifetime rates of suicide attempts between individuals with bipolar disorder, unipolar disorder, and controls. Of their bipolar sample, 29.2% had a lifetime
3.2 Bipolar I

Two retrospective studies (Frank et al., 2002; Goodwin and Hamilton, 2001) support increased risk of suicidal ideation and behavior. The former assessed 66 subjects with bipolar disorder I using Panic-Agoraphobic Spectrum-Self Report (PAS-SR) in order to quantify typical and atypical symptoms of panic. These include somatic symptoms, anticipatory anxiety symptoms, and agoraphobia. Subjects were divided into High (≥ 35) and Low (≤ 35) groups depending on their PAS-SR score. Forty-eight and a half percent of subjects with High scores had suicidal ideation and 18.2% of subjects with Low scores had suicidal ideation. The former group was four times more likely to report suicidal ideation (odds ratio = 4.2). The second study used data from the National Comorbidity Survey and was described previously. As previously stated early onset fearful panic is associated with increased suicidal behavior. The risk of mania as a psychiatric comorbidity in early onset panic with fear and late onset panic with fear was statistically significant (p<0.05) with adjusted odds ratios of 43.4 and 17.1 respectively.

3.3 Bipolar mixed

Three retrospective studies using subjects with a mixed bipolar state support increased risk of suicide when comorbid panic disorder is present. Two studies (Dilsaver et al., 1997; Dilsaver and Chen, 2003) assessed social phobia, panic disorder, and suicidality during the “mania” state of subjects with pure and depressive-mania; subjects with depressive-mania are reviewed now and subjects with pure euphoric mania are described later in this paper. Intra-episodic panic disorder (IEPD) is discussed as panic disorder concurrent with the manic state (Dilsaver et al., 1997). Of 19 patients with depressive-mania, 63.2% were suicidal, 84.4% had IEPD, and 57.9% had both. IEPD is 20 times more common (odds ratio = 21.5, p<0.0001) in depressive-mania than in pure-mania. The third study (Balazs et al., 2006) defined mixed depression as major depressive disorder or dysthmic disorder plus ≥3 co-occurring hypomanic symptoms. Mixed depression subjects (N=63) had significantly higher rates of thinking about death, thinking about self-harm, thinking about suicide, thinking about suicide plans, and panic disorder compared to those without mixed depression. Almost half of the suicide attempters with mixed depression had comorbid panic disorder; none of the suicide attempters without mixed depression had comorbid panic disorder.

3.4 Bipolar rapid cycling

One retrospective study (MacKinnon et al., 2003) assessed families with a pro-band of bipolar disorder. Subjects (N=1574) with rapid switching were more than twice as likely to have panic disorder as those without rapid switching. The authors comment that

suicide attempt; 29% of the sample without panic disorder had a lifetime suicide attempt and 31.4% of the sample with panic disorder had a lifetime suicide attempt. They conclude that comorbidity of panic disorder may contribute to increased suicidality in bipolar patients.

Two studies by Goodwin and Hamilton (2001, 2002) use data from the National Comorbidity Survey and Epidemiological Catchment Area Survey with sample sizes of 421 and 1,689 respectively. They evaluated panic attacks as a predictor for subsequent psychopathology and described four subtypes of panic (early onset without fear, early onset with fear, late onset without fear, late onset with fear). Early onset includes age ≤ 20 years and late onset includes age > 20 years; fear following first panic attack was assessed by asking the question “After the first attack, were you immediately afraid of having another attack?” The four groups were compared across a number of variables including mental disorders, suicidal ideation, and suicide attempts. They conclude that early onset fearful panic is associated with increased incidence and earlier onset of psychopathology as well as increased suicidal behavior. Of note, bipolar disorder is an independent correlate of early onset fearful panic, with an adjusted odd ratio = 7.9 (p<0.05).

Two retrospective studies assessed adolescents with bipolar disorder NOS. Dilsaver et al. (2006) studied Latino adolescents (N=115), 47.8% of whom had comorbid panic disorder. The presence of panic disorder was not associated with an increased number of suicide attempts but was associated with an increased report of suicidal ideation. Goldstein et al. (2005) used a pediatric sample (N=405) drawn from the Course and Outcome of Bipolar Youth (COBY) database and found that 32% had a least one lifetime suicide attempt. Of suicide attempters in this sample, 23% were diagnosed with bipolar NOS, 67% with bipolar I, and 10% with bipolar II; diagnoses were not delineated for analysis. Of bipolar patients who attempted suicide, 12% were diagnosed with panic disorder (statistically significant from non-attempters, p<0.001). Their findings suggest that the strongest predictors of suicide attempt in patients with bipolar disorder are clinical illness history variables (psychiatric hospitalization, self injurious behavior, mixed episodes, psychosis) and comorbid conditions (substance use disorder, panic disorder).
heretofore suicide and rapid switching have not been linked, but their data supports an association and this may be similar to the association observed in bipolar mixed states. The authors conclude that rapid switching in familial bipolar disorder is common and associated with both increased panic disorder and suicide attempts.

The following papers do not support an increased risk of suicide in people with comorbid bipolar and panic disorders. Study information is listed in Table 2.

3.5. Bipolar NOS

Six papers, two using adolescent samples, do not support increased risk of suicide in subjects with bipolar disorder and comorbid panic disorder. One prospective study (Warshaw et al., 2000) examined suicidal behavior in 498 subjects with a current or past diagnosis of panic disorder in order to determine the effect of several variables including psychiatric comorbidity. Several variables (i.e. past suicidal behavior, current major depressive episode, borderline personality disorder etc.) were predictive of suicidal behavior; bipolar or schizoaffective disorder (grouped together) was not a predictor of suicidal behavior ($p=0.47$); being married and having children were protective factors. The other prospective study (Slama et al., 2004) of bipolar subjects ($N=307$) with and without a history of suicidal behavior included univariate analysis for all clinical and demographic variables. The authors found that 10.9% without a history of suicide attempt had panic disorder, whereas 4.7% with a history of suicide attempt had panic disorder ($p=0.06$). A multivariate analysis that controlled for the duration of disease, total number of mood episodes, and early age of onset of mood disorder demonstrated that absence of panic disorder was associated with suicidal behavior ($p=0.032$). This finding was not replicated ($p=0.097$, odds ratio=0.42) in a second logistic regression analysis that only included variables that were significant in the first regression analysis.

Grunebaum et al. (2006) describe a stress-diathesis model of suicidal behavior in bipolar patients [i.e. interaction of stress (mood disorder) and diathesis (aggressive traits and suicidal ideation)]. In their retrospective study of 96 subjects, suicide attempters and non-attempters did not differ in manic symptom severity, general psychopathology, and frequency of panic attacks, amongst other variables. Attempter did have higher scores of aggression, impulsivity, and recent suicidal ideation. Of 64 suicide attempters, 1.5% had panic attacks during the current mood episode and of 32 non-attempters, 1.3% had panic attack during the current mood episode ($p=0.64$ between groups).

A retrospective study (Schurhoff et al., 2000) of 210 subjects with bipolar disorder delineates early onset bipolar disorder (onset $<18$ years) from late onset bipolar disorder (onset $>40$ years) and notes clinical differences

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Table 2

<table>
<thead>
<tr>
<th>Study author/year</th>
<th>Study design</th>
<th>Sample (N)</th>
<th>Study population</th>
<th>Measurement</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warshaw et al. (2000)</td>
<td>Prospective</td>
<td>11</td>
<td>HARP</td>
<td>DSM-III-R, SCID-P, SADS-L</td>
<td>Comorbid BD not a predictor of suicidal behavior in current or past PD</td>
</tr>
<tr>
<td>Slama et al. (2004)</td>
<td>Prospective</td>
<td>307</td>
<td>French university hospitals</td>
<td>DSM-IV, DIGS, FIGS</td>
<td>Absence of PD was associated with suicidal behavior</td>
</tr>
<tr>
<td>Grunebaum et al. (2006)</td>
<td>Retrospective</td>
<td>96</td>
<td>NY State Psychiatric Institute</td>
<td>HAM-17, BDI, BPRS, GAS, SPRS</td>
<td>No difference manic or panic symptoms between suicide attempters/non-attempters</td>
</tr>
<tr>
<td>Schurhoff et al. (2000)</td>
<td>Retrospective</td>
<td>210</td>
<td>Two Parisian hospitals</td>
<td>DSM-IV, RDC, DIGS</td>
<td>No difference in rates of suicide attempts between early and late onset panic</td>
</tr>
<tr>
<td>Lewinsohn et al. (1995)</td>
<td>Retrospective</td>
<td>18</td>
<td>OADP</td>
<td>DSM-III-R, K-SADS</td>
<td>No differences when compared bipolar subjects with and without lifetime non-affective disorders with suicide attempts</td>
</tr>
<tr>
<td>Birmaher et al. (2002)</td>
<td>Retrospective</td>
<td>8</td>
<td>USA child and adolescents clinic</td>
<td>DSM-III-R, K-SADS-P</td>
<td>No difference in prevalence of suicide attempts between PD comorbid with BD, non-panic anxiety disorders comorbid with BD, non-anxious psychiatric controls comorbid with BD</td>
</tr>
<tr>
<td>Dilsaver et al. (1997)</td>
<td>Retrospective</td>
<td>129</td>
<td>HCPC</td>
<td>DSM-III-R, DSM-IV, RDC, SADS</td>
<td>No increased suicide risk in comorbid PD and euphoric mania</td>
</tr>
<tr>
<td>Dilsaver and Chen (2003)</td>
<td>Retrospective</td>
<td>25</td>
<td>HCPC</td>
<td>DSM-III-R, SCID, SADS, RDC</td>
<td>No increased suicide risk in comorbid PD and euphoric mania</td>
</tr>
<tr>
<td>Wu &amp; Dunner (1993)</td>
<td>Retrospective</td>
<td>100</td>
<td>UW Center for Anxiety and Depression</td>
<td>DSM-III-R, HAMD-18</td>
<td>Rapid cycling subjects without higher suicide rates but with more panic attacks</td>
</tr>
</tbody>
</table>

HARP=Harvard/Brown Anxiety Disorders Research project. OADP=Oregon Adolescent Depression Project. HCPC=Harris County Psychiatric Center, Texas. UW=University of Washington.
samples). However, when they compared bipolar subjects with and without lifetime non-affective disorders on variables including treatment, suicide attempts, and current/past year Global Assessment Function (GAF), they found no significant differences. The second study of youths aged 5–19 years compared subjects with bipolar disorder and panic disorder (N=8), subjects with bipolar disorder and anxiety disorder other than panic disorder (N=22), and subjects with bipolar disorder and non-anxiety comorbidity (N=112). They expected that youths with panic disorder have higher rates of bipolar disorder and that this comorbidity results in increased severity of symptoms and suicidality. The authors note that panic attacks are frequent in children and adolescents (5.4–10.2%) while panic disorder is much less common (0.5–0.8%). There was no significant difference in the prevalence of suicide attempts between the three groups; however, there was a trend for the subjects with comorbid panic disorder and bipolar disorder to have higher rates of suicidal ideation than either group alone.

3.6. Bipolar I

Two retrospective studies (Dilsaver et al., 1997; Dilsaver and Chen, 2003) assessed social phobia, panic disorder, and suicidality during the “manic” state of subjects with pure and depressive-mania; subjects with pure-mania are considered currently. The second study had 25 patients with pure-mania: one patient was suicidal, one patient had IEPD, and no patients had both. This differs significantly (p<0.0001) from rates for the depressive-mania group in the same study. They conclude that anxiety disorders are associated with depressive symptoms of mania rather than pure-mania symptoms.

3.7. Bipolar rapid cycling

One retrospective study (Wu and Dunner, 1993) compared 100 rapid cycling subjects with 120 non-rapid cycling patients. They stress that although rapid cycling is defined as at least four episodes per year, many individuals have more episodes and they propose that the number of depressive episodes is associated with increased suicidality. As panic disorder is associated with increased suicide risk, they assessed panic attacks as well. Rapid cycling subjects did not have significantly higher suicide rates but did have more panic attacks. This does not support an association between panic attacks and suicide attempts.

3.8. Bipolar psychosis

One retrospective study (Birmaher et al., 2002) discussed previously also assessed bipolar disorder with psychosis. They looked at three groups: bipolar disorder with panic disorder, bipolar disorder with (non-panic disorder) anxiety, and bipolar disorder without anxiety disorder. Subjects with comorbid bipolar and panic disorder (50%) had significantly more psychotic symptoms than subjects without an anxiety disorder (12.5%, p=0.02). However, there was no significant difference in suicide attempts or ideation between the groups.

The following papers are inconclusive as to whether there is an increased risk of suicide in people with comorbid bipolar and panic disorders. Study information is listed in Table 3.

3.9. Bipolar NOS

A prospective study (Warshaw et al., 1995) of 527 subjects with panic disorder (current or past, with or without agoraphobia) assessed comorbidity with schizoaffective / bipolar disorder; 27 subjects had comorbidity. In their sample, subjects with schizoaffective/bipolar disorders have the highest rates of suicide attempts or gestures (40.7%), there is no evidence of increased risk of suicidal behavior in uncomplicated panic disorder, and they state “our study cannot address the question of whether the presence of panic disorder
increases the chance of suicide attempts in patients with depression or other disorders”.

One retrospective study using subjects with bipolar NOS is inconclusive. Perlis et al. (2004) divided 983 subjects into three groups: <13 years old, 13–18 years old, >18 years old. Rates of panic with agoraphobia were 18.5%, 11.8%, and 8.2%, respectively. Rates of panic without agoraphobia were 8.9%, 9.6%, and 6.0%, respectively. For panic with agoraphobia, there was statistical significance ($p=0.002$) between the pre-pubertal and adolescent groups as well as between the pre-pubertal and adult groups. Suicide attempts were 49.8%, 37%, and 24.6% respectively. Further analysis of suicide attempts within panic subgroups was not performed.

### 3.10. Bipolar I

Vickers and McNally (2004) completed a retrospective study using data from the National Comorbidity Survey ($N=272$) to determine that panic disorder does not affect suicide risk when comorbidity is controlled. The authors describe an opposing view on panic disorder and suicidality. Individuals with panic disorder commonly appear as hypochondriacs with fears of dying and, thus a decreased suicide risk. In the survey, subjects with panic disorder and suicide attempts had significantly higher rates of mania than those without suicide attempts. Although this paper uses subjects with PD rather than BD, it does conclude that an interaction between the two may increase likelihood of suicide attempt.

### 4. Discussion

This review is intended to clarify whether bipolar disorder with comorbid panic disorder imparts a higher risk for suicide than bipolar disorder without comorbid panic disorder. 24 original research papers were reviewed and assessed with regards to the samples’ bipolar diagnosis, panic comorbidity, and measures of suicidality (ideation, attempt, completion); as some papers assessed more than one clinical subgroup of BD, there are 26 reviews; 14 papers support increased risk, 9 papers do not support increased risk, and 3 papers are inconclusive.

According to the recent review by Hawton et al. (2005), completed suicide and suicidality measures in people with BD are associated with single marital status, family history of suicide and affective disorders, early physical or sexual abuse, early onset of psychiatric illness, alcohol and other substance use disorders, expressed hopelessness, and comorbid anxiety disorder. Prior suicide attempt is the single best predictor of suicide. Several papers reviewed here support increased incidence of panic disorder in individuals with BD and an increased risk for suicide attempt and completion in this group. Some research on BD in youths also supports these findings. Early onset and comorbidity specifically worsen the outcome and it may be that early onset panic disorder predisposes to subsequent psychopathology, particularly BD. At the least, early onset bipolar comorbidity (panic attacks and panic disorder) predicts increased suicidal behavior. Specific relationships between panic symptom variables (i.e., early onset and PAS-SR score) and affective symptom variables (i.e., mixed state) may increase risk of suicide. Recent research (Lee and Dunner, 2007; Kauer-Sant’Anna et al., 2007; Rihmer, 2007) assessing anxiety comorbidity, but not panic specifically, in bipolar disorder concludes that comorbid anxiety is associated with suicidal ideation, behavior, and attempts.

In this review there are also several papers that do not support an increased risk of suicidality in this population. A recent study (Nakagawa et al., 2008) found that anxiety associated with cluster b personality disorders increased the risk of suicide in bipolar patients while Axis I anxiety disorders did not. A review (Hagwood and De Leo, 2008) of the literature from January 2006 to May 2007 on anxiety and suicidal behavior highlights the methodological issues that limit the interpretation of
data between studies. Some of these limitations are differences in sample size and demographic, assessment and diagnosis, study design, follow-up duration, and variables controlled for. These methodological issues affect this review and the findings here are not conclusive. However, as stated by Hagwood and De Leo:

“Globally speaking, anxiety disorders have an influence on suicidal behaviour, especially when they occur co-morbid with other mental disorders. Evidence regarding the independent influence of any single anxiety disorder is less consistent in literature and, overall, is less convincing. In any case, the available knowledge is sufficient to inform us that efforts to prevent suicide must not neglect the identification and treatment of anxiety disorders.”

A significant proportion of the literature examined in this review supports such a relationship for panic disorder specifically and underscores the importance of diagnosis and treatment.

In reviewing these articles, more consideration must be given to those which use a prospective study design as retrospective designs are inherently biased by recall and cross-sectional data collection is limited to a particular point in time. Based on the articles reviewed, it appears that comorbid affective and anxiety symptoms increase the likelihood of suicidal ideation and attempts. Those papers supporting increased risk of suicide include one prospective study, large sample sizes, statistical techniques that allow computation of odd ratios, and diverse samples drawn from larger studies (STEP-BD, NCS, ECA). In addition, when assessing youths, the two papers that support increased suicide risk were conducted amongst distinct ethnic groups and included large samples sizes. Two prospective papers (Warshaw et al., 2000; Slama et al., 2004) with adequate sample sizes that do not support increased suicide risk are difficult to interpret. As stated earlier, Warshaw et al. use subjects with PD and there may be a qualitative difference from the subjects used in other studies. Also, in the analysis they combine bipolar and schizoaffective patients. Slama et al.’s finding that absence of PD contributed to suicide attempt was not replicated in their own further analysis.

There are several limitations within the studies reviewed; many use a retrospective design, the sample numbers differ greatly between studies and some studies have small sample sizes, assessment scales differ between studies, age of samples differs between studies, and while some studies separate out panic disorder in relation to suicide, others only assess panic disorder within a general comorbidity group (specifically “anxiety comorbidity”). In addition, some studies specifically assess a subset of bipolar patients but others combine subsets (i.e. bipolar I and II) for analysis. One particular limitation is the variability and inconsistency present in the use of terms relating to suicidal ideation, behavior, attempt, and completion. This limitation is highlighted in the work of Posner et al. (2007), and future use of a standardized assessment tool such as the Columbia Classification Algorithm of Suicide Assessment (C-CASA) will allow for valid and reliable comparisons between studies.

Some investigations allude to convergent biological substrates linking BD, panic, and suicidality. In describing the “manic-panic” connection, MacKinnon and Zamoiski (2006) propose that mood and anxiety disorders are linked in one of three ways: expression of the same genotype, mediation via the same causal risk factors and cellular mechanisms, or distinct etiologies with common pathophysiology. Panic disorder cosegregates with BD (MacKinnon et al., 1997) suggesting both disorders are linked to the same chromosome. One study examining bipolar linkage to chromosome 18q demonstrated five families (of 28) in which the pro-band had panic disorder (Stine et al., 1995). Both disorders occur in episodes and previous episodes predict increased rate of recurrence. Similar to the kindling phenomenon in epilepsy, both bipolar and panic disorders may exhibit tendencies for long term potentiation at the synaptic level resulting in a predisposition for recurrence. Another possibility is that there are distinct etiologies with common anatomical and neurochemical dysfunction. These include the amygdala and hippocampus, monoamines, catechol-O-methyltransferase, and the serotonin transporter gene to name but a few. These shared biological substrates may be amenable to the same treatment strategies. Furthermore, medications indicated for stabilizing depressive and manic/hypomanic mood symptoms in bipolar patients may also ameliorate panic symptoms and reduce suicidality. One might hypothesize that the combination of panic symptoms with specific bipolar symptoms affects suicidality, and as Chen and Dilsaver report it is the individual with depressive-mania that is more at risk than the individual with euphoric manic. The importance of recognizing and treating comorbid panic in patients with BD is underscored by the association with increased suicidal risk. While it is common for psychiatrists to screen for comorbid disorders, there are no treatment guidelines available. Future research should study specific bipolar subgroups, focus on anxiety and panic symptoms rather than diagnosis, evaluate the exacerbation/amelioration of panic symptoms in treated bipolar patients (and vice
versa), and look at the role of specific pharmacological treatment in patients with comorbid mood and anxiety disorders.

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