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Differences between unipolar depression and bipolar II depression in women

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Abstract

Background—Bipolar disorder II (BPII) and unipolar depression (UD) are both characterized by episodes of major depression (MDE), however DSM-IV criteria for MDE are identical, regardless of diagnosis. As a result, misdiagnosis of BP II and UD is common, leading to inappropriate treatment. Because women are twice as likely as men to experience MDE, differentiating UD from BP II in the context of depression is especially important for women. We examined symptoms and clinical features of MDE in women with UD and BPII to compare presentations of the two disorders in women.

Methods—We compared characteristics of depressed women meeting DSM-IV criteria for BPII (n=48) or UD (n=48), matched on age.

Results—Feelings of worthlessness occurred in 98% of participants with UD versus 85% with BPII (p=0.03). Participants with UD experienced either insomnia or hypersomnia, but participants with BPII were more likely to experience both simultaneously (p=0.04). Those with UD were significantly less likely to have >5 prior mood episodes compared to those with BP II (12% versus 61%; p<0.0001) and had a later age of onset (p= 0.003).

Limitations—Small sample size and exclusion criteria (i.e., comorbid substance abuse) may limit generalizability of findings.

Conclusions—Among a sample of women, number of prior episodes, feelings of worthlessness, age of onset, and sleep patterns distinguished between UD and BP II depressive episodes. A better understanding of differential presentation of BP II versus UD depression in women may help guide clinicians to more accurate diagnoses and, ultimately, better treatment.

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Contributors:

Dr. Rastelli conducted the literature review related to this manuscript, formulated initial hypotheses, organized all data in preparation for analyses, drafted the initial version of the manuscript, and participated in manuscript revisions.

Mr. Weingarden assisted with hypothesis generation, manuscript preparation, and manuscript revision.

Dr. Cheng conducted all analyses related to the current study and participated in manuscript preparation and revision.

Dr. Frank oversaw data collection, participated in hypothesis generation and testing, and contributed to manuscript revisions.

Dr. Swartz designed and implemented data collection, oversaw manuscript preparation, edited all drafts of the manuscript, and prepared the final draft of the manuscript.

Keywords

depression; bipolar disorder type II; women

INTRODUCTION

Although recurrent unipolar depression (UD) and bipolar disorder (BP) are both mood disorders, clinical distinctions between them have been recognized since the time of Hippocrates (Goodwin and Jamison, 1990) and are well described in iterations of the DSM dating from the 1980's (American Psychiatric Association, 1980). Although phenomenologically distinct, bipolar disorder II (BPII) has proven particularly difficult to differentiate from UD as both are characterized by recurrent episodes of major depression, and DSM-IV defined criteria for depressive episodes are identical across these two disorders (American Psychiatric Association, 1994). As most patients with BP II present for treatment when depressed rather than hypomanic, it is not surprising that it is difficult to differentiate cross-sectionally between BPII and UD (Swartz et al., 2012b). This issue has important clinical implications as treatments for the two disorders differ, and treatments used for UD may exacerbate the course of illness in BP disorders resulting in increased risk of manic switch or cycle acceleration (Bowden, 2005; Newport et al., 2012; Perlis et al., 2010).

Differentiation of UD from BPII may be especially relevant in women as both of these disorders are more prevalent in women than men (Kessler et al., 2005; Merikangas et al., 2007). Lifetime prevalence of UD is estimated to be 16.6%, however women are almost twice as likely as men to experience this disorder (Kessler et al., 2003). BP II is less common than UD, with lifetime prevalence in the United States estimated to be 1.1% (Merikangas et al., 2011). Again, it appears that BP II may be more prevalent in women relative to men (Hendrick et al., 2000).

BPII is commonly misdiagnosed as recurrent UD (Ghaemi et al., 2000). Some studies have shown that up to 40% of patients with recurrent depressive episodes may in fact suffer from BPII (Berk and Dodd, 2005). Misdiagnosis may occur because patients do not complain about hypomania as it is experienced as egosyntonic or pleasurable (Swartz et al., 2012b). It may also occur because clinicians do not adequately probe for prior histories of hypomania as reliability of diagnosis can improve up to 16% with strategies that directly target enhanced recall of hypomanic episodes (Benazzi, 2003). Although BPII may be also misdiagnosed as borderline personality disorder (Gunderson et al., 2006), anxiety disorder (Berk and Dodd, 2005), or adjustment disorder, the primary confound is UD, leading to delays in correct diagnosis of up to 10 years (Ghaemi et al., 2000).

Although DSM IV diagnostic criteria for major depressive episodes in the context of UD and BP II are identical, studies suggest subtle differences between symptom profiles across disorders. For instance, data suggest that 64.2% of atypical depressions occur in the context of BP II (Benazzi, 1999a), and that almost half of individuals with BP II experience features of atypical depression whereas only one quarter of individuals with UD have these symptoms (Benazzi, 1999b; Benazzi and Rihmer, 2000). In a multisite European study, relative to participants with UD, those with BP II disorder were more likely to have a younger age of onset of depression, higher frequency of suicidal thoughts, higher rates of hypersomnia, and greater levels of psychomotor agitation (Hantouche and Akiskal, 2005; Hantouche et al., 1998). Other studies have shown that compared to those with UD, individuals with BP II have earlier age of illness onset (Benazzi, 1999d; Moreno et al., 2012), greater incidence of past suicide attempts (Kupfer et al., 1988), more psychomotor retardation (Hantouche and Akiskal, 2005; Kupfer et al., 1988), and higher rates of

recurrence (Angst et al., 2003). Individuals with BP II were found to have higher rates of hypersomnia, weight gain, leaden paralysis, and interpersonal rejection sensitivity (Amsterdam and Garcia-Espana, 2000) as well as more comorbid anxiety, physical complaints, and anger (Bowden, 2005) than those with UD. Notably, some studies did not find differences between UD and BP II depression. Specifically, in individuals with psychotic depression, Benazzi found no differences between those with UD and BP II (Benazzi, 1999c).

Most prior attempts to disentangle the relationship between UD and BP depression have focused on BP I disorder specifically (Goldberg and Harrow, 2011; Perlis et al., 2006). Few studies have examined the relationship between BP II and UD, despite the fact that BP II is more prevalent than BP I (Angst et al., 2003; Merikangas et al., 2011). No prior study has focused specifically on characteristics of depressive episodes in women, despite the fact that women are disproportionately affected by both UD and BP II (but not BP I). The goal of the current study is to examine characteristics of major depressive episodes in women suffering from BP II versus UD.

METHODS

This study was performed at the Western Psychiatric Institute and Clinic of the University of Pittsburgh and included data from two previously published studies described below. All study procedures were reviewed and approved by the Biomedical Institutional Review Board of the University of Pittsburgh. Potential participants provided informed written consent after receiving a complete description of the study, including a full description of risks associated with study participation.

Study 1: This trial compared interpersonal psychotherapy (Weissman et al., 2000) to escitalopram as acute treatments for UD (Frank et al., 2011). Participants were outpatients in a DSM-IV-defined episode of major depression as determined by the Structured Clinical Interview for DSM-IV, Clinician Version (SCID) (First et al., 1995), with a minimum score of 15 on the 17-item Hamilton Depression Rating Scale (HRSD) (Hamilton, 1960). A primary diagnosis of schizophrenia, schizoaffective disorder, BP I or II disorder, current anorexia or bulimia, and antisocial personality disorder constituted exclusions. Participants with current alcohol or substance abuse or dependence were excluded only if their drinking or substance use was unrelated to their depression. Individuals with severe, uncontrolled medical illness, those who had been unresponsive to an adequate trial of escitalopram or interpersonal psychotherapy in the current episode and women unwilling to practice an acceptable form of birth control were also excluded. Although the parent study included participants in Italy and the USA, the current sample was restricted to women residing in Pittsburgh.

STUDY 2: Individuals in this study were drawn from an open study of interpersonal and social rhythm therapy (IPSRT) (Frank, 2005) for acute BP II depression (Swartz et al., 2009) or from a comparative trial of IPSRT versus quetiapine for acute BP II depression (Swartz et al., 2012a). Participants were eligible for inclusion in the protocol based on the following criteria: age 18–65; lifetime diagnosis of BP II disorder as determined by the SCID, currently depressed; 25-item version of the HRSD score ≥ 15 (Thase et al., 1991); and Young Mania Rating Scale (YMRS) score < 10 (Young et al., 1978). Participants were excluded from the study if they met any of the following criteria: currently receiving treatment with psychoactive medications; diagnosis of substance abuse or dependence within the prior six months; diagnosis of borderline or antisocial personality disorder as determined by the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II) (First et al., 1997); or unstable medical condition that could produce symptoms that

would confound accurate assessment of mood. Lifetime and current psychiatric diagnoses were assigned using the SCID.

We compared 96 female study participants meeting DSM IV criteria for BP II disorder (n=48) or UD (n=48), currently depressed. Participants were matched on age: mean age UD=32.5±11.3, BP II=32.8±11.7. In order to characterize depressive episodes we examined individual items from the SCID. McNemar or Bowker tests and paired t tests were used to compare categorical and continuous variables, respectively.

RESULTS

Table 1 shows the demographic characteristics of the sample. There were no differences in demographic characteristics between the groups except the income was significantly higher in the BP II group (p=0.03). Note that the two studies used slightly different systems to categorize income. To compare groups, we divided income into low, medium and high levels, where low income included those categorized as either < \$7,500 or < \$10,000 in their respective studies. Table 2 summarizes the clinical characteristics of both groups. There were no differences in depression scores between groups: mean HRSD-17 scores were 19.8 (±4.8) and 19.2 (±3.7) for the UD and BP II samples, respectively. However, women with BP II experienced their first depressive episode at a younger age than those with UD [17.3 (± 6.9) versus 21.7 (±10); p = 0.003]. On individual items of the SCID, women with UD had fewer mood episodes: 12% (5/43) of UD females had 5 prior mood episodes while 61% (26/43) of BP II females had 5 prior mood episodes (p<0.0001). Distribution of sleep complaints differed significantly between groups: those suffering from UD were complained of *either* insomnia or hypersomnia whereas those with BP II more likely to complain of *both* insomnia and hypersomnia during the same episode (p =0.04). We also found that individuals with UD were significantly more likely to endorse feelings of worthlessness compared to those with BP II 98% (47/48) versus 86% (41/48); (p= 0.03).

Table 3 summarizes lifetime and current DSM-IV Axis I co-morbidity. Current anxiety disorders (which included generalized anxiety disorder, panic disorder, posttraumatic stress disorder, and obsessive disorder) were very common: 58% (28/48) and 54% (26/48) of the UD and BP II samples, respectively, but there were no differences between groups. Substance use and anxiety disorders were the most common lifetime diagnostic comorbidities in individuals with both UD and BP II (23% 11/48 and 40% 19/48 for substance abuse for UD and BP II respectively; 27% 13/48 and 40% 19/48 for anxiety disorders for UD and BP II respectively) but there were no statistically significant differences between groups in rates of lifetime comorbidity.

DISCUSSION

Depressive episodes are common to both UD and BP II disorder and yet time to the correct diagnosis can be as long as 10 years (Ghaemi et al., 2000; Hantouche and Akiskal, 2005). Depressive episodes are more prevalent in women than men (Kessler et al., 1993) and have more effects on mortality and psychosocial impairment than do mania and hypomania (Merikangas et al., 2011), but specific clinical or biological markers to distinguish BP II depression from UD depression are lacking.

In this sample of depressed women, those meeting criteria for BP II were significantly more likely to have a larger number of prior mood episodes when compared with those UD depressed women of the same age. Using five previous episodes to create a dichotomous variable showed statistical significance and was associated with a large effect size (0.96). This variable, therefore, may be a useful clinical marker for clinicians treating depressed

women. We also observed that BP II females are more likely to complain of both insomnia and hypersomnia in the same episode than one type of sleep disturbance suggesting a higher degree of sleep instability in these individuals. In combination with the finding of more frequent mood episodes, this adds credence to the previously hypothesized ideas of “temperamental instability” in individuals with BP II (Akiskal et al., 1995).

Our findings conflict with previous reports demonstrating no difference in lifetime number of depressive episodes between individuals with BP II and UD (Moreno et al., 2012). We also did not find evidence to support prior reports that individuals with BP II depression have more atypical symptoms than those with UD (Benazzi, 1999a). Our findings, however, concur with data from the NESARC study which found an early age of onset in individuals with BP II compared to UD and a comparable frequency of atypical symptoms between BP II and UD, although that study included both males and females (Moreno et al., 2012). Because our study is the first to examine characteristics of depressed women only, it is difficult to know whether discrepancies in findings are related to gender differences in the sample, differences in sampling strategies, or some other factor

Improved understanding of differences between symptoms across mood disorders in women may help contribute to diagnostic accuracy and, ultimately, improved capacity to deliver appropriate treatments to women with depressive episodes.

LIMITATIONS

Number of previous episodes was collected retrospectively, therefore recall bias could limit the accuracy of this information. However, the same method of data collection was applied across the UD and BP II samples, therefore this approach would not differentially favor either group. The exclusion criteria of Study 1 and 2 could create a selection bias, limiting inclusion in these analyses to those individuals with reduced comorbidity compared to the general population. In particular, exclusion of those individuals with borderline personality disorder from the BP II group may limit generalizability, given the high rates of comorbidity in both groups (Brieger et al., 2003; Gunderson et al., 2006). Finally, the sample size is relatively small, limiting our ability to detect differences between groups that might become apparent were the samples larger.

CONCLUSION

Improved capacity to identify features of depressive episodes that are specific to UD versus BP II disorder may help to improve diagnostic accuracy by allowing clinicians to develop profiles of symptoms that are characteristic of UD versus BP II, especially in women who are twice as likely as men to experience a depressive episode. Knowing that women with BP II are more likely to have an earlier age of onset, experienced >5 mood episodes, complain of feelings of worthlessness, and experience unstable sleep (both insomnia and hypersomnia) than those with UD may help improve accuracy of diagnosis in this population. Ultimately, treatments may be developed to target these symptom profiles which could, in turn, lead to improved outcomes for patients with mood disorders.

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Table 1

Demographic Characteristics of Women with Unipolar Disorder (UD) and Bipolar II Disorder (BP II)

Demographic characteristics		UD (n = 48)	BPII (n = 48)	P value
Age (years)		32.5 ($\pm$ 11.3)	32.8 ($\pm$ 11.7)	ns
Race (8 missing)	White	33 (82.5%)	34 (85%)	ns
	Black	3 (7.5%)	5 (12.5%)	
	Asian	1 (2.5%)	0 (0%)	
	Other/unknown	3 (7.5%)	1 (2.5%)	
Marital Status (1 Missing)	never married	30 (63.8%)	30 (63.8%)	ns
	married	9 (19.2%)	12 (25.5%)	
	separate/divorced	8 (17%)	5(10.6%)	
Education (3 missing)	12 years or less	7 (15.6%)	7 (15.6%)	ns
	more than 12 years	38 (84.4%)	38 (84.4%)	
Employment (1 missing)	student	8 (17%)	4 (8.5%)	ns
	homemaker	2 (4.3%)	2 (4.3%)	
	part time	6 (12.8%)	11 (23.4%)	
	full time	19 (40.4%)	16 (34%)	
	unemployed	12 (25.5%)	8 (17%)	
	Other/ disabled/ Leave of absence	0 (0%)	6 (12.8%)	
Income (\$/year) (3 missing)	low <7500 or 10000	16 (35.6%)	11 (24.4%)	0.03
	average	27 (60%)	22 (48.9%)	
	high 50000	2 (4.4%)	12 (26.7%)	

Table 2

Clinical Characteristics of Women with Unipolar Disorder (UD) and Bipolar II Disorder (BP II)

Clinical Characteristics		UD (N=48)	BPII (N=48)	p
Anhedonia		48(100%)	47(97.9%)	ns
Depressive mood		48 (100%)	47(7.9%)	ns
Concentration problems		45 (93.8%)	45(93.8%)	ns
Fatigue		46(95.8%)	45(93.89%)	ns
Worthlessness feelings		47(97.9%)	41(85.4%)	0.03
Sleep problems (1 missing)	insomnia	25(56.2%)	28(59.6%)	0.04
	hypersomnia	16(34%)	6(12.8%)	
	both insomnia and hypersomnia	0 (0%)	8(17%)	
Psychomotor alteration (3 missing)	agitation	18(40%)	15(33.3%)	ns
	retardation	17(37.8%)	14(31.1%)	
	both agitation and retardation	0 (0%)	4(8.9%)	
Suicide (2 missing)	thought	12(26.1%)	11(23.9%)	ns
	ideation	3(6.5%)	2(4.4%)	
	plan	3(6.5%)	3(6.5%)	
	attempt	0(0%)	0(0%)	
Weight	loss	18(37.5%)	22(45.8%)	ns
	gain	12(25%)	11(22.9%)	
	both weight loss and gain	0(0%)	2(4.2%)	
Psychotic symptoms		2(4.2%)	1(2.1%)	ns
Impairment		48(100%)	48(100%)	ns
Post partum onset		0(0%)	1(1.8%)	ns
Atypical features		5(10.4%)	6(12.5%)	ns
Melancholic features		11(22.9%)	16(33.3%)	ns
Catatonic features		0(0%)	0(0%)	ns
More than 5 previous episodes (5missing)		5(11.6%)	26(60.5%)	<0.0001
HRSD-17		19.8 (±4.8)	19.2 (±3.7)	ns
Age at onset (years) (5 missing)		21.7 (±10)	17.3 (± 6.9)	0.003

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