Evidence From Studies Of Recurrent Depression and Bipolar Disorder Supports a Two-Dimensional Model Of Mood Disorders

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Abstract
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EVIDENCE FROM STUDIES OF RECURRENT DEPRESSION AND BIPOLAR DISORDER SUPPORTS A TWO-DIMENSIONAL MODEL OF MOOD DISORDERS

A THESIS
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ABSTRACT

Mood disorders represent a major health burden for society and impact individuals’ ability to function socially and professionally. Recent research has challenged the current DSM-IV-TR categorical diagnostic system for unipolar and bipolar mood disorders. This thesis reviews existing research in support of both categorical and dimensional models of mood disorder. A dimensional model appears to be supported based on current research. This thesis proposes a two-dimensional model of mood disorder and suggests directions for future research. It is anticipated that the acceptance of a dimensional model of mood disorders might lead to changes in assessment, diagnosis, and treatment of mood disorders.
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INTRODUCTION

Mood disorders are a class of psychological disorders that impact people’s perception and experience of the world around them (Bowden, 2005). Mood disorders, including unipolar and bipolar mood disorders, have high costs for individuals and society as a whole. In addition to the individual’s suffering and risk for premature death as a result of mood disorder, a holistic view of the problem includes the costs to society.

These costs can include reduced work productivity, increased use of the health care system, increased substance abuse and dependence, and financial costs from such programs as Medicaid and Social Security disability benefits. According to Murray and Lopez (1996), mental disorders account for more than 15% of the burden of disease in the United States, more than all forms of cancer combined. Further, unipolar major depression and bipolar disorders both rank among the top ten causes of disability worldwide (Murray & Lopez, 1996). Given the worldwide impact of this massive problem, it would be prudent for both economic and health reasons to expand the existing knowledge of mood disorders. Successful treatment of mood disorders can reduce many of the eventual costs to society by resulting in prevention of suicide, increased productivity, and paradoxically, reduced use of the healthcare system.

Although mood disorders have been recognized for centuries, the efficacy of mood disorder treatment is still variable. Many forms of depression and bipolar disorder remain treatment resistant and the recurrence of major affective episodes is the norm. For individuals whose demographics do not match those of the experimental groups in
existing studies, and for individuals with comorbid substance abuse, psychiatric, or medical diagnoses, current treatment models lack a secure evidence base and may lack efficacy. Even for those individuals who closely parallel the typical experimental group for treatment protocol research, evidence based treatment can be hard to find. There is not a single evidence-based treatment with approval from the American Psychological Association to treat bipolar disorders, for example (Chambless et al., 1998). Individuals with a diagnosis of a bipolar disorder must rely exclusively on pharmacological treatments or psychotherapy that is not sufficiently evidence-based. Given this information, clinicians and researchers must consider whether the current gold standard treatments should be modified with adequate deference to the existing research.

Improving the use of existing psychological and pharmacological treatments and developing more useful treatments depends on an accurate understanding of individual types of mood disorder. Without a detailed and accurate understanding of mood disorders, development of new treatments may be based on potential inaccuracies. Fortunately, researchers continue to study the mood disorders in order to expand the field’s knowledge of the disorders being treated, and this is resulting in an expanded body of knowledge from which mental health treatment providers can conceptualize the mood disorders.

Currently, the psychological and pharmacological treatments for mood disorders tend to be directly or indirectly based upon the knowledge contained within the most recent Diagnostic and Statistical Manual of Mental Disorders, currently in its fourth edition (DSM-IV-TR; American Psychiatric Association [APA], 2000). The state of research for mood disorders has advanced beyond that contained within the DSM-IV-TR,
which raises concern that mental health practitioners may be relying on an imperfect and outdated source as a complete and exclusive reference. In order to provide enough information to the mental health field to allow for an update in the knowledge base, research needs to be conducted and disseminated thoroughly. The goal of the present review of the literature is to provide a resource that collects the most recent research of mood disorders. This research diverges from the classic literature cited within the DSM-IV-TR in some important ways, and may lead to a new conceptualization and organization of mood disorders. For example, the DSM-IV-TR (APA, 2000) has classically presented the mood disorders in a categorical conceptual model, whereas the research reviewed below lends support for a dimensional model of mood disorder. Some research has not challenged the concept of a categorical model of mood disorders, but has provided evidence for the existence of a third bipolar disorder (Benazzi, 2007c) or challenged the arbitrary four day cutoff for hypomania (Benazzi, 2001). All of this research will be discussed in greater detail below, but it is important to note that the new ideas are nearly always presented in contrast to the existing diagnostic system.

Within the current diagnostic system, the mood disorders are separated from one another on the basis of polarity. Unipolar mood disorders, which almost exclusively refer to the depressive pole, are considered to be distinct from the bipolar affective disorders, which contain episodes from both poles. This distinction has been supported by previous research regarding treatment outcomes and different symptom clusters, which will be expounded upon below. This model of mood disorder is a categorical model, because it presents the different mood disorders as existing within distinct categories that require different conceptualization and treatment.
An alternative model of mood disorders could be called a two-dimensional model. In this case, the dimensions could be conceptualized as both degree of recurrence and polarity of affective episodes. The dimension characterized by degree of recurrence would have single-episode disorders at one end and highly recurrent disorders at the opposite side. The dimension characterized by direction of polarity would have unipolar depressed at one side, unipolar manic at the other side, and disorders with some combination of depression, mania, and hypomania distributed between the two extremes. This model of mood disorders is more inclusive of the diversity of course and polarity observed in the clinical environment and the research presented below.

This concept has implications for conceptualization and treatment of the disorders in question, including what type of psychotherapy or psychopharmacological intervention should be used for the most effective and safe treatment. The majority of contemporary research has increasingly provided evidence for a dimensional model of mood disorders, but research supporting both models is presented following a brief introduction to the mood disorders. Finally, it should be noted that in the following literature review, greater attention has been paid to the recurrence of mood disorders than to the polarity of mood disorders. This is simply because the polarity of mood disorders has been fully described and presented in the DSM-IV-TR (APA, 2000), and it is not the concept or nature of polarity that is being challenged by this new model.
UNIPOLAR MOOD DISORDER

Depression may have been first described by Hippocrates, in 4th century B.C. as melancholia, which included "prolonged despondency, blue moods, detachment, anhedonia, irritability, restlessness, sleeplessness, aversion to food, diurnal variation, and suicidal impulses" (Megna & Simionescu, 2006, p. 1). The construct has changed little since Hippocrates' time, and is now defined within the DSM-IV-TR as major depressive disorder (MDD; APA, 2000).

The specific criteria for MDD last a minimum of two weeks and include depressed mood, anhedonia, unintentional and significant weight loss or gain, insomnia or hypersomnia, psychomotor retardation or agitation, fatigue, feelings of worthlessness, difficulty concentrating, and suicidal ideation (APA, 2000). Five of the nine criteria must be met, at least one of which must be either depressed mood or anhedonia. Further, the episode must not meet criteria for a mixed episode, clinically significant impairment must be evident, the symptoms cannot be the direct affects of a medical condition or substance, and the symptoms must not be better accounted for by another psychological disorder. MDD can be either a single episode or of a recurrent nature, and can be described in terms of its severity as mild, moderate, severe without psychotic features, or severe with psychotic features.

The DSM-IV-TR allows for further description of the nature of the depressive episode by use of diagnostic specifiers. This allows clinicians to indicate whether or not the depression represents a relapse and whether it appears to match an existing subtype,
of which there are five, including chronic, catatonic, melancholic, atypical, and postpartum. In the case of recurrent depression, this also allows for a specifier to describe the level of recovery between episodes and whether or not the depression follows a seasonal pattern (APA, 2000).

For the purposes of the present discussion, the acronym MDD is used in reference to the disorder as it is recognized by the current diagnostic system, and unipolar depression will be used to refer to depression as a construct. This will aid in the reader's understanding that unipolar depression is often contrasted to bipolar depression. The terms MDD and unipolar depression can be used interchangeably and refer to the same general construct.

Unipolar depression is one of the most common presenting problems in mental health treatment facilities (Dozois & Dobson, 2002). According to the U.S. Department of Health and Human Services, MDD annually affects 6.7% of the adult United States population and represents the leading cause of disability for individuals aged 15-44 (1999). In addition, up to 30% of completed suicides can be linked to a diagnosis of MDD, and researchers have estimated the lifetime suicide risk for individuals with MDD to be as high as 15% (Bowden, 2005; Megna & Simionescu, 2006). The costs of unipolar depression are not merely restricted to the directly observable human suffering. Although figures are not available for the financial costs of unipolar depression exclusively, mental health diagnoses as a whole are responsible for approximately 150 billion dollars worth of lost productivity and direct mental health costs (U.S. Department of Health and Human Services, 1999).
Although unipolar depression represents a significant cause of human suffering and financial burden, all news is not negative. There are a number of psychological and psychopharmacological treatments for depression. The American Psychological Association has accepted three psychological treatments as well-established empirically-validated treatments, a label which requires a minimum of two studies incorporating between-group designs and demonstrating superiority to placebo or another established treatment (Chambless et al., 1998). The treatments that meet the rigorous criteria include cognitive therapy, behavior therapy, and interpersonal therapy. In addition, there are five major categories of psychopharmacological treatments, including monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin and norepinephrine reuptake inhibitors (SNRIs), and atypical antidepressants (Adams, Miller, & Zylstra, 2008).

Psychologists are not currently authorized to prescribe medications in most states. Therefore, the remainder of this section is focused on the three American Psychological Association-approved psychological treatments for depression. The first form of psychological treatment is cognitive therapy. This treatment was developed primarily by Aaron Beck and is based upon the theory that negative thinking plays a role in the development and maintenance of depression and that these thoughts must be challenged and restructured in order for the depressive episode to resolve (Beck, Rush, Shaw, & Emery, 1979). Techniques used in this form of therapy might include cognitive restructuring and daily thought records. The American Psychological Association has accepted cognitive therapy as a well-established treatment based upon Dobson’s (1989) meta-analysis of cognitive therapy’s efficacy for depression.
The second form of treatment accepted as well-established by the American Psychological Association is behavioral therapy. This form of therapy incorporates classic behavioral techniques to the specific symptoms of depression. Behavioral therapy for depression is based on the theory that increasing pleasurable activities through behavioral activation and activity scheduling will reduce depressive symptoms. Behavioral therapy became accepted by the American Psychological Association following a component analysis of the treatment by Jacobsen et al. (1996) and a study comparing behavioral therapy to other treatments for depression by McLean and Hakistan (1979).

The third form of treatment presented here is interpersonal therapy. Interpersonal therapy is based upon the hypothesis that maladaptive interpersonal styles lead to situations that are likely to increase the experience of depression (Klerman, Weissman, Rounsaville, & Chevron, 1984). From this perspective, therefore, depression can be effectively treated by teaching more helpful styles of interacting with other people. Techniques used in this form of therapy might include assertiveness training and role-playing. Interpersonal therapy was accepted as well-established by the American Psychological Association following a study from the National Institute of Mental Health (Elkin, Shea, Watkins, Imber, Sotsky, Collins, et al., 1989) and a comparison study of drugs and psychotherapy (DiMascio, Weissman, Prinsoff, Neu, Zwilling, & Klerman, 1979).

There are a number of other treatments for depression that are not included here. It is likely that other effective treatments for depression exist, but at this time there is only empirical support for cognitive therapy, behavioral therapy, and interpersonal
therapy for the psychological treatment of depression (Chambless et al., 1998). It is likely that the American Psychological Association will approve an increasing number of treatments for depression as psychologists conduct the necessary research to establish sufficient empirical support for treatments.
BIPOLAR MOOD DISORDER

A comprehensive understanding of unipolar depression is a foundation for understanding bipolar depression. Bipolar disorder usually includes both major depressive episodes similar or equivalent to the ones that occur in unipolar depression and the hypomanic and manic episodes that serve as the hallmark of the bipolar disorders.

Throughout the history of psychology and prior to the field’s existence, bipolar disorders have existed and been recognized. Within the field of psychology, bipolar disorder was first extensively and empirically described under the title “manic depressive insanity” by Emil Kraepelin, a concept which included all recurrent forms of mood disorder, with and without mania (Akiskal et al., 2000; Baldessarini, 2000). Manic depressive insanity was described as a highly recurrent but non-degenerative disorder characterized by extremes of mood (Benazzi, 2007c). Since Kraepelin’s time, bipolar disorders have alternately been described in terms of course and polarity.

The course of bipolar disorder refers to the recurrent episodes of either hypomania or mania and depression with the full or partial remission of the disorder between episodes. The course of bipolar disorders is still considered to be lifelong but non-degenerative in nature with recurrent episodes of varying lengths and severities (Benazzi, 2007c). The polarity of bipolar disorders refers to the nature of the episodes, which can either be elevated (mania and hypomania) or depressed. The current DSM-IV-TR conceptualization of mood disorders is organized in terms of polarity, and the specific diagnoses are restricted by the types of episodes a patient has experienced.
The DSM-IV-TR (APA, 2000) distinguishes between two major bipolar disorders, called bipolar I disorder (BP-I) and bipolar II disorder (BP-II). The major features of BP-I are the presence of at least one manic or mixed episode, resulting clinically significant impairment, and symptoms not better accounted for by a psychotic or schizoaffective disorder, substance use, or a general medical condition. Typically, bipolar I disorder also includes episodes of depression, although this is not required for diagnosis. The major features of BP-II are the occurrence of at least one depressive episode, occurrence of at least one hypomanic episode, no history of manic or mixed episodes, clinically significant impairment, and that the symptoms are not better explained by another disorder, substance use, or general medical condition. Both BP-I and BP-II include the same set of diagnostic specifiers for depressive episodes as MDD.

Major depressive episodes were more fully described in the unipolar depression section. It is important to note, however, that up to 50% of depressive episodes that are treated in outpatient therapy clinics are actually part of a bipolar disorder (Akiskal, 2005). Manic episodes last a minimum of one week, cause impairment in functioning, and are not caused by substance use. Three of the seven criteria are required for diagnosis of a manic episode if the mood is elevated, and four are required if the mood is only irritable. The seven criteria include grandiosity, decreased need for sleep, pressured speech, flight of ideas, distractibility, increase in goal-directed activity, and excessive involvement in pleasurable but risky activities (APA, 2000). Manic episodes usually require hospitalization and by definition always lead to impairment of functioning. Mixed episodes last at least one week and involve clinically significant impairment that meets criteria for both a major depressive episode and a manic episode. Hypomanic episodes
are often considered to be less-severe forms of mania, but require the same number of manic criteria to be present. The DSM-IV-TR includes a clinical cutoff of four days for the diagnosis of hypomania, but a considerable amount of research supports a two day cutoff (Akiskal et al., 2000; Benazzi, 1999; 2001). In contrast to manic and mixed episodes, however, hypomanic episodes are not considered to impair functioning and may actually result in increased functioning for the individual in about 74% of cases (Benazzi, 2004; Bowden, 2005).

Bipolar disorders are often regarded as representing a more severe level of psychopathology and impairment than occurs with unipolar depressive disorders. With a lifetime risk of a suicide attempt between 25 and 50%, bipolar disorders are associated with an increased risk of suicide compared to unipolar depression (Bowden, 2005). There is also an increased risk of dual diagnosis, or a comorbid diagnosis of substance abuse, with a lifetime prevalence rate of 60% (Bowden). Further, bipolar disorders commonly involve instability in education, career, marriage, and place of residence (Akiskal, 2005). The suffering caused by bipolar disorders was most eloquently described by Ghaemi, Ko, and Goodwin (2002): “apart from the major morbidity and substantial suicide risk that these depressive symptoms present, varieties of BD [bipolar disorder] produce unstable lives, failed careers, high divorce rates, and stormy biographies” (p. 128). A major difference in type of impairment can be observed between BP-I and BP-II. Individuals with a diagnosis of BP-I are most commonly initially hospitalized for mania, at a rate of nearly 80%, whereas individuals with a diagnosis of BP-II are most commonly initially hospitalized for depression (Dunner, Fleiss, & Fieve, 1976).
The psychotherapeutic treatment of bipolar disorders is less established and less commonly practiced than therapeutic treatment for unipolar depression. The American Psychological Association does not have any well-established or probably efficacious treatments listed on the most recent update of empirically validated therapies (Chambless et al., 1998). In terms of psychopharmacological treatments, lithium has long been the frontline treatment of BP-I (Young, Macritchie, & Calabrese, 2000). Unfortunately, lithium’s mechanism of action remains largely unknown, and its therapeutic index, the gap between a therapeutic dose and a toxic dose, is dangerously small and can therefore be extremely dangerous in overdose. In addition, lithium is less effective for the treatment of mixed episodes and rapid cycling bipolar disorder. Treatment compliance is a common challenge in bipolar disorders, particularly with lithium. Unfortunately, one risk of lithium discontinuation is relapse into a manic episode (Young, Macritchie, & Calabrese, 2000).

More recently, alternative medications have been researched and integrated into clinical practice. Among these are anticonvulsants such as carbamazepine and valproate. Valproate has become the most commonly prescribed frontline treatment for bipolar disorder in the United States although the research supporting its use remains inconclusive at best (Young, Macritchie, & Calabrese, 2000). Anticonvulsants are typically more effective when used for prophylaxis than for the acute treatment of manic episodes.

Finally, atypical antipsychotics have become commonly prescribed mood stabilizers. Such medications include olanzapine, risperidone, and clozapine. Olanzapine and risperidone have been found to be effective for the acute treatment of manic
episodes, but are less well established for prophylaxis and long-term use. Risperidone has been reserved for "highly refractory cases" (Young, Macritchie, & Calabrese, 2000, p. 1303).

Unfortunately, none of the medications in use for the treatment of bipolar disorder are sufficiently well-researched to support their continued long-term use without case-by-case examination of the risks and benefits. In addition, the medications discussed above are typically only effective for the treatment of manic and hypomanic episodes, with little assistance in the treatment of depressive episodes. The exception to this is lithium, which has some evidence base for use at preventing relapse of manic, hypomanic, and depressive episodes (Benazzi, 2007a). Often, prevention of depressive relapse is managed by the additional use of an antidepressant medication, but this increases the financial cost to the individual and creates the risk for further medication side effects. Antidepressants can also lead to relapse into manic episodes when used as monotherapy or when the patient is not fully compliant with both medications (Ghaemi & Baldessarini, 2007).

Although the medical profession is continuing to research more effective medications for the management of bipolar disorders, psychology needs to do the same. As previously stated, there is not a single American Psychological Association-approved treatment protocol for bipolar disorder. There are several treatments in the research literature, but most relate to improving medication compliance rather than treatment of the disorder itself (Scott, 1995). This remains a problem, particularly because 25-30% of variance in treatment outcomes for individuals with bipolar spectrum disorders can be attributed to psychosocial factors such as adjustment, loss, and interpersonal difficulties (Scott, 1995). In their landmark text on bipolar disorders, Frederick K. Goodwin and Kay
Redfield Jamison (2007) provided evidence that, although physicians and psychiatrists often do not see the importance of psychotherapy in addition to mood stabilizers, the patients do experience a benefit. Psychotherapy can enable individuals with bipolar disorder to better understand and manage their symptoms, reducing the likelihood and frequency of relapse. It can also help individuals manage the social and psychological consequences of the disorder.

Although there are not any bipolar disorder treatment protocols with the endorsement of the American Psychological Association, there are several potentially effective treatments to use in addition to psychopharmacological intervention with the intention not to treat the disorder itself, but to manage its effects. These treatments include psychoeducation, cognitive-behavioral therapy, interpersonal and social rhythm therapy, and functional family therapy (Goodwin & Jamison, 2007).

Psychoeducation for bipolar disorders focuses mainly on the problems of non-adherence to medications and relapse despite adherence. Individuals with a bipolar disorder diagnosis can be taught to recognize the warning signs of a relapse and to recognize the importance of sleep schedules. Outcome studies of various psychoeducation programs have established that psychoeducation can effectively reduce relapse rates in some cases (Goodwin & Jamison, 2007).

Cognitive-behavioral therapy (CBT) is a form of therapy that combines elements of Aaron Beck's cognitive therapy with elements of behavior therapy (Goodwin & Jamison, 2007). CBT was originally used for the treatment of depression. It has since been adapted for the treatment of bipolar disorder based upon the theory that manic and depressive symptoms often occur at the intersection of stressful life events and negative
cognitive styles (Goodwin & Jamison, 2007). The results of outcome studies of CBT protocols have demonstrated increased medication adherence and lower relapse rates compared to treatment as usual (Goodwin & Jamison).

Interpersonal and social rhythm therapy (IPSRT) is a variation of interpersonal therapy designed for bipolar disorders. This form of therapy is based upon the theory that episodes are often precipitated by grief, interpersonal disputes, role transitions, or role deficits (Goodwin & Jamison, 2007). These four types of problems are hypothesized to interfere with a bipolar individual’s circadian rhythms and daily routines which can lead to an increase in symptoms and risk for relapse into a manic or depressive episode.

Studies of IPSRT have mixed results, but generally support the use of IPSRT as effective during acute phases of treatment (Goodwin & Jamison).

Family/couples therapy has a demonstrated effect in the prevention of depressive and manic relapse. This form of therapy is designed to teach family members of the bipolar patient to reduce their judgment of the diagnosed individual and to aid in the establishment of a more predictable and a lower-stress environment in the home. The family and therapist also work together to develop a “relapse drill” (Goodwin & Jamison, 2007, p. 902), a plan for recognition and early treatment of an affective episode while it is still in its prodromal phase.

Despite the existence of helpful forms of treatment for the effects of bipolar disorder, more research is needed in order to gain the recognition of the American Psychological Association. Also, research is desperately needed to aid in the development of psychological treatment protocols that can actually target the symptoms of the disorder itself rather than its impact. By targeting the disorder at the source of the
problem, treatments should function less as a container for symptoms and distress and more as curative forces. In order for this to be accomplished, however, the field of psychology needs a better understanding of what mood disorders actually are, and in what ways the various types of mood disorder are similar and different. It is the contention of this thesis that, by increasing mental health practitioners' understanding of mood disorders, moving from a categorical to a dimensional model can begin to have an impact on the treatment of bipolar and unipolar mood disorders.
EVIDENCE IN SUPPORT OF A CATEGORICAL MODEL OF MOOD DISORDERS

The categorical model of mood disorders is currently the most widely recognized model because it is the model represented in the DSM-IV-TR. A categorical model holds that unipolar and bipolar mood disorders are qualitatively different from one another and that MDD should be regarded as distinct from bipolar I and bipolar II disorders. Although it has become increasingly controversial in recent years, there remains a body of evidence in support of the categorical model. This collection of evidence can be informally grouped as demographic variables and onset, symptoms and course, and treatment.

Demographic Variables and Onset

Some evidence in favor of the categorical model of mood disorders comes from the age of onset associated with each disorder. Bipolar-II has most frequently been regarded as having an earlier age of onset (Bowden, 2005; Benazzi, 2007d). One study demonstrated that mean age at onset was 18.1 for bipolar depression and 25.6 for unipolar depression although it was not clear whether bipolar II was included in the bipolar sample (Bowden, 2005).

In addition to age at onset, other demographic factors vary between bipolar and unipolar depressions. Gender is the most notable of these factors. Compared to men, twice as many women are diagnosed with unipolar depression, whereas there no significant gender difference in bipolar disorder (Bowden, 2005). Furthermore, women with a diagnosis of bipolar-I or -II tend to experience a greater proportion of depressive symptoms than do men with the same diagnoses (APA, 2000). That depression has been
observed more frequently in women than in men can be attributed to a number of factors. It remains important, however, to note that bipolar and unipolar depression have different proportions of men and women, a fact which may be attributable to a core difference in the two disorders.

Unipolar and bipolar disorders can also be differentiated by the disorders which often precede them in childhood and by the disorders with which they are often comorbid. Unipolar depression has not been explicitly linked with any childhood disorder, but there is some evidence that attention-deficit/hyperactivity disorder is a marker for a potential bipolar diathesis (Savitz, Solms, & Ramesar, 2005). Throughout the course of the mood disorders, MDD is often considered to have relatively high comorbidity with anxiety disorders, including panic disorder and obsessive-compulsive disorder, as well as with anorexia and bulimia, substance-abuse disorders, and borderline personality disorder (APA, 2000). Bipolar disorders, in contrast, have high comorbidity with alcohol abuse at a rate of 30-50%, substance abuse at a rate of over 60%, anorexia and bulimia, panic disorder, and social phobia (APA, 2000; Bowden, 2005; Savitz, Solms, & Ramesar, 2005). Although some overlap in comorbidity can be observed, there are important differences as well, suggesting some difference in the course or cause of these disorders.

There are important differences in the family history of individuals with unipolar versus bipolar disorders. In Benazzi’s recent (2006b) review, participants with bipolar-I had more family history of bipolar-I disorder than of bipolar-II. Participants with bipolar-II had more family history of bipolar-II than of bipolar-I. This suggests there is a qualitative difference between the two disorders, and that family histories and genetics
may be different for bipolar-I than those for bipolar-II. Other researchers have found evidence for a strong genetic influence in bipolar disorders, with heritability scores between 60 and 85% (Savitz, Solms, & Ramesar, 2005). Unfortunately, no research could be found which compared the family histories of major unipolar depression with bipolar depression. It is not known, therefore, whether this generalizes to provide support for a categorical distinction between unipolar depression with bipolar depression.

Symptoms and Course

Notably, qualitative differences between depressive syndromes have been reported for unipolar and bipolar depression. Bipolar depressive episodes are more likely to involve such symptoms as irritability, hypersomnia, mood lability, guilt feelings, and suicidal ideation (Benazzi, 2006b; Bowden, 2005; Hantouche & Akiskal, 2005). Some researchers have argued that psychomotor retardation is also more frequently occurring in bipolar disorder (Bowden, 2005) whereas other researchers have argued that it is better conceptualized as a predominant feature of unipolar depression (Hantouche & Akiskal, 2005). In contrast to the bipolar depressive syndrome, unipolar depressive episodes are more likely to include symptoms such as psychomotor retardation, loss of interest, and insomnia (Hantouche & Akiskal).

There are also differences in the rates at which various DSM-IV-TR diagnostic specifiers are used to describe depression. Mixed depression and atypical depression have both been reported with greater frequency in bipolar disorders than in unipolar disorders. Mixed depression has been observed in about 60% of individuals with bipolar-II diagnoses but only in 30% of individuals with unipolar depression diagnoses (Benazzi, 2006b; Bowden, 2005). Askiskal and Benazzi (2005) argued that atypical depression can
best be viewed as a variant of bipolar-II rather than a subtype of unipolar depression, an argument that has some degree of consensus (Benazzi, 2007d; Bowden, 2005).

The course of bipolar and unipolar depressive disorders is also different, which continues to support that the two are categorically different. Bipolar II disorder has been associated with a greater total number of affective episodes when compared to MDD, which implies there is a difference in the cycle of the two disorders (Akiskal & Benazzi, 2005; Benazzi, 2007d). In addition, bipolar depressions “tend to have shorter duration and are associated with greater anergy” (Hantouche & Akiskal, 2005, p. 130).

Another, more alarming difference in the course of bipolar and unipolar mood disorders are differences in the rates of completed suicides and suicidal ideation. According to the DSM-IV-TR (APA, 2000), 10-15% of individuals with bipolar disorder will complete suicide. Individuals with bipolar disorder have a risk of at least one suicide attempt at a rate between 25 and 50%, compared to the 15% risk of a suicide attempt in unipolar depression (Bowden, 2005).

Treatment Considerations

In addition to the difference in the symptoms and course of bipolar and unipolar disorders, there is also evidence that the two types of mood disorder respond differentially to treatment. Whereas certain types of psychotherapy and antidepressants are considered ideal for the treatment of unipolar depression, psychotherapy has often been deemed ineffective for bipolar disorder, and antidepressants can be iatrogenic in some cases of bipolar depression. For bipolar disorder, lithium carbonate and other mood stabilizing agents have been established as the primary mode of treatment, and these medications have been rarely used for the treatment of unipolar depression.
Tricyclic antidepressants and MAOIs are rarely used for the treatment of bipolar disorder, so most research in this area is in regard to SSRIs and SNRIs. Such antidepressants have been associated with two maladaptive phenomena in bipolar disorder, manic switching and rapid cycling (Benazzi, 2006b; Bowden, 2005; Thase, 2006a). Manic switching is the reversal of symptoms from depressed to manic or hypomanic after the introduction of an antidepressant medication. This can clearly be risky for an individual with bipolar disorder, and implies that there is some difference in the etiology of the two types of depression. Rapid cycling is the increase in frequency of mood episodes, which occurs at the expense of euthymic periods of time. Again, this suggests that antidepressants function differently when treating bipolar depression and that there is some underlying difference in the two syndromes that lead to different treatment responses.

Lithium carbonate, anticonvulsants, and antipsychotics have been established for acute and prophylactic treatment in bipolar disorder. These medications tend to be selectively effective for bipolar disorders, and have never been established for use to prevent recurrence of depression in MDD. The fact that lithium is effective with bipolar disorder but not unipolar depression has long been cited as evidence for the categorical distinction between recurrent unipolar depression and the cycling associated with the bipolar disorders (Benazzi, 2006b).

To summarize, there is a substantial body of evidence that supports the position that unipolar and bipolar disorders are qualitatively different and distinct enough to be considered as belonging to discrete categories rather than lying along the same continuum. This body of information includes differences in course, treatment response,
and symptom clusters, even within depressive episodes. Furthermore, the DSM-IV-TR, which represents the consensus of the mental health field in general and psychiatrists in particular follows the categorical model. Given that this model has been fairly long-standing within the field of psychology and has a large degree of support within the scientific literature, it would take a large amount of evidence to change general opinion.

The following section presents the opposite viewpoint, the dimensional model. Research supporting the categorical model has tended to compare bipolar I to MDD, except where bipolar II was specifically mentioned. Given that research compared the two most extremely polar examples of mood disorder, it is unsurprising that a categorical model was supported. Research supporting a dimensional model has tended to compare bipolar II disorder to MDD on the basis that the two are more similar, and is therefore likely to arrive at slightly different conclusions.
EVIDENCE IN SUPPORT OF A DIMENSIONAL MODEL OF MOOD DISORDERS

As was mentioned above, a great deal of evidence is required in support of a new model before an old one should be dismissed. In order to replace a categorical model with a dimensional model, the dimensional model should better explain the course and prognosis of a disorder, and should lead to more effective treatment. There exists a wealth of evidence which provides support for the position that a dimensional model of mood disorders is more helpful and meaningful than a categorical model. For the sake of conceptual clarity, the evidence can be grouped into demographics and onset, clinical presentation of the disorders, and treatment considerations of the mood disorders.

Demographics and Onset

For individuals with either unipolar or bipolar depressive disorders, family history reveals increased rates of MDD compared to the population as a whole (Bowden, 2005). In fact, MDD is the most common mood disorder in families of individuals with a bipolar I or bipolar II diagnosis, a finding which supports the continuity between the bipolar and unipolar depression (Benazzi, 2006b; 2007c). The importance of this shared family history for individuals with a unipolar or bipolar mood disorder is that it implies a shared diathesis, most probably genetic. If there is a similar genetic vulnerability to both types of mood disorder, it is illogical and artificial to force them into separate categories.

A gender difference has often been observed and cited between BP-I and MDD, with MDD occurring more frequently in women than in men and no major gender difference for BP-I. When BP-II is included, its gender distribution more closely parallels
that of MDD, with more females diagnosed than males (Bowden, 2005; Shih, Belmonte, & Zandi, 2004). This provides support for the dimensional model because the gender distribution directly contradicts the categorical model and can be better explained by the existence of some underlying continuum.

Age of onset also supports the existence of a dimension of mood disorders. The age of onset for individuals with highly-recurrent unipolar depression is more similar to the age of onset for bipolar II disorders than for non-recurrent unipolar depression (Saggese, Lieberman, & Goodwin, 2006). In other words, recurrent depression is similar to BP-II in terms of age of onset.

Another concept related to the onset of bipolar and unipolar depressive disorders is the idea of diagnostic conversion from MDD to BP-I or BP-II. Oftentimes, this is described as misdiagnosis which fails to take into account that depression typically presents prior to mania and hypomania. The mood disorders represent a group of disorders in which unipolar depression converts into a bipolar mood disorder at a rate of about 40-50% (Angst, 2004; Benazzi, 2006b). In fact, some researchers have discovered that the time between first depressive episode and first manic or hypomanic episode is approximately five years (Ghaemi, Ko, & Goodwin, 2002) with approximately 8 to 8.9 years of clinical treatment prior to correct diagnosis (Ghaemi, Ko, & Goodwin, 2002; Thase, 2005). This implies that the two share a similar origin and initial clinical presentation, which supports a dimensional model of mood disorder (Benazzi, 2006b; Cassano et al., 2004).
Symptoms and Course

A number of researchers have studied similarities and differences in the clinical presentations of the different mood disorders, both in terms of symptom clusters and course of the disorders. An overwhelming majority of studies that have examined BP-I and BP-II separately have found that in many ways, BP-II parallels MDD more closely than it parallels BP-I. This evidence would support a dimensional model of mood disorders due to the implication that BP-II is an intermediate disorder between MDD and BP-I, rather than being a less severe version of BP-I.

The first piece of evidence from these studies resulted from comparing the clinical presentation of highly recurrent (more than five episodes) unipolar depression to the clinical presentation of low recurrent (less than five episodes) unipolar depression and BP-II disorder. The results of this study by Saggese, Lieberman, and Goodwin (2006), showed that highly recurrent unipolar depression was more similar to BP-II than to low recurrent unipolar depression in terms of age of onset, chronicity of symptoms, and level of comorbidity. This suggests that the course and symptom cluster of highly recurrent unipolar depressions and BP-II disorder are similar and that the course is a more important consideration in this case than the polarity (Thase, 2006b). Although the five-episode cutoff seems arbitrary, it has in fact been validated as a meaningful cutoff point for the presence of bipolarity even in the absence of a hypomanic or manic episode (Akiskal & Benazzi, 2006). The importance of this finding is that it creates a link between the two mood disorders in a way that argues for their existence along a continuum of mood disorders.
Other studies have compared recurrent unipolar depression to BP-II and some have found a link between the presence of atypical depression and bipolarity. For example, Akiskal and Benazzi (2005) compared the statistical distribution of atypical symptoms across BP-II and MDD. The authors argued that if there was a bimodal distribution in the symptoms this would provide evidence for the categorical model of mood disorders and if there was a lack of bimodal distribution this would provide evidence for a dimensional model of mood disorders. The authors did not find a bimodal distribution, which means the atypical depressive symptoms existed in similar clusters across the two disorders. Again, this provides support for the dimensional model of mood disorders because atypical depression has a similar presentation in MDD as it does in BP-II.

In an earlier study, Benazzi (1999) also found that participants with atypical depression and a diagnosis of either MDD or BP-II did not have significant differences in non-symptom clinical factors. These factors included age of onset, gender distribution, duration of episodes, number of recurrences, and severity of episodes, providing further support for the similarity and dimensional nature of these mood disorders.

Another piece of information frequently cited as evidence for the dimensionality of mood disorders is the existence of depressive mixed episodes. A depressive mixed state is defined by the DSM-IV-TR as the simultaneous presence of a manic and a depressed episode (APA, 2000), but researchers have found that a more empirically validated definition is a depressive episode plus three or more intradepressive hypomanic symptoms (Benazzi, 2007b). The existence of mixed episodes was a primary reason that Kraepelin chose to consider the mood disorders a single disorder with multiple
presentations, simply because the very existence of opposite polarity symptoms within the same episode suggests that the two cannot be meaningfully separated (Benazzi, 2007b).

A study of individuals with either MDD or BP-II found that although mixed depression was more common in BP-II, it was also present at a rate of about 30-32% in those individuals who had been previously diagnosed as unipolar (Benazzi, 2007c; 2007d). Again, although mixed depression was present at a much higher rate, between 64.5 and 70% for those individuals with BP-II, its very existence for individuals with a previous unipolar diagnosis suggests that when careful assessment is utilized, bipolar signs are revealed at a high frequency in supposedly unipolar individuals (Benazzi, 2007c; 2007d). Although this may represent an unfortunate pattern of misdiagnosis within the field, it also demonstrates the dimensional nature of mood disorders.

A lack of bimodality in symptom clusters has also been found for intradepressive hypomanic symptoms that do not reach the threshold for a mixed episode (Benazzi, 2007b; Benazzi, 2006b). In other words, for depressed individuals with hypomanic symptoms and a diagnosis of either MDD or BP-II the number and type of intradepressive hypomanic symptoms were similar. These findings support a dimensional model of mood disorder because the clinical picture and cluster of symptoms are often more similar than different between MDD and BP-II.

Another incident of opposite polarity symptoms within a single episode is dysphoric mania, or a manic episode with intramanic depressive symptoms. Dysphoric mania represents an argument for a continuum approach to mood disorders not only
because of the opposite-polarity symptoms, but also because even one depressive symptom within a manic episode predicts low response to lithium (Akiskal et al., 2000).

Other evidence in support of a dimensional model of mood disorders is less intuitive. The very nature of unipolar and bipolar disorders suggests more similarity than difference. Both types of mood disorder are generally thought to be life-long, highly recurrent, and non-degenerative (Benazzi, 2006b). Although they have episodes of opposite polarity, the evidence cited above seems to indicate that depressive and manic episodes are not always mutually exclusive.

Another frequently overlooked but highly important fact is the importance of depressive episodes in both disorders. Although mania and hypomania are often more salient to clinicians and researchers, individuals with bipolar disorders actually spend far more time in depressive episodes than in manic, hypomanic, or mixed states (Benazzi, 2006b). In fact, a study conducted by Ghaemi, Ko, and Goodwin (2002) found that individuals with a bipolar disorder spent 50% of their lives in a depressive episode and only 11% of their lives in a manic or hypomanic episode. Although both types of episode have a significant impact on functioning, depression is by far the most impactful in regards to time spent in an episode. Thase (2005) further argued that depression in bipolar disorder is "associated with significant morbidity and increased mortality" (p. 266). Again, these facts are important because, although our current diagnostic system separates the mood disorders categorically, they in fact have many clinical similarities that may be more important for assessment and treatment of these disorders than are their differences.
Another symptom cluster that is similar between bipolar and unipolar mood disorders relates to cognitive styles. In a comparison study of individuals with bipolar I disorder, individuals with recurrent major unipolar depression, and healthy controls, researchers compared cognitive styles that related to dysfunctional attitudes and self-esteem (Jones et al., 2005). The researchers found that when current mental state was taken into account there were not significant differences in dysfunctional attitudes and self-esteem between the bipolar I participants and the unipolar participants. Both groups scored lower on measures of self-esteem and higher on measures of dysfunctional attitudes than did healthy controls (Jones et al., 2005). The results of this study indicate that cognitive functioning may have important similarities for the spectrum of mood disorders, and that both deviate from normal cognition in a similar manner. This provides further support for the theory that a dimensional model is appropriate for mood disorders.

Kraepelin's classic research includes unstable temperament as one of the foundations of mood disorder (Benazzi, 2006b). Research has supported this classic model, and Benazzi (2006b) recently reported data that suggested "mood lability, mood swings, [and] ups and downs" (p. 5) commonly occur in both MDD and BP-II; at rates of approximately 35 and 65%. This mood lability, often referred to as cyclothymic temperament, parallels the more extreme and long-term mood changes which are notable in bipolar disorder. Although it is more common in BP-II than MDD, the fact that mood lability is present in over one-third of MDD cases suggests that the mood disorders have a great deal of overlap in symptoms.

Many researchers have interpreted the similarities in mood disorders to mean that in addition to BP-I, BP-II, and MDD there may be a soft bipolar disorder, or 'bipolar
spectrum disorder.' These researchers argue that the incorporation of a soft bipolar disorder is the best way to ensure proper psychological and psychopharmacological treatment for individuals who fail to meet full criteria for BP-I or -II but who exhibit bipolar symptoms or family history. A bipolar spectrum disorder would include MDDs with evidence of antidepressant-induced hypomania, spontaneous hypomania which fails to meet the duration requirement, mixed states, agitated depression, and bipolar family history (Akiskal et al., 2000; Ghaemi, Ko, & Goodwin, 2002).

Other researchers have urged the inclusion of bipolar-III into the next edition of the DSM, which would include all recurrent unipolar depressions with antidepressant-induced hypomanic episodes (Akiskal et al., 2000). Benazzi (2007d) described these approaches to mood disorders as a mixed approach, where the most extreme examples of BP-I, BP-II, and MDD would be described categorically as they are by the current system, but a version of bipolar spectrum disorder would be added to satisfy a dimensional approach. This solution could be a helpful one in terms of meaningfully communicating symptom clusters between mental health professionals. It is extremely important that soft bipolar disorders are recognized and diagnosed because the number of hypomanic symptoms is correlated with paranoid and suicidal ideation, both of which create danger for the diagnosed individual (Cassano et al., 2004).

Treatment Considerations

The third category of evidence in favor of a dimensional or spectrum model of mood disorders is treatment considerations for the mood disorders. The present decade has been witness to increased understanding of the actual functions of antidepressants and mood stabilizers, and some of this research has implications for the understanding of
bipolar and unipolar depression. Antidepressant medications have long been considered iatrogenic in bipolar disorders by functioning as pro-cyclic agents, or agents known to increase the rate of affective switching and decrease the well intervals between episodes (Ghaemi, Ko, & Goodwin, 2002). Evidence suggests that the pro-cyclic effect can also be observed for recurrent unipolar depression. That is, although they function to reduce the duration of depressive episodes, antidepressant medications also reduce the duration of asymptomatic phases between episodes (Saggese, Lieberman, & Goodwin, 2006). This suggests that although their action is more noticeable in BP-I, antidepressants have the same risks in MDD. This suggests that the antidepressants do not differentially affect bipolar and unipolar depression, and that the two may have important similarities.

Antidepressant medications have also been shown to function as catalysts for hypomanic episodes, even for individuals with MDD and no prior history of hypomania (Benazzi, 2007c; Thase, 2006a). In addition, antidepressant-induced hypomania has been shown to have the same symptom clusters as spontaneous hypomania, which suggests that antidepressant-induced and spontaneous hypomanias are not qualitatively distinct phenomena (Benazzi, 2007c). This suggests that antidepressant-induced hypomania lies along the bipolar spectrum and that unipolar and bipolar mood disorders are not categorically different disorders.

Lithium has been established as effective for the prevention of manic and hypomanic episodes in bipolar disorder. Some researchers have reported that lithium is also effective for the prevention of depressive episodes in recurrent unipolar and bipolar depressions (Benazzi, 2007a; Saggese, Lieberman, & Goodwin, 2006). In fact, Benazzi (2007a) presented evidence that lithium may be as effective as antidepressants at
preventing depressive relapse in MDD. Again, this suggests that the medication has the same action in bipolar and unipolar depression, and that the two categories of depression are more similar in nature than different. A dimensional approach to the conceptualization and treatment of mood disorders is therefore supported.
DISCUSSION

The majority of research in this area is subject to the same criticism. One such criticism is that bipolar and unipolar mood disorders are only rarely studied using random sampling, and cannot be studied using random assignment. Samples of mood disordered participants are typically collected as clients present to research-based clinics associated with universities. Therefore, samples are typically self-selective. A prime example of this type of research is that done by Benazzi, who runs a mood-disorders clinic in rural Italy and uses these clients as ongoing research participants (2003; 2006a; 2007e). Although there are typically very few exclusion criteria, typically comorbid personality disorder or substance dependence, the sample remains limited to those clients who live relatively close to the clinic and deliberately seek treatment.

Another limitation of the current research is that much of the research in support of a dimensional model has been conducted by those researchers who argue in favor of a dimensional model (Akiskal & Benazzi, 2005; Benazzi, 2007a). Therefore, although the researchers take steps to reduce the impact of potential bias, it is possible that there is an expectation bias acting in the research.

One of the most concerning problems within some of the existing mood disorder research is that many studies draw broad conclusions about ‘bipolar disorder’ either without separating participants with BP-I from those with BP-II (Dunner, Fleiss, & Fieve, 1976) or while excluding BP-II participants altogether (Cassano et al., 2004). This was a frequent problem in research until very recently. More recently, this particular problem
has been overcome by such researchers as Benazzi (2007a; 2007b) and Akiskal (2005) who either study only one of the two bipolar disorders or differentiate between the two groups. This improves the likelihood that information will be accurate the type of mood disorder in question, but exclusion of other forms of bipolar disorder can also lead to the loss of important data.

There are also important strengths in the existing body of research. As was previously stated, participants were only excluded on the basis of personality disorder or substance dependence diagnoses on the basis that it is often difficult to differentiate between the symptoms of mood disorders and these other diagnoses. This was the maximum reported exclusion criteria from the research conducted by Benazzi (1999; 2001; 2007a) and Akiskal (2005). With this in mind, it is likely that the research is applicable across demographics. Unfortunately, the largest-scale study of this type is ongoing one conducted by Benazzi in Italy. More large-scale research along this vein is still needed in the United States and other countries.

Finally, a major strength of current mood disorder research is the willingness of researchers to reexamine and challenge the status quo. As was stated previously, the DSM-IV-TR has many strengths, but is currently nearly ten years behind the state of the research. Therefore, it is important to continue to challenge existing assumptions. In proposing a new model of mood disorder, it is hoped that this literature review can continue to challenge assumptions in a manner that is supported by the most current research.

In terms of the literature that has been reviewed here, the overwhelming conclusion is that the current categorical model is not supported by research. As was
noted above, the majority of evidence in support of a categorical model of mood disorder excluded BP-II participants from samples. Support was found for categories because the most extreme cases were compared to one another. When less disparate cases have been compared, particularly MDD and BP-II, research has consistently favored a dimensional approach to the conceptualization and diagnosis of mood disorders when compared to a categorical model.

All of the research examined for this literature review in which the categorical model has been challenged has included the proposal of some version of a dimensional model of mood disorders. Some researchers have proposed the existence of a ‘bipolar spectrum disorder’ that functions as a catch-all between the existing mood disorder diagnoses (Ghaemi & Baldessarini, 2007). Others have proposed the inclusion of bipolar III disorder into the DSM, which would be described as recurrent unipolar depression with antidepressant-induced hypomania (Akiskal et al., 2000).

It is the contention of this review of existing literature that the best-fitting model for available data is a two-dimensional model of mood disorder. As stated previously, one of the dimensions is the degree of recurrence and the second dimension is the nature or polarity of the mood episode. Any individual mood disorder case can have some degree of recurrence from a single episode to a highly recurrent course. This same mood disorder case can involve episodes of a single polarity, most typically depression, or of both polarities, by the experiencing of hypomanic and/or manic episodes. Therefore, any individual case can be conceptually mapped along both dimensions in order to enhance the understanding of a particular mood disorder case.
The evidence in support of such a dimensional model was explored above. To reiterate the main themes, however, there are similarities in the demographics of individuals with BP-II and MDD, as well as similarities in terms of symptom onset, course of the disorder, and treatment of the disorder. These similarities are in direct opposition to a categorical model of mood disorders.

Research does not provide support for the continued categorization of mood disorders into MDD, BP-I, and BP-II without renovation of the diagnostic system in a manner which is consistent with a dimensional model. However, given the degree of influence such a categorical approach has over current mainstream clinical practices, it is unlikely that the diagnostic system will evolve rapidly. Instead, more research is required to provide support for a dimensional model before the diagnostic system can be expected to respond. It is possible that continued research could also have the affect of allowing the conceptual model to evolve, particularly because the model is relatively new and preliminary.

In order to support the field of psychology's growth, additional research is needed to expand the body of knowledge concerning all currently existing categories of mood disorder. It is important to compare demographic, onset, symptom, course, and treatment information to continue to provide support for or evidence against a new two-dimensional model of mood disorders. In addition, due to the small number of researchers in this field and the reliance on a small number of samples, it would be useful to conduct studies on new samples to ensure that the results withstand further investigation. For example, Benazzi has created an impressive body of research on mood disorders in Italy (1999; 2007a), and a comparable study in the United States or elsewhere is needed.
CONCLUSION

It is anticipated that the trend towards greater recognition of the dimensional nature of affective disorders will continue. The benefits of this movement will include an enhancement of the empirical basis for ongoing diagnosis and treatment development, better understanding of individual psychopathology, and improved understanding of the nature of mood disorders. It is also strongly urged that mental health clinicians more carefully assess for bipolarity. Many of these disorders are currently being misdiagnosed as MDD due to lack of attention to subclinical hypomania, family history, and mood stabilizer response. More careful assessment and diagnosis should enable better treatment of individuals whose major depression is bipolar in nature despite having no reported history of hypomania or mania. Finally, another benefit of an increased understanding of the dimensional nature of mood disorders is that a more empirically-based understanding of the disorder in question enables the development of more effective psychotherapeutic treatments.
REFERENCES


