

# State of the art

## *Various forms of depression*

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**D**epression is still seen as a single clinical entity, especially in primary care. However, the subtyping of depression is fundamental for its correct treatment. The current subtyping of depression is based on *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, Text Revision (*DSM-IV-TR*) criteria.<sup>1</sup> The major depressive episode is the basic definition of depression given in *DSM-IV-TR*. The diagnostic criteria for major depressive episode require (i) five or more symptoms present during the same 2-week period, most of the day, nearly every day, representing a change from the previous level of functioning; at least one of the symptoms must be depressed mood or loss of interest/pleasure; (ii) the symptoms of depression: depressed mood (which can be irritable in children), diminished interest or pleasure in activities, weight loss or weight gain, decreased eating or

*The current subtyping of depression is based on the Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision (DSM-IV-TR) categorical division of bipolar and depressive disorders. Current evidence, however, supports a dimensional approach to depression, as a continuum/spectrum of overlapping disorders, ranging from bipolar I depression to major depressive disorder. Types of depression which have recently been the focus of most research will be reviewed: bipolar II depression, mixed depression, agitated depression, atypical depression, melancholic depression, recurrent brief depression, minor depressive disorder, seasonal depression, and dysthymic disorder. Most research has focused on bipolar II depression, mixed depression (defined by depression and superimposed manichypomanic symptoms), and atypical depression. Mixed depression, by its combination of opposite polarity symptoms, has been found to be common by systematic probing for co-occurring manichypomanic symptoms. Mixed depression is a treatment challenge for clinicians, because antidepressants alone (ie, not protected by mood-stabilizing agents) may worsen its manichypomanic symptoms, such as irritability and psychomotor agitation, which the Food and Drug Administration (FDA) has listed as possible precursors to suicidality.*

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increased eating, insomnia or hypersomnia, psychomotor agitation or psychomotor retardation, fatigue, loss of energy, feelings of worthlessness, excessive guilt, diminished ability to think, diminished ability to concentrate, indecisiveness, suicidality (thoughts of death, suicidal ideation, suicide attempt); (iii) the symptoms must not meet criteria for a mixed episode; (iv) the symptoms must cause clinically significant distress or impairment of functioning; and (v) the symptoms must not be related to substances, medical disorders, or bereavement. According to *DSM-IV-TR*, the clinical picture of depression is the same for all mood disorders. *DSM-IV-TR* divides depression into two basic categories: bipolar depression and (unipolar) depressive disorders. Subtypes of bipolar depression are bipolar I depression (history of mania), bipolar II depression (history of hypomania), and cyclothymic depression (frequently alternating hypomanic episodes and short depressions not meeting full criteria for a major depressive episode, lasting at least 2 years). Subtypes of unipolar depression are major depressive disorder and dysthymic disorder (which does not meet full criteria for a major depressive episode, and must last at least 2 years). Depression is graded by severity into mild, moderate, severe, and psychotic. *DSM-IV-TR* lists a series of cross-sectional specifiers of the major depressive episode (catatonic, melancholic, atypical, postpartum), and longitudinal course specifiers (chronic, ie, full criteria for a major depressive episode met for at least 2 years; full interepisode recovery present or absent; seasonal; rapid cycling).

The *DSM-IV-TR* diagnostic criteria for depression, based on the categorical distinction between bipolar disorders and depressive disorders, are the opposite of Kraepelin's unitary view of mood disorders. According to Kraepelin,<sup>2</sup> mania, hypomania, depression, mixed states, and mood temperaments were variants of the same disorder, manic-depressive insanity (illness). Manic mixed states (mixed mania/hypomania) and depressive mixed states (mixed depression) were one of the main building blocks supporting Kraepelin's unitary view of mood disorders. Mixed states are different combinations of manic, hypomanic, and depressive symptoms in the same mood episode. A logical conclusion was that if symptoms of opposite polarity could be present in the same episode, manic/hypomanic states and depressive states could not be distinct disorders. Also, recurrent depression (no history of mania or hypomania) was included in manic-depressive insanity by Kraepelin (i) because of its recur-

rent course; (ii) because manic episodes could have a later onset in its course; and (iii) because manic or hypomanic symptoms often co-occurred during depressions. In Kraepelin's view, severe and less severe mood disorders were "without sharp boundaries," and had "a common root with gradual transitions between the individual forms." Kraepelin's view is the basis of the current continuity or spectrum view of mood disorders, based on a dimensional approach which is the opposite of the *DSM-IV-TR* categorical approach (ie, clear boundaries among mood disorders).

The focus of this review will be on the new advances in the classification and description of several forms of depression.

## The mood spectrum

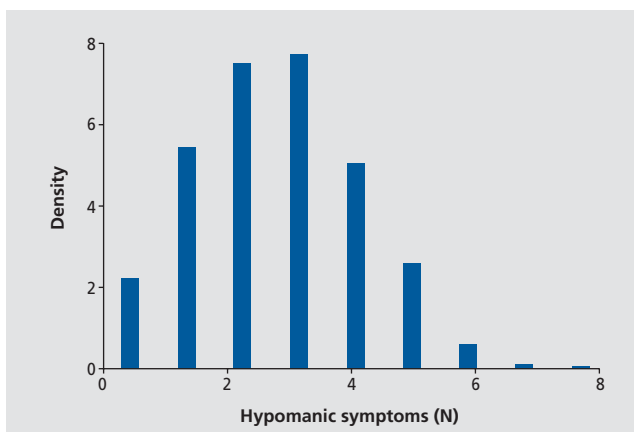
According to the spectrum view of mood disorders,<sup>3-17</sup> depression is not divided into independent categories as in *DSM-IV-TR*. Instead, several types of depression lie along a continuum, which does not have sharp boundaries between the categories, following a dimensional approach. The dimensional view of depression describes depression mainly by the grading of its severity and by associated features. Angst<sup>3-5</sup> described bipolar I depression (history of mania) and several subtypes of bipolar II depression (history of hypomania) on the basis of the severity of hypomania (hypomania with and without functional impairment) and on the severity of depression (major depressive episode, dysthymia, minor depression, recurrent brief depression). Angst also described several subtypes of non-bipolar depression, ie, major depressive disorder, dysthymia, minor depression, and recurrent brief depression. Akiskal<sup>6,7</sup> described bipolar I depression (history of mania), several bipolar II depression subtypes based on the severity of hypomania ("sunny" bipolar II, "dark" bipolar II) and on a co-occurring cyclothymic temperament (defined by frequent instability of mood, thinking, and behavior), bipolar III depression related to substances, and bipolar IV depression combining depression and hypomanic symptoms (depressive mixed state or mixed depression). Cassano<sup>8</sup> described a mood spectrum in which depressive and manic/hypomanic symptoms could mix in various combinations. Cassano found that patients with major depressive disorder (no history of mania or hypomania) often had a lifetime history of manic/hypomanic symptoms. Benazzi,<sup>14,15</sup> following Kendell and Jablensky's<sup>18</sup> approach to diagnostic validity (based on finding a

bimodal distribution of distinguishing symptoms between two related syndromes), studied the distribution of the atypical symptoms and of the co-occurring hypomanic symptoms between bipolar II depression and major depressive disorder. As the atypical symptoms and the co-occurring hypomanic symptoms have been reported to be more common in bipolar II depression than in major depressive disorder, a clustering of these symptoms on one side was the expected finding. Instead, the distribution of these symptoms was not bimodal but normal-like, supporting a continuity between bipolar II disorder and major depressive disorder. *Figure 1* shows the histogram of the distribution of co-occurring hypomanic symptoms between bipolar II depression and major depressive disorder in a new large sample collected by the present author (unpublished data).

In the mood spectrum, several subtypes of depression, useful for clinical practice, have been described: bipolar I depression, bipolar II depression, mixed depression, agitated depression, atypical depression, melancholic depression, recurrent brief depression, minor depressive disorder, seasonal depression, and dysthymic disorder.

### Bipolar depression versus major depressive disorder

The clinical picture of bipolar depression has been defined, until recently, by that of bipolar I depression. It has been repeatedly shown that bipolar I depression, compared with major depressive disorder, is more likely to involve hyper-



**Figure 1.** Histogram of the distribution of co-occurring hypomanic symptoms between bipolar II depression and major depressive disorder (n=650, bipolar II disorder=389, major depressive disorder=261).

somnia and psychomotor retardation, while major depressive disorder has been reported to be more likely to involve insomnia and psychomotor agitation.<sup>19</sup>

Evidence has supported a distinction between bipolar I disorder and bipolar II disorder, on the basis of gender differences (females as common as males in bipolar I disorder, females more common than males in bipolar II disorder), family history differences (relatives of bipolar I disorder probands have more bipolar I disorder than bipolar II disorder, while relatives of bipolar II disorder probands have more bipolar II disorder than bipolar I disorder), and high diagnostic stability.<sup>10-13,20,21</sup>

The clinical picture of bipolar II depression, versus major depressive disorder, has been found to have more atypical symptoms (hypersomnia, overeating) and more co-occurring hypomanic symptoms (including psychomotor agitation).<sup>15,22,23</sup> The different frequency of psychomotor agitation in bipolar I depression (lower) versus bipolar II depression (higher) may have an impact on treatment, as antidepressants alone may increase the severity of psychomotor agitation. As the diagnosis of bipolar II disorder is often missed,<sup>4,24,25</sup> bipolar II depression may be misdiagnosed as major depressive disorder, and the often co-occurring hypomanic symptoms may be undetected, leading to the use of antidepressants not protected by mood-stabilizing agents.

### Mixed depression (depressive mixed state)

Mixed depression is not classified in *DSM-IV-TR*. *DSM-IV-TR* describes a mixed state only in bipolar I disorder, requiring mania and a concurrent major depressive episode. Mixed depression is defined by the combination of depression and manic/hypomanic symptoms, usually below the minimum number required for the diagnosis of mania and hypomania, and *not including elevated mood* by definition. Mixed depression has been described in bipolar I disorder, bipolar II disorder, and major depressive disorder.<sup>15,21,26-50</sup> Mixed depression follows the classic descriptions by Falret (1854)<sup>51</sup> in “circular insanity,” Hecker (1898) in “cyclothymia” (corresponding to *DSM-IV-TR* bipolar II disorder),<sup>52</sup> and by Kraepelin in “manic-depressive insanity”<sup>53</sup> (corresponding to *DSM-IV-TR* bipolar I disorder, bipolar II disorder, and major depressive disorder). The most common *DSM-IV-TR* manic/hypomanic symptoms of mixed depression are irritability, mental overactivity (flight of ideas, racing thoughts, crowded thoughts), and behavioral overactivity (psychomotor agi-

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tation, overtalkativeness). Different frequencies of mixed depression have been reported, which may be related to *treated versus untreated* samples (as treatment may suppress manic/hypomanic symptoms), different definitions of mixed depression, different settings, and different assessment methods. Mixed depression, defined as a major depressive episode plus two or more co-occurring manic/hypomanic symptoms, was present in up to 70% of combined bipolar I disorder and bipolar II disorder samples. Mixed depression, defined as a major depressive episode plus three or more co-occurring hypomanic symptoms, was present in around 60% of bipolar II disorder and in around 30% of major depressive disorder *untreated* depressed outpatients. The hypomanic symptoms of mixed depression were often not reported spontaneously by patients. The systematic probing for hypomanic symptoms co-occurring during depression led to the highest frequencies of mixed depression. This kind of assessment would not have been possible by following strictly the *DSM-IV* structured clinical interview (SCID), which does not allow assessment of hypomania co-occurring during a major depressive episode.<sup>24,25</sup> Hypomania and depressive symptoms can mix, sometimes meeting *DSM-IV-TR* criteria for a major depressive episode. Dysphoric (mixed) hypomania (hypomania plus major depressive episode, no elevated mood) was not common among depressed outpatients (frequency found to be around 15%), and it was similar to mixed depression on bipolar validators, supporting a continuity between hypomania and depression.<sup>41,49,50</sup>

A strong association between bipolar (bipolar I and bipolar II) family history and mixed depression supported the bipolar nature of mixed depression of bipolar disorders and of major depressive disorder. Not only was bipolar family history more common in mixed depression versus nonmixed depression, but also a dose-response relationship was found between number of hypomanic symptoms co-occurring during depression and bipolar family history loading in bipolar II disorder and major depressive disorder (ie, the higher the number of co-occurring hypomanic symptoms, the higher the bipolar family history loading). Mixed depression in major depressive disorder, compared with nonmixed major depressive disorder, had a bipolar family history and an age at onset closer to that of bipolar II disorder.

Mixed depression was also validated by several factor analysis studies, showing a “hypomanic” factor superimposed on nonbipolar depression, and a factor structure

of the hypomanic symptoms of mixed depression similar to that of hypomania occurring outside depression (apart from the elevated mood factor).

Several dimensional and categorical definitions of mixed depression were tested. It was more the number of co-occurring hypomanic symptoms than specific hypomanic symptoms, combinations of symptoms, and hypomanic factors that was found to be more strongly linked to bipolar validators. The most validated definition, on the basis of its strong links to bipolar family history and bipolar II disorder (thus showing both a diagnostic validity and a diagnostic utility, ie, a high positive predictive value for bipolar II disorder) was that of a major depressive episode plus three or more co-occurring hypomanic symptoms.

Kraepelin, among the mixed states, described “excited depression,” whose opposite polarity (manic) symptom was psychomotor agitation. The diagnostic validity of *agitated depression* was tested. Agitated depression was described in bipolar I disorder and in bipolar II disorder. In bipolar I disorder it was often a psychotic depression, while in bipolar II disorder it was often nonpsychotic. Agitated depression was found to be often mixed (ie, it had many concurrent manic/hypomanic symptoms). It was only when agitated depression was mixed that it was different from nonagitated depression on bipolar validators. When agitated depression was not mixed, it was not different from nonagitated depression on bipolar validators. These findings did not support the diagnostic validity of agitated depression, as psychomotor agitation was found to be a marker of a depression that was highly likely to be mixed.<sup>17,32,33,42,46</sup>

Mixed depression, defined by three or more co-occurring hypomanic symptoms, showed a high positive predictive value for bipolar II disorder. This is an important finding, because bipolar II disorder is highly underdiagnosed. By careful, skillful probing for history of hypomania (often supported by interviewing key informants), the frequency of bipolar II disorder was found to be similar to that of major depressive disorder, in both community samples and outpatient clinical samples.<sup>4,53-56</sup> The increased detection of bipolar II disorder was related mainly to the use of semistructured interviews, to probing for hypomania focusing more on overactivity than on mood change, and to interview by clinicians, while previous community studies underdiagnosing bipolar II disorder followed strict diagnostic criteria and used structured interviews by lay interviewers. The treatment

impact of bipolar II disorder misdiagnosed as major depressive disorder may be important, as antidepressants used alone (ie, no concurrent mood-stabilizing agents) may increase the risk of switching to mania/hypomania, and may increase the severity of the irritability and psychomotor agitation of mixed depression that the US Food and Drug Administration (FDA) has reported to be possible precursors to suicidality.<sup>57-62</sup>

The *DSM-IV-TR* list of manic/hypomanic symptoms does not include specific symptoms (apart from perhaps elevated mood and grandiosity). Symptoms similar to those of mixed depression (especially irritability and psychomotor agitation) can be found in other Axis I disorders, especially in the anxiety disorders which frequently co-occur in mood disorders.<sup>1</sup> “Crowded thoughts,” ie, the flooding of the mind by ideas which cannot be stopped, are similar to obsessive ruminations and to the ruminations of excessive worry. Irritability is frequent in major depressive disorder,<sup>63</sup> and psychomotor agitation can be a sign of major depressive disorder or of anxiety. “Anxious depression” was defined as a major depressive disorder plus the “psychic anxiety” item of the Hamilton Depression Rating Scale,<sup>64</sup> which includes excessive worrying.<sup>65</sup> The relationship between psychomotor agitation and anxiety symptoms in major depressive disorder is unclear (a correlation was found to be present or not).<sup>66,67</sup> A comparison of the Montgomery and Asberg Depression Rating Scale (MADRS)<sup>68</sup> items related to anxiety between two large samples of bipolar II disorder and major depressive disorder did not find score differences, which should have been found if mixed depression (which is more common in bipolar II disorder) were related to anxiety.<sup>69</sup> The bipolar nature of irritability, psychomotor agitation, and racing/crowded thoughts was shown, in mood disorders, by a strong link to bipolar family history (controlling for bipolar II disorder), and by a dose-response relationship between the number of co-occurring hypomanic symptoms and bipolar family history loading.<sup>15,35,36,42,62,63</sup> This does not mean that these symptoms are always bipolar, only that they are more likely to be bipolar than not in mood disorders. Further support to the bipolar nature of the co-occurring hypomanic symptoms of mixed depression came from finding in this depression dimensions/factors of mania/hypomania (a “mental activation” factor and a “behavioral activation” factor).<sup>43-45,70</sup>

The response of mixed depression to antidepressants could be a useful tool for studying the anxiety versus the

bipolar nature of its “hypomanic” symptoms, as a bipolar nature would be supported by a worsening of these symptoms by antidepressants. There are few specific studies on this topic. In a combined bipolar I disorder and bipolar II disorder sample, mixed depression treated by antidepressants was more likely to switch than nonmixed depression.<sup>39</sup> In major depressive disorder, low-dose fluoxetine improved mild irritability and psychomotor agitation,<sup>71,72</sup> but imipramine led to many discontinuations due to central nervous system (CNS) side effects. The impact of antidepressants on mixed depression may thus be related to different biochemical effects, increasing nor-epinephrine apparently being more likely to worsen mixed depression. However, in major depressive disorder, high-dose fluoxetine was also found to induce psychomotor agitation (in 40% of cases).<sup>73</sup>

### Atypical depression

According to *DSM-IV-TR*, a major depressive episode with the atypical features specifier (atypical depression) can be present in almost all mood disorders. Distinguishing features of atypical depression are the following: (i) it is more likely to be present in bipolar disorders (especially bipolar II disorder); (ii) it is more likely to be present in seasonal depression; (iii) it is more likely to be present in younger than in older individuals; (iv) it has a lower age at onset compared with nonatypical depression; (v) it is more common in females; (vi) it has higher axis I comorbidity compared with nonatypical depression; and (vii) it has more bipolar family history versus nonatypical depression.<sup>23,74-93</sup> According to *DSM-IV-TR*, the atypical features specifier is defined by mood reactivity plus weight gain or increased eating, hypersomnia, leaden paralysis, and the personality trait interpersonal rejection sensitivity (at least two). The diagnostic validity of atypical depression is based on weak evidence: its better response to monoamine oxidase inhibitors (MAOIs) than to tricyclic antidepressants (TCAs),<sup>79</sup> and latent class analysis,<sup>77,78,90</sup> which has identified, among the major depressive episode symptoms, a class defined by the reversed vegetative symptoms of hypersomnia and overeating. *DSM-IV-TR* diagnostic criteria for atypical depression have recently been questioned on several grounds.<sup>80,82,84,85,88,89,91</sup> Specifically, it has been questioned whether mood reactivity should be the stem criterion for atypical depression, and evidence has been found supporting a definition of atypical depression

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mainly based on the reversed vegetative symptoms of hypersomnia and overeating (plus leaden paralysis). This definition has been used in several epidemiological studies on atypical depression. Its response to antidepressants should be tested versus *DSM-IV-TR* atypical depression, in order to see if the same disorder is covered by the two definitions. This new definition of atypical depression is more clinician-friendly, and should reduce the underdiagnosis of atypical depression, as some *DSM-IV-TR* features such as mood reactivity and interpersonal rejection sensitivity are not very reliable.

## Melancholic depression

According to *DSM-IV-TR*, a major depressive episode with the melancholic specifier (melancholic depression) can be found in almost all mood disorders. Melancholic depression is more common in older age and in more severe and psychotic depressions.<sup>94,95</sup> Its *DSM-IV-TR* diagnostic criteria require loss of pleasure in activities or lack of reactivity to pleasurable stimuli, plus distinct quality of mood, depression worse in the morning, early-morning awakening, marked psychomotor retardation or agitation, significant decreased eating or weight loss, and excessive guilt (at least three).

*DSM-IV-TR* states that psychomotor changes are “nearly always present.” This last statement comes from Parker's studies,<sup>94,95</sup> which came to the conclusion that the core feature of melancholic depression was psychomotor change (usually retardation), and that melancholic depression was more common in bipolar depression than in major depressive disorder. While psychomotor retardation has been classically found to be more common in bipolar I depression than in major depressive disorder, findings have been different in outpatient bipolar II depression.<sup>96,97</sup>

When outpatient bipolar II depression was compared with outpatient major depressive disorder, it was found that psychomotor agitation was more common in bipolar II depression, and retardation in major depressive disorder. Psychomotor change was found in less than 50% of depressed outpatients, running against the *DSM-IV-TR* statement on the primacy of psychomotor change for the diagnosis of melancholic depression. It seems that the clinical picture and frequency of melancholic depression are related to the bipolar subtype and to the setting (it has been reported that melancholic depression is more common in inpatients).

## Minor depressive disorder

The *DSM-IV-TR* research criteria for minor depressive disorder require, compared with major depressive episode criteria, at least two but less than five of the same set of depressive symptoms, nearly every day, most of the day, for at least 2 weeks, and that the criteria for major depressive episode, dysthymic disorder, mania, hypomania, and cyclothymic disorder are not met.

Angst et al<sup>3,98</sup> found that the diagnostic stability of several nonbipolar depressive disorders (major depressive disorder, dysthymia, recurrent brief depression, and minor depression) was low (ie, high shifting from one disorder to another one), questioning the categorical classification of nonbipolar depression and supporting a spectrum of nonbipolar depressive disorders.

Judd et al<sup>10-13</sup> found, in bipolar I disorder and in bipolar II disorder, that, during the long-term course, minor depressions and depressive symptoms were much more prevalent than mania/hypomania and major depressive episodes (three times more frequent than syndromal depression and mania/hypomania), especially in bipolar II disorder. In both disorders, the number, duration, and severity of depressive symptoms fluctuated over time, as well as manic/hypomanic symptoms, supporting a dimensional/spectrum view of depression and mania/hypomania. Judd et al found that bipolar II depression was more likely than bipolar I depression to be long-lasting and to have a fluctuating course of severity and duration (ie, major and minor depressions, and depressive symptoms), and to have more anxiety disorder comorbidity. On the other hand, bipolar I disorder was more likely to have long-term fluctuating manic/hypomanic/cycling episodes and manic/hypomanic symptoms. Patients were symptomatically ill for 50% of the weeks studied. In major depressive disorder, Judd et al found that minor depressions and depressive symptoms were much more common (three times) than major depressive episodes, and that symptom number, severity, and duration changed frequently, alternating over time. Patients were symptomatically ill for 60% of the weeks studied. The findings supported a spectrum view of nonbipolar depressive disorders.

The diagnostic validity of minor depression was supported by Rapaport et al.<sup>99</sup> Minor depression was defined by the symptoms of the major depressive episode, which had to be less than five but more than two, lasting at least 2 weeks. Minor depression, compared with major depres-

sive disorder, had more mood and cognitive symptoms, but not the classical neurovegetative symptoms. History of major depressive disorder was present in only 30%, the main finding supporting its diagnostic validity. The current status of minor depression is unclear.

### Recurrent brief depressive disorder

Recurrent brief depressive disorder research criteria require meeting major depressive episode criteria, apart from the duration, which should be between at least 2 days but less than 2 weeks. It should occur at least once a month for 12 consecutive months. It must not meet criteria for major depressive episode, dysthymic disorder, mania, hypomania, or cyclothymic disorder.

Angst et al<sup>100,101</sup> found that the diagnostic stability of several nonbipolar depressive disorders (major depressive disorder, dysthymia, recurrent brief depression, and minor depression) was low (ie, high shifting from one disorder to another one), questioning the categorical classification of nonbipolar depression and supporting a spectrum of nonbipolar depressive disorders. Pezawas et al<sup>102</sup> studied longitudinally recurrent brief depression in an adolescent community sample. Recurrent brief depression was defined according to *DSM-IV-TR* research criteria. The frequency of all depressive disorders was 21%; the frequency of recurrent brief depression was 1% without history of major depressive disorder and 1% with history of major depressive disorder. Compared with major depressive disorder, recurrent brief depression did not occur more in females than in males (a typical feature of nonbipolar depression), and frequency of comorbid axis I disorders was different. The frequency of suicide attempts, compared with major depressive disorder, was 8% vs 12%. Recurrent brief depression was not associated with bipolar disorders. However, use of fully structured interviews by lay interviewers underreports bipolar II disorder.<sup>4,24,25</sup> Angst and Hochstrasser<sup>100</sup> found that recurrent brief depression (defined as in *DSM-IV-TR*) had a lifetime community prevalence of 10% to 16%, it could shift to major depressive disorder and vice versa, had a 35% diagnostic stability, usually lasted 1 to 3 days, had different axis I comorbidity compared with major depressive disorder (more anxiety disorders), high frequency of suicide attempts (14% vs 21% in major depressive disorder), and high treatment seeking. Angst et al also found that recurrent brief depression was similar to major depressive disorder on most validators such

as age at onset, family history, and impairment of functioning. Carta et al<sup>103</sup> found a community lifetime prevalence of recurrent brief depression of 8%. A literature review by Merikangas et al<sup>104</sup> on recurrent brief depression found that validation criteria did not discriminate between recurrent brief depression and major depressive disorder, that it did not appear to be a milder subtype of depressive disorders, and that it was unrelated to the premenstrual syndrome. The current status of recurrent brief depression is unclear.

### Seasonal affective disorder

According to *DSM-IV-TR*, seasonal affective disorder is not a distinct disorder, but a specifier of the major depressive episode of bipolar disorders and depressive disorders. It is unclear if it is more common in bipolar disorders, but it seems to be more common in bipolar II disorder than in bipolar I disorder. The diagnostic criteria of the “seasonal pattern specifier” require a regular temporal relationship between the onset of major depressive episodes and a particular time of the year, full remissions (or a shift to mania/hypomania) at a characteristic time of the year, a temporal seasonal relationship in the last 2 years and no nonseasonal depressions during the same period, and seasonal depressions should far outnumber the nonseasonal depressions that may have occurred in the lifetime. The seasons of onset are usually autumn and winter (but there is also a summer subtype), and remissions usually occur in spring or summer. Seasonal depressions may be also subsyndromal. Symptoms of seasonal depression are often atypical ones such as hypersomnia and overeating, and depressions are usually mild to moderate. Probands may have seasonal affective disorder in first-degree relatives, but it is unclear whether its frequency is higher than in nonseasonal depression probands. In summer, at least 30% have hypomanic episodes. Diagnostic stability is low, being present in 20% to 40% of patients, which questions the diagnostic validity of seasonal affective disorder. Bulimia and anxiety disorders frequently co-occur. Community prevalence of seasonal affective disorder may range between less than 1% and more than 10%, and it is related to latitude (lower in warmer and sunnier countries). It is more common in women and in young age. Seasonal affective disorder is thought to be mainly caused by lack of light in winter (short photoperiod), and phototherapy seems to be a useful treatment.<sup>105-107</sup>

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## Dysthymic disorder

According to *DSM-IV-TR*, dysthymic disorder is a low-grade, persistent depression, causing clinically significant distress or impairment of functioning. Its diagnostic criteria require depressed mood for at least 2 years, plus poor eating or overeating, insomnia or hypersomnia, low energy, low self-esteem, poor concentration or difficulty making decisions, and hopelessness (at least two). No major depressive episode must have been present during the first 2 years, or a major depressive episode must have had full remission for at least 2 months before the onset of dysthymic disorder. After the first 2 years, a major depressive episode may be superimposed. There must be no history of mania, hypomania, mixed state, or cyclothymic disorder. *DSM-IV-TR* specifies a much more common early-onset subtype (onset before age 21 years). It seems that vegetative symptoms are less common than in major depressive episode. Up to 75% of individuals with dysthymic disorder will have a major depressive disorder. The main difference from the major depressive episode is the duration, which must always be at least 2 years. The difference in the number of symptoms (a minimum of five in major depressive episode, a minimum of three in dysthymic disorder) makes retrospective assessment difficult. The prospective studies of nonbipolar depression by Angst and Judd have shown a high instability of the various cat-

egories of *DSM-IV-TR* nonbipolar depression, as symptom number, severity, and duration fluctuate over time, supporting a dimensional approach.<sup>3,10,98</sup> Up to 30% of dysthymic disorder individuals can switch to hypomania when treated by antidepressants (more often when there is a family history of bipolar disorder), suggesting a link to bipolar II disorder.<sup>108</sup>

## Conclusion

In conclusion, the several subtypes of depression described seem to support a dimensional approach to the classification of mood disorder, following the continuity/spectrum concept of mood disorders. In clinical practice it is still useful to follow a categorical approach at the first stage (diagnostic utility), but bearing in mind that bipolar depressions and nonbipolar depressions have a fluctuating course and also have mixed episodes of depression and superimposed manic/hypomanic symptoms. The impact on treatment of these findings may be important for bipolar disorders and depressive disorders. If, when, and how long to use antidepressants and mood-stabilizing agents in the light of the spectrum concept of mood disorders have to be defined, setting the stage for a new series of studies. □

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### Diversas formas de la depresión

Los subtipos actuales de la depresión están basados en la división en categorías de los trastornos bipolares y depresivos según el Texto Revisado del Manual Diagnóstico y Estadístico de los Trastornos Mentales en su Cuarta Edición (DSM-IV-TR). Sin embargo, la evidencia actual apoya una aproximación en dimensiones para la depresión, como un espectro/continuo de trastornos que se sobrepone, y que van desde la depresión bipolar I al trastorno depresivo mayor. En este artículo serán revisados los tipos de depresión que han constituido el foco de atención de la mayoría de las investigaciones: depresión bipolar II, depresión mixta, depresión agitada, depresión atípica, depresión melancólica, depresión breve recurrente, trastorno depresivo menor, depresión estacional y trastorno distímico. La mayor parte de la investigación se ha focalizado en la depresión bipolar II, la depresión mixta (definida por depresión con superposición de síntomas maníacos o hipomaniacos) y la depresión atípica. Se ha encontrado que la depresión mixta, en que se combinan síntomas polares opuestos, es común cuando se ha investigado sistemáticamente la co-ocurrencia de síntomas maníacos o hipomaniacos. La depresión mixta constituye un desafío terapéutico para los clínicos, ya que los antidepresivos solos (es decir, sin protección de estabilizadores del ánimo) pueden empeorar sus síntomas maníacos o hipomaniacos como la irritabilidad y la agitación psicomotora, los cuales la Administración de Alimentos y Drogas (FDA) ha mencionado como posibles precursores de suicidalidad.

### Différentes formes de dépression

Les sous-groupes actuels de la dépression sont basés sur la séparation entre troubles dépressifs et bipolaires du DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, 4e ed., texte révisé). L'approche dimensionnelle de la dépression, comme un continuum de troubles qui se superposent allant de la dépression bipolaire I à la dépression majeure, est néanmoins soutenue par des travaux récents. Les groupes de dépression qui ont fait l'objet de la plupart des recherches récentes sont examinés : dépression bipolaire II, dépression mixte, dépression agitée, dépression atypique, dépression mélancolique, dépression récidivante brève, trouble dépressif mineur, dépression saisonnière et trouble dysthymique. La plus grande partie des travaux se sont intéressés à la dépression bipolaire II, à la dépression mixte (définie par dépression et symptômes maniaques/hypomaniaques superposés) et à la dépression atypique. La recherche systématique de symptômes maniaques/hypomaniaques simultanés a révélé que la dépression mixte, par sa combinaison de symptômes de polarité opposée, était fréquente. La dépression mixte représente un défi thérapeutique pour les médecins car les antidépresseurs seuls (c'est-à-dire non protégés par des stabilisateurs de l'humeur) peuvent aggraver les symptômes maniaques/hypomaniaques comme l'irritabilité et l'agitation psychomotrice, identifiés par la FDA (Food and Drug Administration) comme des précurseurs possibles de suicidalité.

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