Unipolar and bipolar depression: different or the same?†

Daniel J. Smith and Nick Craddock

Summary
The diagnostic boundary between recurrent unipolar depression and bipolar disorder may not be clear-cut and, further, the symptoms of unipolar depression compared with bipolar depression (although similar) are subtly different. Here we review the potential implications for clinical practice and research of new thinking about the relationship between recurrent unipolar depression and bipolar disorder.

Declaration of interest
D.J.S. has received honoraria for speaking at educational meetings organised by AstraZeneca and Eli Lilly.

Are the clinical syndromes of unipolar and bipolar depression the same?

Mitchell and colleagues present an elegant comparison of the clinical course and symptom profile of bipolar vs unipolar depression from a large genetic study of bipolar disorder.1 In line with several similar reports,4–10 they find that, as well as many similarities, there are also subtle differences between the clinical syndromes of unipolar and bipolar depression. These differences include symptoms such as higher rates of psychomotor retardation, greater difficulty thinking, more early morning worsening of mood and more frequent psychotic symptoms in bipolar depression relative to unipolar depression.11 A possible limitation of Mitchell et al’s study is that participants were required to report in retrospect the profile of their depressive symptoms occurring during their worst-ever depressive episode, something that is obviously open to recall bias. Nevertheless, there exists a growing body of research suggesting that we need to develop and test diagnostic approaches to bipolar disorder which go beyond merely screening for a history of hypomania or mania. The key point is that not all depressions are the same and that detailed features of the depressive episode itself can contribute to accurately assessing the clinical picture.

Furthermore, the relatively broad DSM diagnostic criteria for a major depressive episode may in recent years have led to many individuals who experienced depressive symptoms on only one occasion being diagnosed with depression when in fact adjustment disorder could be regarded as the more appropriate diagnosis. As pointed out by Kraepelin (and re-stated recently in Goodwin & Jamison’s classic text on manic–depressive illness12), recurrent depression may be nosologically separate from a single lifetime episode of depression and much more closely related to a spectrum of bipolar disorders.

Implications for diagnosis and management

One of the most important clinical implications of differentiating bipolar from unipolar depression during episodes of depression and before an episode of hypomania/mania has occurred or been recognised relates to the possibility of an earlier and more accurate index of suspicion of bipolar disorder (that is, ensuring bipolar disorder is accorded appropriate weighting within the differential diagnosis and taken into account in the management plan). We know that many patients with bipolar disorder are misdiagnosed as having major depressive disorder, often for several years – even after having experienced full-blown episodes of hypomania and

Editorial

Two commonly held beliefs about the relationship between unipolar depression (major depressive disorder) and bipolar disorder are being challenged by a converging body of research from a variety of disciplines including epidemiology, psychopathology and molecular genetics. The first assumption is that recurrent major depressive disorder and bipolar disorder are clear-cut and easily separable diagnostic entities. The second is that there is no difference in the symptom profile of unipolar vs. bipolar depression. Recent evidence, including the work of Mitchell and colleagues1 (this issue), suggests that we may need to acknowledge that both of these assumptions are no longer correct. This is not merely a matter of academic interest but has potentially far-reaching implications for the clinical assessment and management of large numbers of patients with depression worldwide.

Is there a clear zone of separation between unipolar and bipolar depression?

Several recent epidemiological and psychopathological studies have found that manic symptoms, occurring at an intensity and duration just below the DSM-IV diagnostic threshold for a diagnosis of hypomania, are relatively common in patients who experience recurrent episodes of depression that are presumed to be ‘unipolar’.2–6 As a consequence, it appears likely that there will be a slightly broader definition of hypomania – and therefore bipolar disorder – within DSM-5 (www.dsm5.org). This means that a substantial proportion of patients currently diagnosed as having major depressive disorder may qualify for a bipolar disorder diagnosis. It is easy to see that this shift in diagnostic category will have major implications for the way in which we approach the assessment, diagnosis and management of large numbers of patients presenting for help with recurrent depressive symptoms. It may present particular challenges within primary care, with many general practitioners holding a view that diagnosing bipolar disorder goes beyond their remit. Indeed, some general practitioners may already feel that manifestations of bipolar disorder beyond ‘classic’ (type I) bipolar disorder are not valid as clinical entities.7

†See pp. 303–309, this issue.
mania – and that their recall of periods of hypomania is often poor. Developing detailed diagnostic assessments which take account of the symptom profile and course of depressive episodes, similar to the probabilistic approach suggested by Mitchell et al, could potentially identify young adults with depression who may be at high risk of bipolar disorder. This, in turn, could influence the choice of treatment used: for example, perhaps towards more cautious and judicious use of antidepressants and a greater use of psychoeducational approaches, other psychological treatments or even mood stabilisers. It may also be important for advising women about risks of severe episodes of mood disorder in relation to the postpartum period, given the particularly high risk of severe postpartum episodes in women with bipolar disorder.

Implications for research

Mitchell and colleagues rightly suggest that the use of categorical DSM definitions of major depressive disorder and bipolar disorder in large genetic studies may have made it difficult to find susceptibility genes because a proportion of major depressive disorder cases in these studies carry genetic predispositions for bipolar disorder. The careful use of detailed dimensional measures of symptom clusters across traditional (DSM) diagnostic boundaries could help in identifying genetic risk factors for a range of mental disorders.

Mood disorder research should, in our view, not be overly constrained by the need (of funders and journals) to study populations of patients diagnosed according to DSM criteria but should explore the potential utility of dimensional approaches. This strategy could usefully be applied in the fields of neuroimaging, neuroendocrinology and in medication treatment trials. Taking treatment trials as an example, it is interesting to speculate that many previous trials of antidepressants for major depression may have been compromised because they included patients with major depressive disorder with subdiagnostic (but clinically important) features of bipolar disorder. We now know, for example, that there is considerable uncertainty about the usefulness of antidepressants in treating bipolar depression. Mitchell and colleagues suggest that identifying bipolarity in patients with major depressive disorder will be helpful for future genetic studies but identifying these patients might also be useful in the assessment of new treatments for depression (both pharmacological and psychological) by helping to define more homogeneous groups.

The need for a more critical approach to diagnosing depression

Concepts of depression have changed over the years and it has become clear that the cross-sectional ‘tick-list’ approach of DSM has a number of limitations, not least a danger of pathologising normal sadness and overdiagnosing mental disorder. This descriptive operational approach has been an important phase in the development of psychiatry that has allowed greatly improved reliability and been practically useful in many ways. However, the lack of theoretical underpinning and consequent arbitrariness of many definitions has meant the use of diagnoses that have unknown and largely untested validity. The drive for reliability has meant that some subtle, but potentially important, clinical features are often not considered. For example, the quality of depressed mood has been recognised for hundreds of years as indicative of pathological, severe depression but is difficult to measure reliably, particularly for someone without substantial clinical experience. It does not appear in diagnostic guidelines but is an important clinical feature. Researchers have a responsibility to develop and critically evaluate approaches to diagnosing a clinically meaningful syndrome of depression which most clinicians will recognise from their everyday work as something that is highly morbid (even life-threatening) and, usually, in need of treatment. Beyond this, we may need to acknowledge that depression, at least as defined by DSM, is a diagnostic concept that may be so heterogeneous as to be of limited value in both research and much of clinical practice.

Looking to the future: the need for clinical excellence

Can clinical practice and research really continue to be best served by persisting with basing our diagnoses on tick-list-defined cross-sectional categories? A classification based on an understanding of pathogenesis still lies some years in the future. It is not yet possible to know how many distinct disorders it might be useful to recognise or whether major mood disorders are better conceptualised as a continuum or as a set of overlapping pathological processes. We must encourage the careful measurement and reappraisal of psychopathology including using dimensional measures of key domains of psychopathology which can sit alongside the use of categories. Now, and as scientific understanding advances, there is a need for psychiatrists to use their clinical skills to ensure patients benefit from a thorough diagnostic assessment and formulation that can allow the delivery of optimal, evidence-based therapeutic interventions.

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First received 11 Mar 2011, final revision 25 May 2011, accepted 16 Jun 2011

References


Yukio Mishima

Martin Humphreys, Henry Scott Stokes

Kimitake Hiraoka was born in Tokyo in January 1925. As Yukio Mishima, the pen name he used from the age of 16, when his first work was published, he became, and still remains, the best known Japanese author in the West and worldwide. He was a prolific writer to whom he had earlier kidnapped a serving general, Yukio Mishima committed ritual suicide by disembowelling, a companion then beheading him.

On 25 November 1970 he attempted to incite a military coup but failed. With one of four student members of his Tatenokai with whom he had earlier kidnapped a serving general, Yukio Mishima committed ritual suicide by disembowelling, a companion then beheading him.
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BJP 2011, 199:272-274.
Access the most recent version at DOI: 10.1192/bjp.bp.111.092726

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