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Research report

Bipolar depression: Prototypically melancholic in its clinical features

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ABSTRACT

Background: Numerous studies have considered whether bipolar depression is phenomenologically similar or different to unipolar depression. While there have been some relatively consistent individual features identified, no clear clinical phenotype has been defined for bipolar depression.
Methods: A self-report and clinician-rated measure of the Sydney Melancholia Prototype Index ('SMPI') was used to assess prototypic features of melancholic and non-melancholic depression in a sample of 901 patients clinically diagnosed with bipolar disorder or unipolar depression. The majority also completed a self-report (SDS) severity of depression measure, and provided current and historical data on depression, anxiety, global functioning and stressor severity.
Results: Comparative analyses favoured the SMPI-CR above the SMPI-SR measure in terms of discriminatory strengths. The previously determined SMPI-CR difference score cut-off of 4 or more for differentiating melancholic from non-melancholic depression was replicated in this larger sample. SMPI item and prototypic pattern analyses indicated that bipolar depression corresponded closely to unipolar melancholic depression in terms of clinical pattern features but not in regard to a number of socio-demographic, illness course and correlate variables. 'Atypical features' were common across bipolar and unipolar disorders, but somewhat more prevalent in bipolar disorder.
Limitations: There was no distinction made for the bipolar group between subtypes I and II, with the study simply comparing bipolar with unipolar disorders. The apparent superiority of the clinician-rated in comparison to the SMPI-SR measure may reflect a clinician judgement bias.
Conclusions: The SMPI-CR measure indicated that bipolar depression corresponds closely to melancholic depression in terms of its clinical phenotype.

1. Introduction

There has long been interest in the nature of bipolar depression, particularly in regard to its nosological status and phenomenological issues. In relation to the first, Joffe et al. (1999) suggested that it might be more fruitful to position unipolar and bipolar depression as the same illness, a reversion to the earlier view that bipolar disorder and depression were dimensional manifestations of a unitary illness. However, since DSM-III, bipolar and unipolar depressive disorders have been separated, reflecting (see Shorter, 2008) research by several authors (i.e., Winokur, 1991; Angst, 1966; Leonhard, 1957; Perris, 1966). Arguments for their true separation—as against simply the longitudinal presence or absence of manic/hypomanic episodes would be advanced by showing differential (i) causes, (ii) episode-related and course of illness clinical variables, (iii) biological underpinnings (perhaps as pursued by genetic, neurotransmitter or neuroimaging studies), and (iv) response to quite differing treatments (especially in relation to antidepressant and mood stabilising medications). Support for distinctive differences is limited, with Cuellar et al. (2005) suggesting this to be a reflection of methodological limitations to study selection and assessment of those with a bipolar disorder. Such limitations include which bipolar disorders to include, choice of retrospective or cross-sectional studies, and how symptom criteria are best defined. Generally authors fail to consider an equally salient methodological issue—the nature of the comparison group of 'unipolar depression.' The general assumptive view is that unipolar depression (with DSM-defined major depression being the commonest diagnostic comparator) is an entity. If, however, it is a heterogeneous domain diagnosis capturing a range of differing melancholic and non-melancholic conditions, then the prevalence of such differing constituent conditions in any unipolar sample will alone cloud identification of commonalities and differences across bipolar and unipolar depressive sub-groups.

In relation to the second issue of phenomenological distinction between bipolar and unipolar depression, there have been several

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broad overviews of individual studies. Cuellar et al. (2005) concluded from their review of key studies that there were only four relatively consistent symptoms, with bipolar depressed subjects being more likely than those with unipolar depression to report anhedonia, and less likely to report anxiety, activity and somatisation. In a recent report, and where the researchers combined those with bipolar I and II disorders reporting on their most severe lifetime depressive episode (Mitchell et al., 2011), the bipolar subjects were more likely than those with unipolar depression to have higher rates of psychomotor disturbance, impaired concentration, early morning wakening, diurnal variation, psychotic symptoms and mixed features.

In an earlier review, Mitchell et al. (2008) first noted that there are "currently no accepted diagnostic criteria for either research or clinical purposes," and importantly examined for differences related to differing bipolar sub-sets (i.e., I or II) – as against bipolar disorder per se – for comparison with unipolar depression. They tabulated symptomatology data from 52 studies (i) comparing bipolar I and bipolar II subjects with unipolar subjects, and (ii) studying unipolar subjects who converted to having a bipolar disorder. Their approach of conceding potential phenomenological differences across bipolar I and bipolar II depressed patients is an important one in addressing the phenomenology of 'bipolar depression'. In our own studies (overviewed in Parker, 2008), and where we distinguished bipolar I from bipolar II disorders on the basis of the respective presence or absence of psychotic features during manic/hypomanic states, we quantified that some 40% of the bipolar I patients but none of the bipolar II patients experienced psychotic episodes during the depressed phase, but that both groups were highly likely to report depressive states weighted to melancholic features. We therefore concluded that bipolar I depression was generally manifested with psychotic or melancholic clinical features and bipolar II depression with non-psychotic melancholic features. If valid, this would explain the variable over-representation of psychotic features in bipolar depressed patients as a reflection of the percentage representation of bipolar I subjects.

While quite varying features were identified as over-represented or under-represented across the many studies reviewed by Mitchell et al. (2008) in relation to each bipolar subtype, those authors indicated that bipolar I patients were more likely to have episodes of psychotic depression, to show characteristic melancholic features (such as psychomotor disturbance) and to show so-called 'atypical features' such as hyperphagia and hypersomnolence. Forty et al. (2008) reported a study of a large sample (i.e., 443 individuals with a bipolar I disorder and 593 with a unipolar major depressive episode), and narrowed the list of individual differential features by undertaking a logistic regression analysis. That analysis identified bipolar I depression differentiating from unipolar depression by (i) psychotic features, (ii) diurnal mood variation and hypersomnia during depressive episodes, (iii) a greater number of depressive episodes and (iv) a shorter episode duration.

There have been relatively few studies comparing bipolar II depression with unipolar depression. Hantouche and Akiskal (2005) compared groups of those with bipolar II ($n=196$) and unipolar depression ($n=256$) in dimensional analyses of symptom factorial scores rather than examining for differential prevalence in features, and identified greater hypersomnia and psychomotor activation in the bipolar group. Benazzi (2006) compared 379 depressed bipolar II and 271 unipolar depressed patients, and quantified that the bipolar group were more likely to report 'atypical features' (i.e., increased eating, weight gain, hypersomnia), psychomotor agitation, impaired concentration and worthlessness.

Our longstanding research focus has considered whether bipolar depression is prototypically melancholic depression in its nature (whether psychotic or non-psychotic melancholic depression), but with the obvious caveat that bipolar patients (like whether unipolar melancholic patients) may also develop non-melancholic depressive episodes as a consequence of stressful life events and other factors, a reality that limits any parsimonious hypothesis that bipolar depression is simply or invariably melancholic depression. However, by asking patients about their most characteristic and severe episodes, those who experience both melancholic and non-melancholic episodes might be expected to be far more likely to nominate and report on their melancholic episodes. Our research focus has shaped the design of several studies undertaken by our group. In an earlier monograph, Mitchell and Sengoz (1996) overviewed two such studies. In the first, depressed patients assigned as experiencing melancholic depression by three differing criteria measures were subdivided into those with unipolar and bipolar courses, and with age and gender-matched sub-sets derived. The bipolar sub-set reported more previous and briefer depressive episodes, and while not differing significantly on 37 *symptoms* examined, returned higher agitation and lower retardation psychomotor *sign* scores. In a second similar study of well characterised melancholic patients sub-divided into age and gender-matched unipolar and bipolar patients, the bipolar patients again reported briefer episodes and tended to report more previous episodes. While they did not differ on signs of psychomotor disturbance they were more likely to report initial insomnia, hypersomnia and suicidal features. In neither study did the groups differ in depression severity. Such analyses identified some differences in terms of illness course (i.e., more frequent and briefer depressive episodes in bipolar patients) but with largely similar cross-sectional features favouring bipolar depression being akin to melancholia as observed in unipolar patients.

Clarifying whether bipolar depression is quintessentially melancholic in nature or not is highly dependent, however, on how 'melancholia' is defined and measured. Symptom measurement is somewhat problematic as none of the so-called endogeneity symptoms show absolute specificity (Parker et al., 1996), at best only showing modest differential prevalence. We have also progressively recognised limitations to rating psychomotor signs as a measure or proxy estimate of melancholia, in light of psychomotor disturbance being less evident in younger patients with seemingly true melancholia. Thus, in our more recent studies we have examined whether melancholia might be more precisely defined by adding non-clinical illness correlates to candidate symptoms, a reprised model having been adopted in the Newcastle Index (Carney et al., 1965) and in the DSM-III-R classification of melancholia. In our first such study (Parker et al., 2010), we established that adding course of illness and context variables to a set of refined symptoms distinctly improved differentiation of melancholic and non-melancholic depression made by symptom definition alone.

As a consequence, we developed the SMPI measure (Sydney Melancholia Prototype Index). It comprises a single page listing 12 items weighted to melancholic depression and 12 items weighted to the non-melancholic depressive conditions in respective left-hand and right-hand columns. Subjects are requested to tick those items from either column that they regard as 'characteristic' in terms of their depressive experience. Items assess symptoms historically favoured as differentiating melancholic and non-melancholic depression and which we have refined over several studies, as well as assessing premorbid interpersonal functioning, distal and proximal stressors, the context and impact of any preceding episode stressors on inducing and maintaining the depression, as well as ongoing emotional dysregulation levels. At the bottom of the page, subjects are invited to judge whether their overall 'profile' is captured best by Description A (left-hand column descriptors), Description B (right-hand column), is somewhat closer to A than to B, is somewhat closer to B than to A, or is effectively an equal mix or A and B descriptors—a 'prototypic' measurement approach. Subsequently, we developed an equivalent clinician-rated version of the measure.