Clinical differences between bipolar and unipolar depression

Liz Forty, Daniel Smith, Lisa Jones, Ian Jones, Sian Caesar, Carly Cooper, Christine Fraser, Katherine Gordon-Smith, Sally Hyde, Anne Farmer, Peter McGuffin and Nick Craddock

Summary
It is commonly – but wrongly – assumed that there are no important differences between the clinical presentations of major depressive disorder and bipolar depression. Here we compare clinical course variables and depressive symptom profiles in a large sample of individuals with major depressive disorder (n=593) and bipolar disorder (n=443). Clinical characteristics associated with a bipolar course included the presence of psychosis, diurnal mood variation and hypersomnia during depressive episodes, and a greater number of shorter depressive episodes. Such features should alert a clinician to a possible bipolar course. This is important because optimal management is not the same for bipolar and unipolar depression.

Declarations of interest
Funding from the Wellcome Trust, the UK Medical Research Council and GlaxoSmithKline.

Distinguishing between major depressive disorder and bipolar disorder is important because there are differences in the optimal management of these conditions. Antidepressant treatment of bipolar depression can adversely affect long-term prognosis by causing destabilisation of mood and more frequent depressive episodes, and can lead to the development of treatment resistance. Most people with bipolar disorder experience depression rather than mania as their first episode of illness. It is clinically desirable to recognise, or at least to suspect, bipolar depression at an early stage of a bipolar illness. Here, we compare the clinical course and depressive symptoms of the two forms of depression by analysing phenotypic data for over 1000 patients who were recruited to our genetic epidemiological studies of mood disorders.

Method
The sample comprised 443 individuals with type I bipolar disorder and 593 with recurrent major depressive disorder. Participants were recruited systematically from the case-loads of community mental health teams, and non-systematically from advertisements placed in local general practices and local media. Patients were excluded from the original genetic studies if they: had a lifetime diagnosis in local general practices and local media. Patients were excluded from the original genetic studies if they: had a lifetime diagnosis of major depressive disorder and bipolar disorder (n=443). The sample comprised 443 individuals with type I bipolar disorder and 593 with recurrent major depressive disorder. Participants were recruited systematically from the case-loads of community mental health teams, and non-systematically from advertisements placed in local general practices and local media. Patients were excluded from the original genetic studies if they: had a lifetime diagnosis.

Results
The proportions of women in the major depression group and the bipolar group were 70.2% and 71.3% respectively. The median age at interview was 49 years for the major depression group and 47 years for the bipolar group. Forty-six per cent of the major depression group were recruited systematically, compared with 37% of the bipolar group. The median illness duration was 19 years for the major depression group and 20 years for the bipolar group. The major depression group had a median BDI score at interview of 16, compared with 8 in the bipolar group. Forward stepwise logistic regression was used to establish the best depression-related predictors of bipolar v. unipolar group membership. All lifetime variables relating to depressive episodes that were significant at the 1% level in univariate analyses were entered into the regression. To control for sample differences in recruitment and current mental state, BDI score at interview and method of recruitment were included in the regression. Gender was also included in the logistic regression analysis. Significant predictors of diagnosis are shown in Table 1.

Although there were, of course, similarities between unipolar and bipolar depression, we found important clinical differences: characteristics that best predicted bipolar rather than unipolar
depression were the presence of psychosis, diurnal mood variation and hypersomnia during depressive episodes, a greater number of depressive episodes and a shorter duration of the longest depressive episode. Participants with major depressive disorder were characterised by the presence of excessive self-reproach, loss of energy and diminished libido.

**Table 1** Lifetime clinical characteristics predicting bipolar v. unipolar group membership

<table>
<thead>
<tr>
<th>Major depressive disorder</th>
<th>Bipolar disorder</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants, n (total n=1036)</td>
<td>593</td>
<td>443</td>
<td></td>
</tr>
<tr>
<td>Psychotic features during depression, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>61 (10.5)/522 (69.5)</td>
<td>134 (30.2)/309 (69.8)</td>
<td>0.160 (0.08–0.32)</td>
</tr>
<tr>
<td>No. of episodes of depression: median (IQR) range</td>
<td>4 (2)–40</td>
<td>5 (6)–1–70</td>
<td>0.952 (0.89–0.98)</td>
</tr>
<tr>
<td>Longest episode of depression, weeks: median (IQR) range</td>
<td>69 (60)/8–624</td>
<td>26 (20)/2–416</td>
<td>1.011 (1.01–1.02)</td>
</tr>
<tr>
<td>Diurnal mood variation, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>285 (50.4)/281 (49.6)</td>
<td>219 (59)/152 (41)</td>
<td>0.536 (0.31–0.94)</td>
</tr>
<tr>
<td>Excessive self-reproach, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>342 (7.1)/48 (12.3)</td>
<td>148 (42.8)/198 (57.2)</td>
<td>0.371 (0.21–0.67)</td>
</tr>
<tr>
<td>Loss of energy, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>386 (95.8)/18 (4.5)</td>
<td>123 (34.8)/230 (65.2)</td>
<td>6.031 (1.00–36.27)</td>
</tr>
<tr>
<td>Hypersomnia, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>120 (21.5)/437 (78.5)</td>
<td>148 (42.8)/198 (57.2)</td>
<td>0.371 (0.21–0.67)</td>
</tr>
<tr>
<td>Diminished libido, n (%)&lt;sup&gt;b&lt;/sup&gt;: present/absent</td>
<td>231 (63.3)/133 (36.5)</td>
<td>123 (34.8)/230 (65.2)</td>
<td>7.537 (4.14–13.74)</td>
</tr>
</tbody>
</table>

**Discussion**

Our results are consistent with, and extend the findings of, previous studies that have shown that ‘atypical’ depressive features (such as hypersomnia and weight gain) may be more common in bipolar disorder than in major depression.<sup>7–9</sup> Compared with previous studies, our study has several advantages, including the large number of participants and the high degree of consistent and comprehensive clinical data collected. Distinguishing between bipolar disorder and major depressive disorder is of great clinical importance because optimal management of the two conditions is very different. For example, anti-depressants should be used with caution in bipolar depression because of the risk of precipitating mood switches, cycling, or mixed or agitated states.<sup>10</sup> It is desirable that clinicians use all available information to guide management (including choice of treatment, advice to patient and intensity of monitoring). The clinical features of depression are not a definitive guide to diagnosis but can help to alert the clinician to a possible bipolar course. These findings also have important implications for future research on type II bipolar disorder and sub-threshold bipolar disorders. Evidence suggests that 25–50% of individuals with recurrent major depression (particularly those within atypical, early-onset or treatment-refractory subgroups) may in fact have a broadly defined bipolar disorder.<sup>11</sup> We currently know little about how best to treat such patients. Future studies will need to move beyond strict diagnostic categories and examine sub-groups of patients defined by extended phenotypic measures such as dimensional assessments of bipolar features, bipolar symptom clusters and longitudinal illness course variables.

An important limitation of our study is that there might have been differences between the two groups of participants that we were not able to examine, such as subtle differences in treatment regimens or patterns of comorbid illness. We also note that although the proportion of women in the major depressive disorder sample is typical of studies of this nature, the proportion of women in the bipolar disorder sample is higher than is typically reported (nearly three-quarters compared with a half) and that this may limit the generalisability of our findings. A further limitation was the use of retrospective rather than prospective assessments, even though we used an in-depth semi-structured clinical interview supplemented by case-note review. Prospective ratings, though preferable, can be prohibitively expensive.

**References**

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Access the most recent version at DOI: 10.1192/bjp.bp.107.045294

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