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Research report

## Identifying hypomanic features in major depressive disorder using the hypomania checklist (HCL-32)

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#### Abstract

*Background:* Recent studies have challenged the traditional unipolar/bipolar divide with increasing support for a more dimensional view of affective disorders. We here examine the occurrence of hypomanic symptoms in individuals with a history of major depression selected to exclude indicators of underlying bipolarity.

*Methods:* The presence of hypomanic symptoms was assessed by the Hypomania Checklist (HCL-32) self-report questionnaire in a sample of almost 600 patients meeting DSM-IV criteria for Bipolar I disorder (BPI N=260) or Major Recurrent Depressive disorder (MDDR N=322). Subjects were recruited and assessed using consistent, robust methodology.

*Results:* We found that a score of 20 or more on the HCL-32 yielded the best combination of sensitivity (68%) and specificity (83%) to distinguish between BPI and MDDR. Within our highly selected and well defined MDDR sample (for which exclusion criteria included personal or family histories of bipolar or psychotic illness), 17% of MDDR subjects scored over the threshold of 20 on the HCL-32.

*Conclusions:* The HCL-32 identified a substantial number of patients meeting DSM-IV criteria for recurrent major depression (even when selected to exclude personal and family histories of bipolar illness) who reported bipolar symptoms at a level similar to that reported by patients meeting diagnostic criteria for bipolar disorder. This demonstrates the limitations of using DSM-IV criteria to distinguish those with and without bipolar features of illness.

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### 1. Introduction

Kraepelin's (1921) description of manic depressive illness included syndromes featuring both mania and

depression, as well as recurrent depression alone. Modern diagnostic systems take into account the chronicity of the disorder and classify affective disorders as either unipolar or bipolar in nature, a distinction introduced into modern psychiatry by Leonhard (1959). Recent thinking has begun to question the categorical splitting of mood disorders into bipolar and unipolar disorders and there is increasing support

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for a more dimensional view of affective disorders (Akiskal, 2003; Angst et al., 2003; Cassano et al., 2004; Ghaemi et al., 2002; Angst, 2007).

The Hypomania Check List (HCL-32) self-report questionnaire is a tool designed to screen for hypomanic components in patients with Major Depressive Disorder (MDD) (Angst et al., 2005a). It has been used in different countries and languages (Meyer et al., 2007; Wu et al., 2008; Vieta et al., 2007). In a study of Italian and Swedish patients with bipolar I (BPI, N=102) or bipolar II disorder (BPII, N=164) or MDD (N=160), Angst et al. (2005a) found that a cut-off score of 14 or more on the HCL-32 yielded the best combination of sensitivity (true bipolars) (80%) and specificity (true non-bipolars) (51%) to distinguish between bipolar disorder (BP) and MDD. They concluded that the HCL-32 is a sensitive instrument for distinguishing between BP and MDD, although it does not distinguish between BPI and BPII disorders.

The primary aim of this study was to assess the presence of hypomanic symptoms in a highly selected "unipolar" sample. In order to do this we first established the cut-off score on the HCL-32 that best distinguished between MDD and BPI, in our large, well characterised UK sample.

### 2. Method

The sample comprised 513 bipolar patients (BPI Bipolar I disorder) and 774 unipolar patients (MDDR Recurrent Major Depressive Disorder) recruited to ongoing molecular genetic studies of affective disorder (Korszun et al., 2004; Green et al., 2006; Raybould et al., 2005; Williams et al., 2006; McGuffin et al., 2005). Subjects were recruited systematically from Community Mental Health Teams and non-systematically from advertisements placed in local General Practices and local media. All participants were aged 18 years or over and were of UK/Eire white ethnicity (due to the fact that patients were recruited for molecular genetic studies).

Subjects were excluded from the original genetic studies if they: i) had a lifetime diagnosis of intravenous drug dependency; ii) had only experienced affective illness as a result of alcohol or substance dependence; iii) had only experienced affective illness secondary to medical illness or medication; or iv) were biologically related to another study participant. In addition, patients in the MDDR group were excluded if they: i) had a first or second degree relative with a clear diagnosis of bipolar affective disorder or schizophrenia, schizotypal disorder, persistent delusional disorder, acute and transient psychotic disorders or schizoaffective disorder; or ii) had ever experienced mood incongruent psychosis or psychosis outside of mood episodes.

Participants were interviewed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990) which provides detailed information about lifetime psychopathology. Psychiatric and General Practice case-notes were reviewed. These data were combined to form a written case vignette. Based on this vignette, best-estimate lifetime diagnoses were made according to DSM-IV (APA, 2000) criteria. Each patient was diagnosed, and had key clinical variables rated independently by at least two members of the research team and consensus was reached. Team members involved in the interview, rating and diagnostic procedures were either fully trained research psychologists or psychiatrists. Inter-rater reliability was formally assessed using joint ratings of 20 cases with a range of mood disorder diagnoses. The mean overall kappa statistic was 0.85 for DSM-IV diagnoses. This study received all necessary Multi-Region and Local Research Ethics Committee (MREC and LREC) approval and all participants provided written informed consent.

All participants recruited to our mood disorders studies were sent a follow-up postal questionnaire pack in 2007. The mean number of years between the initial research interview and the completion of the follow-up questionnaire pack was 3.8. The questionnaire pack included, amongst other self-report questionnaires, the hypomania checklist (HCL-32) (Angst et al., 2005a). The HCL-32 is a self-report measure that comprises a checklist of possible symptoms of hypomania that are rated yes (present or typical of me) or no (not present or not typical). The questionnaire also includes a question about current mood state (relative to usual mood state) where subjects rate themselves on a seven point scale (worse than usual - neither worse no better than usual better than usual). The Beck Depression Inventory (BDI) (Beck and Steer, 1987) and the Altman Self-Rating Mania Scale (ASRM) (Altman et al., 1997) were also included in the questionnaire pack as measures of current mental state.

The Mood Disorders Research Team keeps in regular contact with study participants (including patients, unaffected controls and family members) via annual newsletters. The questionnaire pack was sent to all participants on our newsletter mailing list. The response rates for participants in our bipolar (BPI) and unipolar (MDDR) samples were 57% (N=291) and 48% (N=373) respectively. Participants who did not complete the HCL-32 correctly (i.e. missed out any questions, or answers were inconsistent) were excluded

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