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Differences in symptom expression between unipolar and bipolar spectrum depression: results from a nationally representative sample using Item Response Theory (IRT)

Nicolas Hoertel, M.D., M.P.H.^{1,2,3,4,*}, Carlos Blanco, M.D., Ph.D.¹, Hugo Peyre, M.D., M.P.H.^{5,6}, Melanie M. Wall, Ph.D.^{1,7}, Kibby McMahon, B.A.¹, Philip Gorwood, M.D., Ph.D.^{3,8}, Cédric Lemogne, M.D., Ph.D.^{2,3,4}, and Frédéric Limosin, M.D., Ph.D.^{2,3,4}

¹Department of Psychiatry, New York State Psychiatric Institute, Columbia University, New York, USA

²AP-HP, Corentin Celton Hospital, Department of Psychiatry, 92130 Issy-les-Moulineaux, France

³Paris Descartes University, PRES Sorbonne Paris Cité, Paris, France

⁴INSERM UMR 894, Psychiatry and Neurosciences Center, Paris, France

⁵Assistance Publique Hôpitaux de Paris (APHP), Robert Debré Hospital, Child and Adolescent Psychiatry Department, Paris, France

⁶Cognitive Sciences and Psycholinguistic Laboratory, Ecole Normale Supérieure, CNRS, EHESS, Paris, France

⁷Department of Biostatistics, Mailman School of Public Health, Columbia University, New York, USA

⁸Groupe Hospitalier Sainte-Anne, CMME, Paris, France

Abstract

Background—The inclusion of subsyndromal forms of bipolarity in the fifth edition of the DSM has major implications for the way in which we approach the diagnosis of individuals with depressive symptoms. The aim of the present study was to use methods based on item response theory (IRT) to examine whether, when equating for levels of depression severity, there are differences in the likelihood of reporting DSM-IV symptoms of major depressive episode (MDE) between subjects with and without a lifetime history of manic symptoms.

Methods—We conducted these analyses using a large, nationally representative sample from the USA ($n = 34,653$), the second wave of the National Epidemiologic Survey on Alcohol and Related Conditions.

*Corresponding author: Nicolas Hoertel, M.D., M.P.H. Department of Psychiatry, Corentin Celton Hospital, Paris Descartes University, 4 parvis Corentin Celton; 92130 Issy-les-Moulineaux, France, Phone: 33 (0) 1 58 00 44 21, Fax: 33 (0) 1 58 00 44 53, nico.hoertel@yahoo.fr.

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Results—The items sadness, appetite disturbance and psychomotor symptoms were better indicators of depression severity in participants without a lifetime history of manic symptoms, in a clinically meaningful way. DSM-IV symptoms of MDE were substantially less informative in participants with a lifetime history of manic symptoms than in those without such history.

Limitations—Clinical information on DSM-IV depressive and manic symptoms was based on retrospective self-report

Conclusions—The clinical presentation of depressive symptoms may substantially differ in individuals with and without a lifetime history of manic symptoms. These findings alert to the possibility of atypical symptomatic presentations among individuals with co-occurring symptoms or disorders and highlight the importance of continued research into specific pathophysiology differentiating unipolar and bipolar depression

Keywords

depression; unipolar; bipolar; symptoms; item response theory; differential item functioning

Introduction

The inclusion of subthreshold forms of bipolarity (referred to as “Other Specified Bipolar and Related Disorder”) in the fifth edition of the Diagnostic and Statistical Manual of psychiatric disorders (DSM-5) (American Psychiatric Association, 2013) has revived decades of debate regarding whether major depressive disorder and bipolar disorder are distinct and easily distinguishable diagnostic entities (Smith and Craddock, 2011). Given the depression-predominant course of illness in bipolar disorder and the risk for inadequate identification and treatment (Hirschfeld et al., 2003; Perlis, 2005; Stensland et al., 2008), determining whether there are unique features that differentiate bipolar depression from unipolar depression has potentially far-reaching implications for the clinical assessment and management of large numbers of patients with depression (Angst et al., 2011; Ghaemi et al., 2000; Hoertel et al., 2013a; McMahon et al., 2016).

Despite the clinical and research importance of this debate, there remains disagreement as to whether there are unique phenomenological differences in depression symptom expression between bipolar and unipolar depression. While some studies have suggested that unipolar and bipolar depression symptom presentations are more similar than different (Joffe et al., 1999; Robertson et al., 1996), others indicate that certain depressive features may differentiate bipolar depression from unipolar depression. Specifically, bipolar depression may be associated with higher rates of atypical features (Akiskal and Benazzi, 2005; Benazzi, 1999; Mitchell et al., 2001; Moreno et al., 2012; Perlis et al., 2006; Perugi et al., 1998), psychotic symptoms (Mitchell et al., 2001; Olfson et al., 2005; Parker et al., 2000; Solomon et al., 2006), melancholic features (Parker et al., 2000), agitation (Endicott et al., 1985; Hantouche and Akiskal, 2005; Rihmer et al., 2001), psychomotor disturbance (Hoertel et al., 2013b; Mitchell et al., 2008, 2001; Parker et al., 2000; Weinstock et al., 2009) and suicidal ideation (Hoertel et al., 2013b; Moreno et al., 2012; Weinstock et al., 2009). In contrast, individuals with unipolar depression may tend to endorse higher rates of anxiety (Bowden, 2005; Cuellar et al., 2005; Mitchell et al., 2001), insomnia (Benazzi, 1999;

Hantouche and Akiskal, 2005; Mitchell et al., 2008, 1992; Mitchell and Malhi, 2004; Mitchell et al., 2001; Perlis et al., 2006), appetite loss (Mitchell et al., 1992; Mitchell and Malhi, 2004; Mitchell et al., 2001; Olfson et al., 2005) and somatic complaints (Cuellar et al., 2005; Mitchell et al., 2008; Mitchell and Malhi, 2004; Perlis et al., 2006). For example, two studies applied two different statistical approaches to the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (Moreno et al., 2012; Weinstock et al., 2009) and reached opposite conclusions regarding the presence of differences in depression symptom expression between bipolar and unipolar depression.

These mixed results may be attributed, at least in part, to methodological differences such as reliance on samples of convenience precluding extrapolation of their results to the general population, small sample sizes, incomplete assessment of full range of DSM-IV major depressive episode (MDE) criteria, absence of control for overall symptom severity in the comparisons of clinical presentations across groups, as well as the inclusion of a substantial proportion of individuals with MDD and subthreshold hypomania within the MDD diagnostic category (Hoertel et al., 2013c). This last point is critical because prior research conducted in both clinical and general population samples suggests that the prevalence of lifetime history of subthreshold hypomania in individuals with major depressive disorder (MDD) ranges from 30% to 55% (Angst et al., 2011, 2010, 2003; Fiedorowicz et al., 2011; Hoertel et al., 2013b; Judd and Akiskal, 2003; Lewinsohn et al., 1995; Merikangas et al., 2008; Zimmermann et al., 2009), supporting the existence of large overlaps between unipolar and bipolar disorders. Therefore, the change implemented in DSM-5 means that up to half of patients currently diagnosed as having MDD may qualify for an ‘other specified bipolar and related disorder’ diagnosis (Nusslock and Frank, 2011). This shift in diagnostic category has major implications for the way in which we approach the assessment, diagnosis and management of large numbers of patients presenting for help with depressive symptoms. Since individuals with MDD and subthreshold hypomania may more closely resemble to those with bipolar disorder (BD) (Nusslock and Frank, 2011), it is likely that inclusion of subthreshold bipolarity within the unipolar diagnostic category has led prior studies to underestimate differences in depression symptom expression between unipolar and bipolar depression and may explain at least partly discrepancies in results between previous studies (Hoertel et al., 2013c).

To our knowledge, no study has examined in the general population differences in depression symptom expression in individuals with a lifetime history of manic symptoms (broadly referred to as “bipolar spectrum symptom group”) versus those without such symptoms (referred to as “unipolar symptom group”).

Accordingly, our aim was to examine whether there are differences in the likelihood of reporting DSM-IV MDE symptoms between individuals with and without a lifetime history of manic symptoms, when equating for levels of depression severity using item response theory (IRT) methods. Methods based on IRT, which are rapidly becoming the gold standard for examining differential symptom expression (Aggen et al., 2005; Hoertel et al., 2015b, 2014; Peyre et al., 2014; Rivollier et al., 2015; Simon and Von Korff, 2006; Uebelacker et al., 2009, 2010; Weinstock et al., 2009, 2010), provide significant improvements over previous statistical techniques as IRT approaches allow examining the likelihood that a

particular symptom will be reported given a particular level of depression severity (Lord, 1980). We hypothesized that symptom features of depression would substantially differ between individuals with and without a lifetime history of manic symptoms. To conduct these analyses, we used a large representative sample of the US population.

Materials and Methods

Sample

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is a survey of a nationally representative sample of the civilian adult population of the United States, described in detail elsewhere (Grant et al., 2009, 2004a, 2004b). Participants were drawn from the 2004–2005 NESARC (Grant et al., 2009), the second Wave following upon the Wave 1 NESARC. The cumulative response rate at Wave 2 was 70.2%, reflecting 34,653 completed both Wave 1 and Wave 2 interviews. Weighted Wave 2 data were adjusted to be representative of the civilian population on sociodemographic variables including region, age, race/ethnicity and sex, based on the 2000 Decennial Census. The research protocol, including informed consent procedures, received full human subjects review and approval from the US Census Bureau and the Office of Management and Budget. The present analysis consists of all individuals who completed the second wave of the NESARC ($n=34,653$).

Measures

Participants were interviewed face to face with the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (AUDADIS-IV), a fully structured diagnostic instrument designed for experienced lay interviewers (Grant et al., 2009).

Assessments of DSM-IV symptoms of MDE—All NESARC participants were asked whether they had a lifetime history of 2-week episode of depressed mood and/or anhedonia. Participants with a lifetime history of 2-week episode of depressed mood and/or anhedonia were further asked about the other DSM-IV depressive symptoms. Consistent with DSM-IV, a major depressive episode (MDE) was diagnosed when an individual reported at least 2 weeks of persistent depressed mood or anhedonia, accompanied by a total of at least 5 of the 9 DSM-IV symptoms of MDE during the episode. To reduce participants' burden, the diagnosis of MDE focused on the most severe episode (Hasin et al., 2005). Test-retest reliability (Grant et al., 2003; Hasin et al., 2005) and validity (Canino et al., 1999; Grant et al., 2003) of the AUDADIS-IV diagnoses of MDD are good ($k = 0.64–0.67$), and a clinical reappraisal study (Grant et al., 2004a) of major depressive episode indicated good agreement between AUDADIS-IV and psychiatrist diagnoses ($k = 0.64–0.68$). Analyses for this study focused on the nine DSM-IV MDE symptoms (Table 1).

Assessment of lifetime history of manic symptoms—All participants were asked for the lifetime presence of the DSM-IV criterion A for hypomania, assessed with the three following questions: (i) “In your entire life, have you ever had a time lasting at least 1 week when you felt so extremely excited, elated or hyper that other people thought you weren't your normal self?”, (ii) “In your entire life, have you ever had a time lasting at least 1 week when you felt so extremely excited, elated or hyper that other people were concerned about

you?” and (iii) “In your entire life, have you ever had a time lasting at least 1 week when you were so irritable or easily annoyed that you would shout at people, throw or break things, or start fights or arguments?”. Respondents who answered affirmatively to at least one of these questions were considered having a “lifetime history of manic symptoms”. All other responders were referred to “no lifetime history of manic symptoms”.

Analyses

Comparing prevalence of depressive symptoms—Differences in prevalence of each DSM-IV depressive symptom between participants with and without a lifetime history of manic symptoms were tested using chi-square tests in both the full NESARC sample and the subsample of participants with a lifetime DSM-IV diagnosis of MDE.

To examine differential item functioning (DIF) in the symptoms of MDE between individuals with and without a lifetime history of manic symptoms, we used a multigroup confirmatory factor analysis.

Multisample confirmatory factor analysis (MCFA) for DIF analyses

Assessing unidimensionality: Prior to item response theory modeling, including testing for differential item functioning (DIF), it is necessary to confirm the unidimensionality of the set of symptoms. Eigenvalue analysis of the tetrachoric correlation matrices of the nine DSM-IV depressive symptoms was performed separately in individuals with a lifetime history of manic symptoms and in those without such history. A scree plot with an elbow after the first eigenvalue and a well-fitting one-factor model according to standard goodness of fit tests (RMSEA<.06, TLI>.95 and CFI>.95) were used to indicate unidimensionality in both sets of analyses (Hu and Benter, 1999).

Item response theory (IRT)—Item response theory (IRT) modeling was conducted to examine whether the DSM-IV depressive symptoms were endorsed similarly in participants with and without a lifetime history of manic symptoms after adjusting for differences in underlying depression severity (Harford et al., 2013). In IRT, a severity and a discrimination parameter are estimated for each item (i.e., symptoms of MDE in this study) indicating where along the latent severity continuum a symptom has a probability of 50% of being endorsed (for the severity parameter), and how rapidly the probability of observing the symptom changes across increasing levels of the latent severity continuum (for the discrimination parameter).

All factor analyses were conducted in Mplus Version 7.0 (Muthén and Muthén, 2007) which takes into account the NESARC sampling weights and design effects in the parameter and standard error estimation as well as model fit calculations. The default estimator for the analysis was the variance adjusted weighted least squares (WLSMV), a robust estimator that provides the best option for modeling categorical or ordered data (Muthén and Muthén, 2007).

Testing differential item functioning (DIF)—Multisample confirmatory factor analysis (MCFA) was used to test DIF across groups of (a) factor loadings (i.e., item discrimination

parameters) and (b) thresholds (i.e., severity parameters). The different models varied in terms of the parameters constrained to be equal across groups (Millsap and Yun-Tein, 2004). Initially, an unconstrained model was fit allowing all parameters to differ between groups (i.e., individuals with and without a lifetime history of manic symptoms) in both sets of analyses (Table 2). Following a method previously described by McBride and colleagues (McBride et al., 2010), analyses were conducted iteratively to determine which IRT parameters differ between both groups. Nested models were compared using the chi-square difference test (implemented using the DIFFTEST option in Mplus) (Peyre et al., 2014; Rivollier et al., 2015). To detect DIF in IRT parameters of each item, the discrimination and severity parameters of the others items were constrained to be equal between groups. For each item, a chi-square difference test DIF comparing models with and without the discrimination parameter of the item constrained to be equal between groups was used to identify DIF in the discrimination parameter. To identify DIF in the severity parameter, a chi-square difference test DIF was used to compare models with and without the severity parameter of the item constrained to be equal between groups.

To minimize the number of false positives that could derive from the multiple comparisons conducted in this study, we set alpha at 0.05 and used the Benjamini–Hochberg procedure to adjust p-values for all 1 df tests (Benjamini and Hochberg, 1995). Furthermore, small differences in severity between groups can be statistically significant but may not be clinically meaningful (Strong et al., 2009). Thus, it was decided *a priori* that only differences greater than 0.50 in symptom discrimination and severity would be considered as clinically meaningful (Steinberg and Thissen, 2006). Such differences in symptom severity can be interpreted as one “half of the standard unit difference between the values of the (underlying) trait necessary to have a 50–50 chance of responding positively in one group compared to another” (Steinberg and Thissen, 2006). This difference may be associated with differences as large as 10% in the probability of response (Steinberg and Thissen, 2006). Because graphical display is helpful in placing the “effect sizes in a practical and theoretical context” (Wilkinson, 1999), we present the item response curves (IRC) for all symptom parameters (see supplemental Figures S1 to S9). Minimum sample size for DIF analyses is usually considered in the range of 100–200 subjects per group (Zumbo, 1999). Based on a simulation study, Scott et al. (Scott et al., 2010) recommended a minimum of 200 participants per group to ensure adequate performance (i.e., 80% power).

Total information function (TIF)—The TIF and the standard error of measurement (SEM, which is equal to the inverse square root of the TIF) were estimated in each group. The TIF is a graphic representation of the total quantity of information yielded by a set of items at each latent trait level. The area under the TIF curve (AUC) corresponds to the total amount of information provided by the set of items. The standard error of measurement is related to the reliability of the measurement and is equal to the square root of 1 minus reliability (e.g., a SEM of 0.55 is equal to an internal consistency of 0.70) (Weiss and Davison, 1981). The TIF and the SEM represent the information and precision of a set of items across different levels of a latent trait.

Results

Sample characteristics

Of the 34,653 participants included in this study, 15 (0.03%) were excluded from our analysis because they did not answer to any question on depressive or manic symptoms in both waves. Of the 34,638 remaining participants, 6,465 reported a lifetime history of manic symptoms.

Prevalence of symptoms of MDE

Table 1 shows the prevalence of symptoms of MDE in participants with and without a lifetime history of manic symptoms in the full NESARC sample and in the subsample of respondents with a lifetime DSM-IV diagnosis of MDE. In both the full sample and the subsample of participants with a lifetime DSM-IV diagnosis of MDE, the most frequently endorsed depressive symptoms in both groups were sadness, anhedonia, sleep disturbance and concentration difficulties whereas the criterion suicidality was the least commonly reported. In the full sample, the lifetime prevalence rates of all symptoms of MDE were significantly higher in participants with a lifetime history of manic symptoms than in those without such condition. In the subsample of respondents with a lifetime DSM-IV diagnosis of MDE, the symptoms anhedonia, appetite disturbance, psychomotor disturbance, worthlessness/guilt, concentration difficulties and suicidality were significantly more prevalent in participants with a lifetime history of manic symptoms.

DIF results using multisample confirmatory factor analysis

Unidimensionality of symptoms of MDE—In both groups (i.e., individuals with and without a lifetime history of manic symptoms), fit indices indicated an excellent fit to the data in the full sample. In individuals with a lifetime history of manic symptoms, the first factor eigenvalue was 7.2, whereas the second factor eigenvalue was 0.5. For this group, the fit indices were CFI=0.998, TLI=0.997 and RMSEA=0.032. In individuals without a lifetime history of manic symptoms, the first factor eigenvalue was 7.8, whereas the second factor eigenvalue was 0.3. The scree plots are shown in supplemental Figures S1a and S1b. The fit indices were CFI=0.999, TLI=0.999 and RMSEA=0.022. We determined that these fit statistics were adequate to proceed to fitting IRT models. The item response curves (IRC) for both groups are shown in supplemental Figures S2a and S2b.

Differential item functioning (DIF)—In the full sample, after adjusting for multiple testing using the Benjamini-Hochberg procedure, all items displayed statistically significant differences between groups in symptom discrimination but only six (i.e., sadness, anhedonia, appetite disturbance, sleep disturbance, psychomotor symptoms and concentration difficulties) reached our *a priori* threshold for clinical significance (DIF higher than 0.50). In addition, only one item (i.e., sadness) displayed statistically significant differences between groups in symptom severity but this item did not reach our *a priori* threshold for clinical significance (Table 2).

Visual inspection of the item response curves (IRC) for sadness, anhedonia, appetite disturbance, sleep disturbance, psychomotor symptoms and concentration difficulties (given

in supplementary material) revealed that curves of three items (i.e., sadness, appetite disturbance and psychomotor symptoms) were graphically substantially steeper in individuals without a lifetime history of manic symptoms than in those with a history of manic symptoms. These results suggest that the items sadness, appetite disturbance and psychomotor disturbance were better indicators of depression severity (i.e., provide more information about the level of the latent construct representing depression severity) in individuals without a lifetime history of manic symptoms than in those with a history of manic symptoms, in a clinically meaningful way.

Test information function (TIF)—The TIF curve of the group of individuals with a lifetime history of manic symptoms had a lower peak than the TIF curve of the group of those without a history of manic symptoms (vertical shift), indicating that DSM-IV symptoms of MDE are less informative in participants with a lifetime history of manic symptoms than in those without such history (Figure 1).

Because psychiatric comorbidities and depressive symptoms are more prevalent in individuals with bipolar spectrum disorder (Hoertel et al., 2013b; Nusslock and Frank, 2011) and might explain these results, we further examined the TIF curves for both groups 1) in the subpopulation of subjects without any lifetime mental comorbidity (i.e., without any lifetime history of anxiety disorder, substance use disorder or personality disorder) and 2) in the subpopulation of subjects with a lifetime history of 2-week episode of depressed mood and/or anhedonia and without any lifetime mental comorbidity. We found that the vertical shift was substantially reduced (Figures 2 and 3), with a group difference in the total amount of information provided by the set of depressive items (corresponding to the difference in area under the curve (AUC) between the two TIF curves) of 55% in the full sample (Figure 1), of 51% in the subpopulation of those without any lifetime history of psychiatric comorbidity (Figure 2), and of 4% in the subpopulation of those with a lifetime history of 2-week episode of depressed mood and/or anhedonia and without any lifetime history of psychiatric comorbidity (Figure 3). This result suggests that differences between groups are partly explained by differential rates of psychiatric comorbidity and history of 2-week episode of depressed mood and/or anhedonia.

Discussion

To our knowledge, this is the first study to examine differences in the likelihood of reporting DSM-IV symptoms of MDE between individuals with and without a lifetime history of manic symptoms in a nationally representative sample using an IRT-based methodology. The benefit of the IRT-based approach is that it accounts for the potential confounding effect of depression severity in evaluating potential group differences in symptom expression (Asparouhov, 2005). Additional strengths of the present study include (i) the use of a large, representative community sample, (ii) the use of an *a priori* defined threshold of clinical significance so that emphasis was placed on differences that are substantively meaningful rather than only on statistical significance, and (iii) the incorporation in our analyses of information from the sampling methods of the survey design which has been suggested to substantially improve standard error estimates and tests of model fit (Asparouhov, 2005).

Although most prior research found only subtle differences in depressive symptoms between MDD and bipolar disorder (Cassano et al., 1989; Cuellar et al, 2005; Mitchell et al., 2011; Swann, 1994), the specific contribution of manic symptoms to the depression symptom expression in the general population had not been previously examined. The current study results revealed clinically substantial differences in symptom expression between the unipolar symptom group (those without a lifetime history of manic symptoms) and the bipolar spectrum symptom group (those with a lifetime history of manic symptoms). The data suggested that three symptoms of MDE (i.e., sadness, appetite disturbance and psychomotor symptoms) were better indicators of depression severity (i.e., provide more information about the level of the latent construct representing depression severity) in individuals without a lifetime history of manic symptoms than in those with a lifetime history of manic symptoms. Ranging in size from medium to large in magnitude, these effects suggest that there are clinically relevant differences in depression symptom presentation that may be informative in distinguishing unipolar from bipolar spectrum depression. These findings are consistent with prior research supporting phenomenological differences in depression symptom expression between bipolar and unipolar depression (Akiskal and Benazzi, 2005; Bowden, 2005, Cuellar et al., 2005; Hoertel et al, 2013b; Mitchell et al., 2008, 2001, 1992; Moreno et al., 2012; Olfson et al., 2005; Parker et al., 2000; Perlis et al., 2006; Solomon et al., 2006) and extend them because they support that considering a broader definition of bipolar disorder may allow to unmask in the general population important differences between unipolar and bipolar symptom expression in the general population that are not merely due to differences in depression severity between groups.

Our findings suggest that DSM-IV MDE symptoms, when considered in isolation, may be less informative in individuals with a lifetime history of manic symptoms than in those without such history because they may provide lower information at equal levels of depression severity. MDE symptoms (in particular sadness, appetite disturbance, and psychomotor symptoms) might less accurately reflect the pattern of depressive symptoms in individuals with a lifetime history of manic symptoms than in those without such condition. It is also possible that among individuals with a lifetime history of manic symptoms, depressive symptoms may provide less incremental information. Because individuals with a lifetime history of manic symptoms are more likely than the general population to have depressive symptoms and psychiatric comorbidity, the presence of depressive symptoms in that group may provide less additional information than among individuals without a lifetime history of manic symptoms (Alonso and Molenberghs, 2007).

Our findings have two important implications. From the nosological point of view, our findings call attention to the need to develop reliable and valid procedures to identify diagnostic thresholds for depression and mania in the absence of a gold standard and to examine whether those thresholds should vary in the presence of comorbidity (Hoertel et al., 2015a, 2015c). From the clinical point of view, our findings alert to the possibility of different symptomatic presentations among depressed individuals with co-occurring disorders, which could increase the risk of errors in diagnosis and treatment.

This study should be interpreted in light of some limitations. First, clinical information on depressive and manic symptoms was based on retrospective self-report, which could lead to recall bias. Second, participants had to endorse a 2-week period of depressed mood and/or anhedonia to be asked about other DSM-IV depressive symptoms. Therefore, we may have missed information on other depressive symptoms for some participants with lower levels or shorter durations of depressed mood. However, one third of the full NESARC sample endorsed depressed mood or anhedonia sometime in their life and our results are consistent with those of previous studies (Cooper et al., 1988; Whiffen, 1991; Whiffen and Gotlib, 1993). Finally, we identified participants with manic symptoms based on the lifetime presence during over one week of at least one of three hypomanic symptoms used for the screening of a manic or hypomanic episode. This restrictive definition could have led us to underestimate the proportion of participants with a lifetime history of manic symptoms. Alternatively, these three hypomanic symptoms could be associated with psychopathology other than mania, possibly resulting in an overestimation of participants with a history of manic symptoms. However, our approach is consistent with that of prior epidemiological and clinical studies (Angst et al., 2003; Hoertel et al., 2013b; Merikangas et al., 2008; Ramsey et al., 2013; Zimmermann et al., 2009). Furthermore, the lifetime prevalence rate of manic symptoms in our study (18.7%) is consistent with recent data from the Epidemiologic Catchment Area Study (Ramsey et al., 2013) that found that the proportion of individuals with a lifetime history of at least two manic symptoms was 15.6%. In addition, this potential misclassification would have tended to bias our results towards the null hypothesis, suggesting the robustness of our findings.

Conclusion

Despite these limitations, by addressing several constraints of prior research and using Item Response Theory (IRT), the present study supports that the clinical presentation of depressive symptoms may differ substantially between unipolar and bipolar spectrum depression, highlighting the importance of continued research into specific pathophysiology differentiating these disorders to help clinicians ensure patients benefit from a thorough diagnostic assessment and formulation that can allow the delivery of optimal, evidence-based therapeutic interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

We examined differences between unipolar and bipolar spectrum depression symptom expression.

We used item response theory (IRT) methods to equate for levels of depression severity. The clinical presentation of depressive symptoms differed substantially between the two groups.

Continued research into specific pathophysiology differentiating these conditions is needed.

Figure 1.
Test information function (TIF) and its standard error of measures (SEM) of DSM-IV depressive symptoms in individuals with and without a lifetime history of manic symptoms (N=34,638).

Figure 2.

Test information function (TIF) and its standard error of measures (SEM) of DSM-IV depressive symptoms in individuals with and without a lifetime history of manic symptoms, in the subpopulation of those without any lifetime history of psychiatric comorbidity (i.e., no lifetime history of anxiety disorder, substance use disorder or personality disorder) (N=20,706).

Figure 3.

Test information function (TIF) and its standard error of measures (SEM) of DSM-IV depressive symptoms in individuals with and without a lifetime history of manic symptoms, in the subpopulation of those with a lifetime history of 2-week episode of depressed mood and/or anhedonia and without any lifetime history of psychiatric comorbidity (i.e., no lifetime history of anxiety disorder, substance use disorder or personality disorder) (N=6,444).

Table 1

Prevalence of DSM-IV depressive symptoms in participants with and without a lifetime history of manic symptoms in the full NESARC sample and in the subsample of those with a lifetime diagnosis of DSM-IV MDE.

DSM-IV symptoms	Full Sample		Participants with lifetime DSM-IV MDE			
	History of manic symptoms (N = 6,465)	No history of manic symptoms (N = 28,173)	History of manic symptoms (N = 3,350)	No history of manic symptoms (N = 4,589)	OR [95%CI]	p-value
	%	%	%	%		
Sadness	65.9	31.0	93.0	93.3	1.35 [1.27–1.43]	0.676
Anhedonia	60.2	23.5	86.9	82.1	1.27 [1.18–1.35]	<0.001
Appetite disturbance	52.3	18.4	79.8	74.7	1.25 [1.18–1.35]	<0.001
Sleep disturbance	58.0	22.0	89.6	88.1	1.32 [1.23–1.41]	0.098
Fatigue	51.9	19.0	82.6	80.1	1.30 [1.22–1.39]	0.025
Psychomotor symptoms	42.5	12.8	69.0	59.9	1.16 [1.08–1.25]	<0.001
Worthlessness / guilt	46.3	14.0	74.7	65.5	1.18 [1.09–1.27]	<0.001
Concentration difficulties	56.8	20.2	87.9	84.6	1.28 [1.20–1.37]	0.001
Suicidality	36.0	10.7	57.4	47.9	1.12 [1.03–1.20]	<0.001
DSM-IV diagnosis of major depressive episode	51.0	15.4	–	–	–	–

Percentages are weighted values.

p-values in bold are statistically significant ($p < .05$) after adjusting for multiple testing using the Benjamini-Hochberg procedure

Differential item functioning (DIF) of DSM-IV depressive symptoms in participants with and without a lifetime history of manic symptoms in the NESARC sample, using multigroup confirmatory factor analysis.

Table 2

DSM-IV symptoms	History of manic symptoms (N = 6,465)				No history of manic symptoms (N = 28,173)				DIFFTEST a		DIFFTEST b	
	a	Rank a	b	Rank b	a	Rank a	b	Rank b	DIFa	pDifference	DIFb	pDifference
Sadness	2.28	7	0.59	1	3.84	9	0.51	1	1.57	<0.001	-0.08	<0.001
Anhedonia	2.07	6	0.75	2	2.58	5	0.78	2	0.52	<0.001	0.02	0.543
Appetite disturbance	1.71	3	0.97	5	2.26	4	0.99	6	0.55	<0.001	0.01	0.492
Sleep disturbance	3.03	9	0.83	3	3.68	8	0.80	3	0.65	<0.001	-0.03	0.233
Fatigue	1.60	2	1.26	8	1.96	2	1.28	8	0.37	<0.001	0.01	0.219
Psychomotor symptoms	2.04	5	0.99	6	2.71	6	0.94	5	0.67	<0.001	-0.05	0.086
Worthlessness / guilt	1.78	4	1.15	7	2.17	3	1.19	7	0.39	<0.001	0.04	0.058
Concentration difficulties	2.66	8	0.86	4	3.21	7	0.87	4	0.55	<0.001	0.02	0.549
Suicidality	1.18	1	1.51	9	1.50	1	1.49	9	0.32	<0.001	-0.02	0.206

Note:

a = discrimination parameter estimate,

b = severity parameter estimate.

p-values were adjusted for multiple testing using the Benjamini-Hochberg procedure.

Values in bold are statistically ($p < .05$) and clinically significant (method described in the article).

Sampling weights and design effects of the NESARC were taken into account.

DIFFTEST a = comparing models with the factor loading free and fixed for the corresponding item.

DIFFTEST b = comparing models with the threshold respectively free and fixed for the corresponding item.