

Affect Disord. Author manuscript; available in PMC 2012 July 02.

Published in final edited form as:

J Affect Disord. 2009 May; 115(1-2): 87–99. doi:10.1016/j.jad.2008.09.006.

The factor structure of lifetime depressive spectrum in patients with unipolar depression

G.B. Cassano*, A. Benvenuti, M. Miniati, S. Calugi, M. Mula, L. Maggi, P. Rucci, A. Fagiolini, F. Perris, and E. Frank

Department of Psychiatry, Neurobiology, Pharmacology and Biotechnology, School of Medicine, University of Pisa, Italy

Department of Psychiatry, University of Pittsburgh School of Medicine, United States

Department of Psychiatry, University of Naples SUN, Naples, Italy

Abstract

Background—While previous attempts to elucidate the factor structure of depression tended to agree on a central focus on depressed mood, other factors were not replicated across studies. By examining data from a large number of items covering the range of depressive symptoms, the aim of the present study is to contribute to the identification of the structure of depression on a lifetime perspective.

Methods—The study sample consisted of 598 patients with unipolar depression who were administered the Mood Spectrum Self-Report (lifetime version) in Italian (*N*=415) or English (*N*=183). In addition to classical exploratory factor analysis using tetrachoric correlation coefficients, an IRT-based factor analysis approach was adopted to analyze the data on 74 items of the instrument that explore cognitive, mood and energy/activity features associated with depression.

Results—Six factors were identified, including `Depressive Mood', `Psychomotor Retardation', `Suicidality', `Drug/Illness related depression', `Psychotic Features' and `Neurovegetative Symptoms', accounting overall for 48.3% of the variance of items.

Limitations—Clinical information on onset of depression and duration of illness is available only for 350 subjects. Therefore, differences between sites can only be partially accounted using available data.

Conclusions—Our study confirms the central role of depressed mood, psychomotor retardation and suicidality and identifies the factors `Drug/Illness related depression', `Psychotic features' and the neurovegetative dysregulation not captured by the instruments most frequently used in previous studies. The identification of patients with specific profiles on multiple factors may be useful in achieving greater precision in neuroimaging studies and in informing treatment selection.

Keywords

Depression	; Spectrum;	Suicidality;	Factor; 1	Retardation;	Mood	

^{© 2008} Elsevier B.V. All rights reserved

^{*}Corresponding author. Department of Psychiatry, Neurobiology, Pharmacology and Biotechnologies, University of Pisa, via Roma 67 - 56100 Pisa, Italy. Tel.: +39 050 835419; fax: +39 050 21581. gcassano@psico.med.unipi.it (G.B. Cassano)..

Conflict of interest The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

1. Introduction

Current classification systems describe prototypes of mood disorders that overlook the heterogeneity of clinical syndromes in terms of pattern of symptoms, onset, course and response to treatment.

Attempts to define clinical characteristics of subtypes of depression have been already extensively made, based on clinical presentation (atypical vs. melancholic vs. psychotic), type of onset (early-onset, late-onset, post-partum depression, etc.), course of illness (single episode or recurrent depression), or treatment response (Rush, 2007).

The heterogeneity of clinical presentation of depression has been considered to explain why a high number of patients fail to reach a complete or a sustained recovery. Indeed, long term recovery from depression is still a goal to reach, given that more than 10% of patients never fully recover from a depressive episode (Kennedy and Giacobbe, 2007), and 20–40% of patients display long-lasting depressive symptomatology (Keitner et al., 2006).

In order to identify clusters of depressive symptoms for a refined description of clinical subtypes of depression, a number of studies have carried out exploratory factor analysis of items included in the most commonly administered rating scales for depression, such as the Hamilton Rating Scale for Depression (HAM-D), the Center for Epidemiologic Studies Depression Scale (CES-D), the Beck Depression Inventory (BDI), the Zung Self-Rating Depression Scale (SDS) and the Montgomery-Asberg Depression Rating Scale (MADRS) (Mowbray, 1972; Cassano et al., 1976; O'Brien and Glaudin, 1988; Marcos and Salamero, 1990; Gibbons et al., 1993; Keogh and Reidy, 2000; Whisman et al., 2000; Helm and Boward, 2003; Suzuki et al., 2005; Shafer, 2006; Ward, 2006; Berk et al., 2007; Romera et al., 2008; Vanheule et al., 2008). In general, factor analyses of these instruments have consistently identified a 'depressive factor' and a 'somatic/neurovegetative factor'. Other factors identified were "psychomotor retardation" (Schrijvers et al., 2007) and "suicidality" (Witte et al., 2006). However, the instruments on which factor analyses were carried out include criterion symptoms for a depressive episode and do not comprise atypical symptoms, subthreshold or sub-syndromal depressive features that may be clinically significant because they represent precursors, prodromes, residuals of a full-blown episode, or isolated features of depression (Judd et al., 1997). These manifestations are part of the 'mood spectrum' that considers as clinically meaningful depressive features that may occur throughout the lifetime, sometimes isolated, rather than as part of a temporally circumscribed clinical syndrome (Cassano et al., 1999, 2002). In order to evaluate mood spectrum features using a standardized assessment, researchers of the Spectrum Project have developed and validated the Mood Spectrum questionnaire (MOODS-SR) designed to collect signs and symptoms of depression, mania, rhythmicity and vegetative functions (Fagiolini et al., 1999; Dell'Osso et al., 2002).

The aim of this study is to analyze the factor structure of the depressive component of MOODS-SR in patients with unipolar depression, recruited in different studies conducted in the framework of the Spectrum Project. We focused on depression items because we were interested in defining conceptually homogeneous dimensions of depression to be used as separate measures in place of a total score of depression.

2. Methods

2.1. Participants

The sample includes 598 patients with unipolar depression (459 F, 139 M, mean age=38.6, SD=12.2, range 18–67) collected in 4 studies (see Table 1). Study 1 includes 41 Italian

patients with unipolar depression participating in an ongoing study aimed at comparing the compare the clinical characteristics and genetic profile of mood disorders (Mula et al., 2008). Study 2 includes female participants in a study aimed at comparing mood spectrum and anorectic—bulimic spectrum across eating disorders, mood disorders and controls. Study 3 includes US and Italian male and female patients aged 18–66 years participating in the study "Depression: the search for treatment-relevant phenotypes" (Frank et al., 2008). These patients had non-psychotic depression and no history of mania or hypomania. Study 4 includes 87 Italian patients with unipolar depression with (*N*=10) or without (*N*=77) psychotic symptom recruited for a multicenter Italian study aimed at validating an interview to assess the psychotic spectrum (Sbrana et al., 2005).

2.2. Instruments

The MOODS-SR questionnaire, developed in English and Italian, was derived from the corresponding structured interview (Fagiolini et al., 1999) and is focused on the presence of manic and depressive symptoms, traits and lifestyles that may characterize the 'temperamental' affective dysregulation that make up both fully syndromal and subthreshold mood disturbances. The latter include symptoms that are either isolated or clustered in time and temperamental traits that are present throughout individual's lifetime. The MOODS-SR consists of 161 items coded as present or absent for one or more periods of at least 3-5 days in the lifetime. Items are organized into 3 manic-hypomanic and 3 depressive domains each exploring mood, energy and cognition, plus a domain that explores disturbances in rhythmicity (i.e. changes in mood, energy and physical well-being according to the weather, the season and the phase of menstrual cycle, etc.) and in vegetative functions, including sleep, appetite and sexual function. The sum of the scores on the three manichypomanic domains constitutes the score for the manic-hypomanic component and that for the three depressive domains the depressive component. For the purpose of the present report, we selected 74 items from the MOODS-SR lifetime version, 62 encompassing depressive symptoms and features and 12 exploring rhythmicity/vegetative function features related to depression. The instrument was administered in the English version to 183 US patients and in the Italian version to 415 Italian patients.

2.3. Statistical analyses

An exploratory factor analysis (EFA) was conducted using tetrachoric correlation coefficients. These coefficients measure the association between dichotomous items and are based on the assumption that the response to any particular item can be thought of in terms of the crossing of a threshold on an underlying latent continuous distribution (i.e., the latent trait). Respondents with a response strength greater than the threshold will answer 'yes', otherwise they will respond 'no'. By assuming that the response process is normally distributed and knowing the proportion of subjects that respond affirmatively to the items, tetrachoric correlations for all distinct 74(74–1)/2=2701 pairs of items were estimated. The matrix of tetrachoric correlations was then subjected to unweighted least squares factor analysis and then rotated orthogonally using the varimax method (Kaiser, 1958) and the promax method (Hendrickson and White, 1964), to allow for a possible correlation of factors, as suggested by Fabrigar et al. (1999).

The number of factors was determined by inspecting the scree plot, and considering their interpretability and consistency with the criteria that guided the construction of the instrument. Items with a cross-loading on multiple factors were assigned to the factor with the highest loading.

In addition to classical exploratory factor analysis, an IRT-based factor analysis approach was adopted to analyze the data. While classical factor analysis makes use of information

derived from pair-wise correlations of items, IRT-based factor analysis make use of all information in each patient's pattern of item responses, *i.e.* item pairs, triplets, quadruplets, etc. and is therefore called full-information factor analysis (FIFA). This procedure is limited in terms of the number of factors that can be estimated, typically no more than 5 or 6 dimensions. Furthermore, when the number of latent dimensions (k) is large and the number of items is large (n), a minimum of n(k+1) subjects is required to accurately estimate the unknown parameters in the model, and in general the number of subjects should be on the order of ten times the number of items (see Gibbons et al., 2007). In IRT models, the item difficulty, or threshold, parameter b is the point on the latent scale θ where a person has a 50% chance of responding positively to the item. Items with high thresholds are less often endorsed. The slope, or discrimination, parameter a describes the strength of an item's discrimination between people with trait levels (θ) below and above the threshold b. The a parameter may also be interpreted as describing how an item may be related to the trait measured by the scale (Linden and Hambleton, 1997). Differential item functioning (DIF) analysis, a 1-parameter logistic model that estimates only the item threshold under the assumption that the discrimination parameter is constant, was carried out in order to determine whether site or gender had an effect on the latent dimensions identified and whether the individual items measured the latent dimensions in a different way in females and males and in US and Italian participants. In order to establish whether a DIF effect was in place, a model without covariates was first fit and compared with the DIF model. The difference between the log-likelihood of the fit of the DIF and of the non-DIF models is distributed as a chi-square and was used to test the improvement of the DIF model over the non-DIF model.

Analyses were conducted using TESTFACT, Version 4.0 (2003) and BILOG-MG, version 3.0 (2003).

3. Results

The frequency of endorsement of the 74 items of the depressive component of the MOODS-SR is provided in Table 2. Items are organized by decreasing frequency. In our sample, feeling guilty and being sad or empty were the most commonly endorsed items.

3.1. Factor analysis

A classical factor analysis was first carried out. By inspecting the scree plot, a change in the curvature was observed after the 6th factors, suggesting that 6 factors are sufficient to summarize the variance of the items in a parsimonious way and that the subsequent factors are nuisance factors.. After comparing 5- 6- and 7- solutions using the varimax and the promax method, a 6-factor varimax solution was selected as the best in terms of interpretability. This solution accounted overall for 48.3% of the variance of the 74 items. Factor 1 accounted for 28.7% of the variance, the other five factors accounted for 5.2%, 4.2%, 3.8%, 3.2% and 3.0% of the variance, respectively. Factor loadings obtained using varimax rotation are shown in Table 3, arranged in decreasing order within factors. Based on items contents, factors were labeled as:

3.1.1. Factor 1. Depressive mood—This factor includes a number of symptoms and temperamental features that span depressed mood, loss of interests and loneliness, with principal loadings on "persistently sad or empty, blue or down in the dumps" (0.713), "serious, introverted or gloomy" (0.707), "lost interest in hobbies or sport" (0.701), "purposeless, as if everything had lost its significance" (0.690), "lonely" (0.663), "deeply annoyed" (0.624) and "difficulty making new friends" (0.624).

3.1.2. Factor 2. Psychomotor retardation—This factor includes psychomotor retardation in different areas of daily activities, physical weakness and tiredness, with principal loadings on "slowed down" (0.725), "passive, sluggish" (0.718), "difficulty starting to do anything" (0.717), "speech or thinking seemed slowed down" (0.688), "fatigued, weak, or tired for the smallest task" (0.679), "trouble getting out of bed in the morning" (0.630) and "your housework deteriorated" (0.612).

- **3.1.3. Factor 3. Suicidality**—This factor includes items related with suicidal ideation, plans and attempts, with principal loadings on "suicide attempt" (0.865), "want to die or hurt yourself" (0.783), "specific plan to hurt or kill yourself" (0.756), "suicide attempt requiring medical attention" (0.730) and "wishing not to wake up in the morning" (0.645).
- **3.1.4. Factor 4. Drug/illness related depression**—This factor describes the tendency to feel depressed when ill or after having taken substances, with principal loading on "depressed when stopping any of these substances" (-0.687) and "depressed when drinking lots of alcohol or using substances" (-0.635).
- **3.1.5. Factor 5. Psychotic features**—This factor includes paranoid thoughts and psychotic symptoms, with principal loading on "you felt surrounded by hostility, as if everybody was against you" (0.743), "everyone was talking about you" (0.702) and "others were causing all of your problems" (0.610).
- **3.1.6. Factor 6. Neurovegetative symptoms**—This factor includes a number of items that describe problems with sleep, appetite and sexual function, with principal loadings on "repeatedly wake up in the middle of the night and had difficulty falling sleep" (0.568) and "less sexually active" (0.524).

Results of the 6-factor solution obtained with promax rotation are provided in the Appendix A for comparison. While the first 5 factors coincided to a large extent with those generated by the varimax solution, the items that made up the factor "neurovegetative symptoms" did not cluster together. The last factor derived with promax solution, "hopelessness," included only two items ("gloomy future" and "wishing to run away from your current life") with a weak loading on multiple factors.

3.2. DIF analysis by gender and site

The 63 items with a factor loading >0.40 in the varimax solution were retained for subsequent IRT analyses. Full information factors analysis was carried out first. Although the ratio between subjects and items (9.5:1) was close to the ten-to-one ratio recommended for carrying out the analysis, the model failed to converge (data available on request).

DIF analysis was conducted separately on the items belonging to the 6 factors to examine the gender effect. Comparisons between the models without covariates and the DIF models indicated that the latter had a significantly better fit to the data. While no or minor effects on the latent dimensions were found, indicating that population mean scores on the latent dimensions were similar for males and females, some items differed between genders. These included q26 (indifferent about everything that happened to you or your family) and q97 (hear voices), that were more frequent in males and q11 (crying very easily), q15 (nothing you put on looked or felt right) and q155 (difficulty becoming sexually aroused), that were more frequent in females, q65 (fatigued weak, or tired for the smallest task), q90 (difficulty making even minor decisions).

DIF analysis by site revealed remarkable differences between sites. US participants had higher scores (lower thresholds) on 4 of the 6 latent dimensions estimated, including neurovegetative function (-0.782), depressive mood (-0.576), suicide (-0.357), psychomotor retardation (-0.301). Item differences between sites included sleep (q139, q141), appetite (q152, q153), suicide behavior (q107), hearing voices (q97), feeling guilty or remorseful (q93), housework/performance deteriorated (q89), crying very easily (q11) nostalgic (q2), lost interest in how you looked (q14), lost pleasure in your social life (q21), indifferent about everything that happened to you or your family (q26).

4. Discussion

In our study, based on a sizeable pool of subjects with major depression and using items drawn from a validated instrument, a six-factor solution was identified with classical factor analysis using a sound methodology for dichotomous items. Our solution accounted for 48.3% of variance of the items, in line with other studies that explored the factor structure of depression.

MOODS-SR items reflecting DSM-IV criteria for a depressive episode were frequently endorsed in our population and can be found in all identified factors (see Tables 2 and 3 highlighted in bold). However, a number of other features encompassing temperamental traits and atypical symptoms also displayed a high frequency (Table 2) and high loadings on each factor (Table 3) and clustered with criterion symptoms of depression. This is of even greater interest when one considers that this is the first study investigating factors of depression from a lifetime perspective.

The first identified factor, *Depressive mood*, includes "core" symptoms of depression, anhedonia and temperamental features.

Anhedonia is recognized as an important component of depression (Akiskal, 1986; Loas and Boyer, 1996; Leventhal et al., 2006) and is one of the diagnostic criteria for the DSM-IV diagnosis of major depression with melancholia (Rush and Weissenburger, 1994). It is defined as a reduced capacity or inability to experience pleasant emotions and was introduced as one of the core symptoms of the endogenous (or melancholic) subtype of major depression in the DSM-III (1980). The development of anhedonia as a construct was influenced by Klein's conceptual framework of "endogenomorphic" depression, that refers to a particular type of depression characterized by a pervasive impairment of the capacity to experience pleasure or to respond affectively to the anticipation of pleasure (Klein, 1974). Anhedonia was found to correlate significantly with neuroticism, introversion and morbid risk of depression in first-degree relatives of individuals with depression (Schrader, 1997). Furthermore, in his classification of chronic depression, Akiskal described a condition characterized by the presence of neurovegetative change and anhedonia as an antidepressant-responsive form of chronic depression (Akiskal, 1983).

Kraepelin (1923) described four basic affective temperaments (manic, depressive, irritable and cyclothymic) and suggested that they could color the symptoms pattern of acute mood episodes. In that tradition, the baseline affective temperament was characterized, with an emphasis on the role of the latter for the final phenomenology and prognosis of mood disorders (Akiskal et al., 1977; Cassano et al., 1989; Placidi et al., 1998; Akiskal et al., 1998, 2006). The depressive temperament includes at least five of the following characteristics, with an onset before age 21:1) gloomy, pessimistic, humorless; 2) quiet, passive and indecisive; 3) skeptical, hypercritical or complaining; 4) brooding and given to worry 5) conscientious or self-disciplining; 6) self-critical, self-reproaching and self-derogatory; 7) preoccupied with inadequacy, failure and negative events. Several of these features are

present in this factor, further supporting the close relationship between core features of depression and its temperamental correlates.

The second factor, *Psychomotor retardation*, parallels another central feature of depression and includes the contra-polar features of mania, which is characterized by psychomotor activation (Cassidy et al., 2002; Hantouche et al., 2003; Benazzi, 2004; Angst et al., 2005; Koukopoulos et al., 2005; Picardi et al., 2008; Cassano et al., 2008; Schrijvers et al., 2007). Psychomotor changes are reported to be `nearly always present' in the melancholic subtype of major depressive episode in DSM-IV-TR, and are believed by some researchers to be markers of melancholia (Parker and Hadzi-Pavlovic, 1996; Rush and Weissenburger, 1994; Parker, 2000). The identification of patients with psychomotor retardation may have important practical implications in the light of current literature linking retardation to severity of the depression in general (Benazzi, 2002) and of melancholic depression in particular (Parker, 2000). Moreover, in our opinion, the role of psychomotor retardation deserves further investigation in the light of a clinical distinction between unipolar and bipolar depression.

The third factor, *Suicidality*, encompasses suicidal ideation, attempts and severity of attempts. Various studies have confirmed that patients with an affective disorder have a higher risk of suicide attempts than the general population with a case-fatality prevalence (suicides divided by total subjects) varying from 2.0% in outpatients with affective disorders to 6% in suicidal inpatients (Bostwick and Pankratz, 2000). In our sample, up to 45% of patients reported suicidal ideation over the lifetime, but only 18% reported a suicide attempt, in line with the figures reported by Balestrieri et al. (2006). In spite of the large number of studies on suicidality, few of them have focused on the process that lead from weariness of life to death wishes, suicidal plans, suicidal attempts and completed suicide. The "suicidality" factor of the MOODS-SR allows the assessment of each separate step of the suicidal process together with the severity of any previous attempts from a lifetime perspective. In a recent study Cassano et al. (2004) found that the number of manic—hypomanic items endorsed on the lifetime mood spectrum assessment was linked with an increased likelihood of lifetime and current suicidal ideation in patients with recurrent unipolar depression.

The fourth factor, *Drug/Illness-Related Depression*, explores the occurrence of mild or severe mood dysregulations (energy fluctuations, moods instability, or emotional liability) reported by patients during common and not severe physical illnesses (namely, flu, or cold). For example, mood manifestations, including severe depressive episodes, have been described in subjects who are sensitized to tree pollen as exacerbated or triggered by the use of common drugs, such as antihistamines or vasoconstrictors (Widmer et al., 2000; Rondon et al., 2007).

It is well documented that patients with depressive spectrum features are sensitive to substance withdrawal, as occurs with benzodiazepines or alcohol, or that they may be unusually sensitive and reactive to ingested substances, including prescribed or over-the-counter medication, street drugs, or commonly used beverages (Winokur et al., 1998; Chengappa et al., 2000). Because these signs and symptoms have been described in patients with depression as markers `underlying soft bipolarity', past research has focused on their clinical significance (Akiskal et al., 2006).

The fifth Factor, *Psychotic features*, includes paranoid thoughts and psychotic symptoms. The presence of psychotic symptoms in patients with affective disorders has been described since the first observations on *dementia praecox* and the manic depressive illness (Kraepelin, 1904) and it is widely reported also among patients with major depressive episodes (Maj et

al., 2007). Psychotic symptoms during a depressive episode seems to be related to an increased likelihood of underlying bipolarity (Cassano et al., 2004; Goes et al., 2007) especially in patients with recurrent depression. Wood et al. (2002) found that a specific genotype, allegedly associated with the occurrence of full-blown psychotic syndromes, was associated with paranoid ideation and psychoticism in major depressive disorder. More recently (Iga et al., 2007) a polymorphism of brain-derived neurotrophic factor (BDNF) gene has been associated with psychotic features in patients with major depression.

The sixth factor, Neurovegetative Symptoms, explores symptoms of neurovegetative and rhythm disruption such as diurnal mood variation with morning worsening, early morning awakening, marked loss of appetite or marked weight-loss or loss of libido. Long-lasting sleep, appetite and sexual function problems may reduce daily life functioning and work performance. These symptoms have been traditionally considered as `somatic', or 'melancholic' core features of full-blown depressive episodes, and associated with 'endogenous depression', in epidemiological and clinical studies. However, physical and neurovegetative symptoms proved to be useful for subtyping subjects in the NCS Survey (Sullivan et al., 1998) and were frequently reported as residual manifestations of a major depressive episode (Fava, 1999). Moreover, they have been associated with an increased duration of the depressive episode and high risk of chronic course and recurrences (Cassano and Savino, 1997). Finally, it must be acknowledged that neurovegetative episodic subthreshold neurovegetative dysregulations, even if egosyntonic and adaptive, may represent a vulnerability for a full-fledged mood episodes of both manic and depressive polarity (Fava, 1999). Because 'behavioral activation is more important than mood change per se in diagnosing BP-II hypomania', disturbances and rhythmic changes in eating, sexual activity, or sleep, have been considered of relevance when ambiguities regarding the boundaries between unipolar and bipolar disorders were explored (Akiskal, 2005).

Our results suggest that the factors identified were approximately invariant between genders, and that only a limited number of items differentiated males from females. These include items related to depressed mood 'indifferent about everything that happened to you or your family', `crying very easily', `nothing you put on looked or felt right', neurovegetative symptoms 'difficulty becoming sexually aroused', psychomotor retardation 'fatigued weak, or tired for the smallest task', 'difficulty making even minor decisions' and one psychotic feature `hear voices.' This is consistent with the literature that fails to provide clear-cut evidence of gender differences in symptoms in patients with depression (Frank et al., 1988; Young et al., 1990). On the contrary, the differences on factors between sites were more pronounced. This was however expected because, despite the adoption of similar inclusion/ exclusion criteria between US and Italian participants to Study 3 (Depression: the Search for Treatment-Relevant Phenotypes), the US patients exhibited longer duration of illness (median 10.6 vs. 3 years, Mann–Whitney Z=-6.26, pb0.001) and younger age of onset of depression (24.1 \pm 12.5 vs. 30.9 \pm 10.8, *t*-test=-5.2, *p*<0.001). Therefore, the differences between Italian and US participants may represent a proxy for a higher severity of illness and should not be interpreted as genuine variations between sites. However, because in the other studies information on age of onset and duration of illness was not recorded in the database, differences between sites can only be partially accounted using available data.

Our results should be interpreted keeping in mind that the factors identified with orthogonal (varimax) rotation are uncorrelated to each other. While this assumption is at variance with the expectation that depression factors are correlated, it allowed us to generate a solution that is conceptually clear, consistent with our aim to derive distinct dimensions of depression and in line with the literature that identified similar factors using other instruments.

In conclusion, our study provided further evidence that patients with unipolar depression exhibit a number of lifetime symptoms, in additions to classical DSM-IV criteria, including temperamental traits, atypical signs or isolated symptoms, all of them contributing to the final structure of depressive spectrum. Future research should be aimed at differentiating unipolar and bipolar depression.

The identification of patients with specific profiles on multiple factors could be used to achieve higher precision in clinical diagnosis and in brain imaging or neurobiological studies than is currently achieved using subjects who simply meet with the same DSM-IV diagnosis. Better psychopathological characterization of patients may inform treatment selection and ultimately result in better treatment outcome.

Acknowledgments

We thank Dr. Rocco Nicola Forgione and Mrs. Gail Kepple, who kindly provided the data necessary for our analysis, and Ms. Elaine Boland, who assisted with the preparation and proofreading of the manuscript.

Role of funding source This study was funded by NIMH grants MH65376 (PI: E. Frank) and MH30915 (PI: E. Frank), and Fondazione IDEA, Italy (PI: GB Cassano) and a grant from Forest Research Institute.

Appendix

Α

Factor loadings derived from a 6-factor solution with promax rotation (bolded items reflecting DSM-IV criteria for a depressive episode, and bolded italicized items reflecting those with a factor loading <0.40 in absolute value).

	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness- related depression	Psychotic features	Hopelessness
10. persistently sad or empty, blue or down in the dumps	0.553	0.094	-0.017	-0.012	0.022	-0.191
4. serious, introverted or gloomy	0.538	-0.119	0.048	-0.099	0.087	0.025
13. purposeless, as if everything had lost its significance	0.512	0.135	0.081	-0.095	-0.067	-0.184
25. lost interest in hobbies or sport	0.509	0.073	-0.012	-0.129	-0.058	0.059
3. lonely	0.494	-0.062	-0.033	0.102	0.097	0.054
12. constantly complaining	0.466	-0.025	-0.317	-0.120	0.228	-0.090
6. deeply annoyed	0.465	-0.065	-0.056	-0.091	0.069	0.094
22. difficulty making new friends	0.455	-0.045	0.058	-0.098	-0.109	0.090
8. lost your capacity to laugh, have fun, enjoy your life?	0.448	0.030	0.208	-0.132	0.083	-0.275
11. crying very easily	0.438	-0.078	0.071	-0.100	0.079	-0.151
15. nothing you put on looked or felt right	0.431	0.095	-0.150	-0.059	0.047	-0.085
5. bored	0.413	-0.088	0.017	-0.157	0.065	0.090
7. the littlest thing could make you sad?	0.413	0	0.021	-0.016	0.122	0.047
26. indifferent about everything that happened	0.401	0.105	-0.097	-0.074	-0.158	0.079

	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness- related depression	Psychotic features	Hopelessness
to you or your family						
1. frustrated and defeated	0.393	0.020	-0.030	0.105	0.166	-0.019
27. lost interest or pleasure in all or almost all the things you usually enjoyed	0.372	0.194	0.135	-0.087	-0.091	0.077
21. lost pleasure in your social life	0.370	0.088	0.096	-0.081	-0.167	0.126
2. nostalgic	0.351	-0.105	0.042	0.083	0.150	-0.061
23. lost interest in your romantic life	0.349	0.039	0.053	-0.138	-0.180	0.120
9. you found it unusually hard to take rejections, particularly those involving friendships or romantic relationships?	0.337	-0.055	-0.067	-0.031	0.203	0.068
14. lost interest in how you looked	0.325	0.199	0.113	-0.125	-0.119	-0.211
84. disappointed in yourself	0.206	0.150	0.126	0.077	0.136	0.189
153. appetite decrease	0.198	-0.010	-0.017	0.030	-0.175	0.079
151. craving sweets or carbohydrates	0.178	-0.054	-0.109	-0.030	-0.012	0.076
59, physically "slowed down"	-0.096	0.646	-0.191	-0.189	0.082	0.032
58. difficulty starting to do anything	0.088	0.583	-0.214	-0.014	-0.062	0.205
60. speech or thinking seemed slowed down	0.080	0.569	-0.129	-0.056	-0.099	0.134
62. passive, sluggish	0.105	0.563	-0.094	0.097	-0.049	0.110
65. fatigued weak, or tired for the smallest task	0.081	0.499	0.079	-0.049	0.023	0.144
63. trouble getting out of bed in the morning	-0.042	0.470	0.066	0.097	-0.146	0.124
61. time as passing very slowly, hanging heavy	0.064	0.469	-0.047	-0.026	0.093	0.098
89. your housework/ performance deteriorated	0.021	0.435	0.031	0.062	-0.033	0.133
64, difficulty take to care of yourself	0.119	0.426	0.073	0.008	-0.095	0.111
90. difficulty making even minor decisions	0.123	0.388	-0.140	0.085	0.228	0.135
132. difficult to work in the early morning	-0.013	0.387	0.006	0.037	-0.110	0.099
92. mentally dull or confused	-0.058	0.335	0.026	-0.159	0.124	0.135
91. trouble thinking or concentrating	-0.064	0.308	-0.078	-0.048	0.233	0.137
101. using sleep as an escape	0.079	0.267	0.081	0.072	0.015	0.148
88. problems with your memory	-0.015	0.237	-0.024	-0.042	0.092	0.113
66. difficulty to sit still or lie down	-0.103	0.217	-0.113	0.006	0.190	0.084
ne down						

	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness- related depression	Psychotic features	Hopelessness
142. need much more sleep	-0.065	0.213	0.017	0.043	-0.101	0.113
138. you felt sleepy all the time	-0.033	0.210	-0.087	0.072	0.051	0.117
106. suicide attempt	-0.002	-0.167	0.684	-0.021	-0.016	0.199
105. specific plan to hurt or kill yourself	0.117	-0.133	0.576	0.032	0.015	0.195
104. want to die or hurt yourself	0.123	-0.104	0.569	-0.025	0.084	0.237
107. suicide attempt requiring medical attention	0.031	-0.086	0.563	-0.107	0.021	0.181
103. wishing not to wake up in the morning	0.010	0.002	0.443	0.030	0.087	0.226
102. life was not worth living	0.198	0.071	0.382	-0.001	-0.022	0.207
155. difficulty becoming sexually aroused	-0.008	0.099	-0.148	0.029	-0.098	0.097
19. depressed when stopping any of these substances	0.144	0.020	0.009	-0.680	-0.030	0.113
18. depressed when drinking lots of alcohol or using substances	0.231	-0.186	0.081	-0.652	-0.176	0.200
20. became depressed as a result of using alcohol, sleeping pills, anti-anxiety drugs, nicotine, caffeine, stimulants or similar substances even though you took them in order to feel better	0.107	-0.013	0.113	-0.606	-0.157	0.161
17. depressed when taking medications	0.164	0.038	-0.285	-0.563	0	0.128
98. heard voices clearly	-0.440	0.271	0.197	-0.440	0.152	0.078
16. depressed during physical illnesses	0.178	0.073	-0.233	-0.440	0.051	0.040
140. repeatedly wake up in the middle of the night and had difficulty falling sleep	-0.264	-0.298	-0.040	-0.306	0.199	0.094
141. repeatedly wake up much earlier	-0.193	-0.242	-0.026	-0.266	0.166	0.077
154. less sexually active	-0.017	-0.041	0.045	-0.179	-0.120	0.091
152. appetite increased	0.046	0.031	0.061	-0.172	-0.164	0.097
150. no food that appealed	0.011	0.144	0.072	-0.167	-0.131	0.091
95. you felt surrounded by hostility, as if everybody was against you	0.087	-0.051	0.003	0.088	0.545	0.155
96. everyone was talking about you	0.085	-0.035	-0.054	-0.027	0.507	0.134
94.others were causing all of your problems	0.092	-0.156	-0.002	0.081	0.478	0.096
97. heard voices	-0.313	0.081	0.174	-0.368	0.369	0.092
83. very vulnerable	0.067	0.166	0.082	0.111	0.365	0.176

	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness- related depression	Psychotic features	Hopelessness
93. you felt guilty or remorseful	0.036	0.026	0.088	0.092	0.321	0.182
85. body transformed	0.080	0.078	0.030	-0.152	0.257	0.088
87. need to take refuge in religion or player?	-0.075	-0.070	0.064	-0.063	0.231	0.085
139. repeatedly difficulty falling sleep	-0.205	-0.067	-0.136	-0.096	0.226	0.090
82. preoccupied with yourself and your own problems, thoughts and feelings	-0.013	0.084	0.159	0.201	0.222	0.150
81. hypercritical or skeptical	0.183	-0.030	-0.006	0.111	0.186	0.109
86. very preoccupied with money	0.131	0.051	0.026	-0.117	0.182	0.083
99. gloomy future	0.069	0.138	0.124	0.096	0.114	0.183
100. wishing to run away from your current life	0.152	0.045	0.113	0.105	0.133	0.153

References

- Akiskal HS. Dysthymic disorder: psychopathology of proposed chronic depressive subtypes. Am. J. Psychiatry. 1983; 140:11–20. [PubMed: 6336637]
- Akiskal, HS. Mood disturbances. In: Winokur, G.; Clayton, P., editors. The Medical Basis of Psychiatry. Saunders Co; Philadelphia: 1986.
- Akiskal HS. Searching for behavioral indicators of bipolar II in patients presenting with major depressive episodes: the `red sign', the `rule of three' and other biographic signs of temperamental extravagance, activation and hypomania. J. Affect. Disord. 2005; 84:279–290. [PubMed: 15708427]
- Akiskal HS, Djenderedjian AM, Rosenthal RH, Khani MK. Cyclothymic disorder: validating criteria for inclusion in the bipolar affective group. Am. J. Psychiatry. 1977; 134:1227–1233. [PubMed: 910973]
- Akiskal HS, Placidi GF, Maremmani I, Signoretta S, Liguori A, Gervasi R, Mallya G, Puzantian VR. TEMPS-I: delineating the most discriminant traits of the cyclothymic, depressive, hyperthymic and irritable temperaments in a nonpatient population. J. Affect. Disord. 1998; 51:7–19. [PubMed: 9879799]
- Akiskal HS, Kilzieh N, Maser JD, Clayton PJ, Schettler PJ, Traci Shea M, Endicott J, Scheftner W, Hirschfeld RM, Keller MB. The distinct temperament profiles of bipolar I, bipolar II and unipolar patients. J. Affect. Disord. 2006; 92:19–33. [PubMed: 16635528]
- Angst J, Adolfsson R, Benazzi F, Gamma A, Hantouche E, Meyer TD, Skeppar P, Vieta E, Scott J. The HCL-32: towards a self-assessment tool for hypomanic symptoms in outpatients. J. Affect. Disord. 2005; 88:217–233. [PubMed: 16125784]
- Balestrieri M, Rucci P, Sbrana A, Rafani L, Benvenuti A, Gonnelli C, Dell'Osso L, Cassano GB. Lifetime rhythmicity and mania as correlates of suicidal ideation and attempts in mood disorders. Compr. Psychiatry. 2006; 47:334–341. [PubMed: 16905394]
- Benazzi F. Psychomotor changes in melancholic and atypical depression: unipolar and bipolar-II subtypes. Psychiatry Res. 2002; 112:211–220. [PubMed: 12450630]
- Benazzi F. Factor structure of recalled DSM-IV hypomanic symptoms of bipolar II disorder. Compr. Psychiatry. 2004; 45:441–446. [PubMed: 15526254]
- Berk M, Malhi GS, Cahill C, Carman AC, Hadzi-Pavlovic D, Hawkins MT, Tohen M, Mitchell PB. The Bipolar Depression Rating Scale (BDRS): its development, validation and utility. Bipolar Disord. 2007; 9:571–579. [PubMed: 17845271]

Bostwick JM, Pankratz VS. Affective disorders and suicide risk: a re-examination. Am. J. Psychiatry. 2000; 157:1925–1932. [PubMed: 11097952]

- Cassano GB, Castrogiovanni P, Conti L, Nardini AG. Depression as seen by nonpsychiatrist physicians. Compr. Psychiatry. 1976; 17:315–323. [PubMed: 1253593]
- Cassano GB, Akiskal HS, Musetti L, Perugi G, Soriani A, Mignani V. Psychopathology, temperament, and past course in primary major depressions. 2. Toward a redefinition of bipolarity with a new semistructured interview for depression. Psychopathology. 1989; 22(5):278–288. [PubMed: 2602525]
- Cassano, GB.; Savino, M. Chronic and residual major depressions. In: Akiskal, HS.; Cassano, GB., editors. Dysthymia and the Spectrum of Chronic Depression. The Guilford Press; NY: 1997. p. 54-65
- Cassano GB, Dell'Osso L, Frank E, Miniati M, Fagiolini A, Shear K, Pini S, Maser J. The bipolar spectrum: a clinical reality in search of diagnostic criteria and an assessment methodology. J. Affect. Disord. 1999; 54:319–328. [PubMed: 10467978]
- Cassano GB, Frank E, Miniati M, Rucci P, Fagiolini A, Pini S, Shear MK, Maser JD. Conceptual underpinnings and empirical support for the mood spectrum. Psychiatr. Clin. North Am. 2002; 25:699–712.
- Cassano GB, Rucci P, Frank E, Fagiolini A, Dell'Osso L, Shear MK, Kupfer DJ. The mood spectrum in unipolar and bipolar disorder: arguments for a unitary approach. Am. J. Psychiatry. 2004; 161:1264–1269. [PubMed: 15229060]
- Cassano GB, Mula M, Rucci P, Miniati M, Frank E, Kupfer DJ, Oppo A, Calugi S, Maggi L, Gibbons RD, Fagiolini A. The structure of lifetime manic-hypomanic spectrum. J. Affect. Disord. 2008; 112(1–3):59–70. [PubMed: 18541309]
- Cassidy F, Ahearn EP, Carroll BJ. Symptom profile consistency in recurrent manic episodes. Compr. Psychiatry. 2002; 43:179–181. [PubMed: 11994834]
- Chengappa KN, Levine J, Gershon S, Kupfer DJ, Boward MD. Lifetime prevalence of substance or alcohol abuse and dependence among subjects with bipolar I and II disorders in a voluntary registry. Bipolar Disord. 2000; 2:191–195. [PubMed: 11256686]
- Dell'Osso L, Armani A, Rucci P, Frank E, Fagiolini A, Corretti G, Shear MK, Grochocinski VJ, Maser JD, Endicott J, Cassano GB. Measuring mood spectrum: comparison of interview (SCI-MOODS) and self-report (MOODS-SR) instruments. Compr. Psychiatry. 2002; 43:69–73. [PubMed: 11788923]
- Fabrigar LR, Wegener DT, MacCallum RC, Strahan EJ. Evaluating the use of exploratory factor analysis in psychological research. Psychol. Methods. 1999; 4:272–299.
- Fagiolini A, Dell'Osso L, Pini S, Armani A, Bouanani S, Rucci P, et al. Validity and reliability of a new instrument for assessing mood symptomatology: the Structured Clinical Interview for Mood Spectrum (SCI-MOODS). Int. J. Methods Psychiatr. Res. 1999; 8:71–82.
- Fava GA. Subclinical symptoms in mood disorders: pathophysiological and therapeutic implications. Psychol Med. 1999; 29:47–61. [PubMed: 10077293]
- Frank E, Carpenter LL, Kupfer DJ. Sex differences in recurrent depression: are there any that are significant? Am. J. Psychiatry. 1988; 145(1):41–45. [PubMed: 3337291]
- Frank E, Cassano GB, Rucci P, Fagiolini A, Maggi L, Kraemer HC, Kupfer DJ, Pollock B, Bies R, Nimgaonkar V, Pilkonis P, Shear MK, Grochocinski VJ, Scocco P, Buttenfield J, Forgione RN. Addressing the challenges of a cross-national investigation: lessons from the Pittsburgh-Pisa study of treatment-relevant phenotypes of unipolar depression. Clin. Trials. 2008; 5(3):253–261. [PubMed: 18559415]
- Gibbons RD, Clark DC, Kupfer DJ. Exactly what does the Hamilton Depression Rating Scale measure? J. Psychiatr. Res. 1993; 27:259–273. [PubMed: 8295158]
- Gibbons RD, Bock RD, Hedeker D, Weiss D, Bhaumik DK, Kupfer D, Frank E, Grochocinski V, Stover A. Full-information item bi-factor analysis of graded response data. Appl. Psychol. Meas. 2007; 31:4–19.
- Goes, FS.; Sadler, B.; Toolan, J.; Zamoiski, RD.; Mondimore, FM.; Mackinnon, DF.; Schweizer, B.; Bipolar Disorder Phenome Group. Psychotic features in bipolar and unipolar depression. Raymond DepauloJr, J., Jr.; Potash, JB., editors. Vol. 9. Bipolar Disord.; 2007. p. 901-906.

Hantouche EG, Angst J, Akiskal HS. Factor structure of hypomania: interrelationships with cyclothymia and the soft bipolar spectrum. J. Affect. Disord. 2003; 73:39–47. [PubMed: 12507736]

- Helm HW Jr. Boward MD. Factor structure of the Beck Depression Inventory in a university sample. Psychol. Rep. 2003; 92:53–61. [PubMed: 12674257]
- Hendrickson AE, White PO. Promax: a quick method for rotation to orthogonal oblique structure. Br. J. Stat. Psychol. 1964; 17:65–70.
- Iga J, Ueno S, Yamauchi K, Numata S, Tayoshi-Shibuya S, Kinouchi S, Nakataki M, Song H, Hokoishi K, Tanabe H, Sano A, Ohmori T. The Val66Met polymorphism of the brain-derived neurotrophic factor gene is associated with psychotic feature and suicidal behavior in Japanese major depressive patients. Am. J. Med. Genet. B Neuropsychiatr. Genet. 2007; 144:1003–1006. [PubMed: 17510948]
- Judd LL, Akiskal HS, Paulus M. The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. J. Affect. Disord. 1997; 45:5–18.
 [PubMed: 9268771]
- Kaiser HF. The varimax criterion for analytic rotation in factor analysis. Psychometrica. 1958; 85:187–200.
- Keitner GI, Ryan CE, Solomon DA. Realistic expectations and a disease management model for depressed patients with persistent symptoms. J. Clin. Psychiatry Sep. 2006; 67:1412–1421.
- Kennedy SH, Giacobbe P. Treatment resistant depression-advances in somatic therapies. Ann. Clin. Psychiatry. 2007; 19:279–287. [PubMed: 18058285]
- Keogh E, Reidy J. Exploring the factor structure of the Mood and Anxiety Symptom Questionnaire (MASQ). J. Pers. Assess. 2000; 74:106–125. [PubMed: 10779936]
- Klein DF. Endogenomorphic depression. A conceptual and terminological revision. Arch. Gen. Psychiatry. Oct.1974 31(4):447–454. Amer. Psych. Assoc., 1980. DSM-III: Diagnostic and Statistical Manual of Mental Disorders, 3rd edn. APA,, Washington, DC. [PubMed: 4420562]
- Koukopoulos A, Albert MJ, Sani G, Koukopoulos AE, Girardi P. Mixed depressive states: nosologic and therapeutic issues. Int. Rev. Psychiatry. 2005; 17:21–37.
- Kraepelin, E. Clinical Psychiatry: a Text Book for Students and Physicians. The Macmillan Co.; New York: 1904.
- Kraepelin, E. Psychiatrie. Band 3. Johann Ambrosius Barth; Leipzig: 1923.
- Leventhal AM, Chasson GS, Tapia E, Miller EK, Pettit JW. Measuring hedonic capacity in depression: a psychometric analysis of three anhedonia scales. J. Clin. Psychol. 2006; 62:1545–1558. [PubMed: 17019674]
- Linden, WJ.; Hambleton, RK., editors. Handbook of modern item response theory. Springer-Verlag; New York, NY: 1997.
- Loas G, Boyer P. Anhedonia in endogenomorphic depression. Psych. Res. 1996; 60:57–65.
- Maj M, Pirozzi R, Maliano L, Fiorillo A, Batoli L. Phenomenology and prognostic significance of delusions in major depressive disorder: a 10-year prospective follow-up study. J. Clin. Psychiatry. 2007; 68:1411–1417. [PubMed: 17915981]
- Marcos T, Salamero M. Factor study of the Hamilton Rating Scale for Depression and the Beck Melancholia Scale. Acta Psychiatr. Scand. 1990; 82:178–181. [PubMed: 2239363]
- Mowbray RM. The Hamilton Rating Scale for depression: a factor analysis. Psychol. Med. 1972; 2:272–280. [PubMed: 5079190]
- Mula M, Pini S, Monteleone P, Iazzetta P, Preve M, Tortorella A, Amato E, Di Paolo L, Rucci P, Cassano GB, Maj M. Different temperament and character dimensions correlate with panic disorder comorbidity in bipolar disorder and unipolar depression. J. Anxiety Disord. Feb 29.2008 [Electronic publication ahead of print].
- O'Brien KP, Glaudin V. Factorial structure and factor reliability of the Hamilton Rating Scale for Depression. Acta Psychiatr. Scand. 1988; 78:113–120. [PubMed: 3223312]
- Parker G. Classifying depression: should paradigms lost be regained? Am. J. Psychiatry. 2000; 157:1195–1203. [PubMed: 10910777]

Parker, G.; Hadzi-Pavlovic, D. Melancholia: A Disorder of Movement and Mood. Cambridge University Press; New York: 1996.

- Picardi A, Battisti F, De Girolamo G, Morosini P, Norcio B, Bracco R, Biondi M. Symptom structure of acute mania: a factor study of the 24-item Brief Psychiatric Rating Scale in a national sample of patients hospitalized for a manic episode. J. Affect. Disord. 2008; 108:183–189. [PubMed: 18029028]
- Placidi GF, Signoretta S, Liguori A, Gervasi R, Maremmani I, Akiskal HS. The semi-structured affective temperament interview (TEMPS-I). Reliability and psychometric properties in 1010 14-26-year old students. J. Affect. Disord. 1998; 47:1–10. [PubMed: 9476738]
- Romera I, Delgado-Cohen H, Perez T, Caballero L, Gilaberte I. Factor analysis of the Zung self-Rating depression scale in patients with major depressive disorder in primary care. BMC Psych. 2008; 8:4
- Rondon C, Romero JJ, Lopez S, Antunez C, Martin-Casanez E, Torres MJ, Mayorga C, R-Pena R, Blanca M. Local IgE production and positive nasal provocation test in patients with persistent nonallergic rhinitis. J. Allergy Clin. Immunol. 2007; 119:899–905. [PubMed: 17337294]
- Rush AJ, Weissenburger JE. Melancholic symptom features and DSM-IV. Am. J. Psychiatry. 1994; 151:489–498. [PubMed: 8147445]
- Rush AJ. The varied clinical presentations of major depressive disorder. J. Clin. Psychiatry. 2007; 68:4–10. [PubMed: 17640152]
- Sbrana A, Dell'Osso L, Benvenuti A, Rucci P, Cassano P, Banti S, Gonnelli C, Doria MR, Ravani L, Spagnolli S, Rossi L, Raimondi F, Catena M, Endicott J, Frank E, Kupfer DJ, Cassano GB. The psychotic spectrum: validity and reliability of the Structured Clinical Interview for the Psychotic Spectrum. Schizophr. Res. 2005; 75:375–387. [PubMed: 15885528]
- Schrader GD. Does anhedonia correlate with depression severity in chronic depression? Compr. Psychiatry. 1997; 38:260–263.
- Schrijvers D, Hulstijn W, Sabbe BG. Psychomotor symptoms in depression: a diagnostic, pathophysiological and therapeutic tool. J. Affect. Disord. 2007; 109(2008):1–20. [PubMed: 18082896]
- Shafer AB. Meta-analysis of the factor structures of four depression questionnaires: Beck, CES-D, Hamilton and Zung. J. Clin. Psychol. 2006; 62:123–146. [PubMed: 16287149]
- Sullivan PF, Kessler RC, Kendler KS. Latent class analysis of lifetime depressive symptoms in the national comorbidity survey. Am. J. Psychiatry. 1998; 155:1398–1406. [PubMed: 9766772]
- Suzuki A, Aoshima T, Fukasawa T, Yoshida K, Higuchi H, Shimizu T, Otani K. A three-factor model of the MADRS in major depressive disorder. Depress Anxiety. 2005; 21:95–97. [PubMed: 15884092]
- Vanheule S, Desmet M, Groenvynck H, Rosseel Y, Fontaine J. The Factor Structure of the Beck Depression Inventory II: An Evaluation. Assessment. Jan 8.2008
- Young MA, Scheftner WA, Fawcett J, Klerman GL. Gender differences in the clinical features of unipolar major depressive disorder. J. Nerv. Ment. Dis. 1990; 178(3):200–203. [PubMed: 2307973]
- Ward LC. Comparison of factor structure models for the Beck Depression Inventory-II. Psychol. Assess. Mar. 2006; 18:81–88.
- Whisman MA, Perez JE, Ramel W. Factor structure of the Beck Depression Inventory-Second Edition (BDI-II) in a student sample. J. Clin. Psychol. 2000; 56:545–551. [PubMed: 10775046]
- Widmer F, Hayes PJ, Whittaker RG, Kumar RK. Substrate preference profiles of proteases released by allergenic pollens. Clin. Exp. Allergy. 2000; 30:571–576. [PubMed: 10718856]
- Winokur G, Turvey C, Akiskal H, Coryell W, Solomon D, Leon A, Mueller T, Endicott J, Maser J, Keller M. Alcoholism and drug abuse in three groups-bipolar I, unipolars and their acquaintances. J. Affect. Disord. 1998; 50:81–89. [PubMed: 9858067]
- Witte TK, Joiner TE Jr. Brown GK, Beck AT, Beckman A, Duberstein P, Conwell Y. Factors of suicide ideation and their relation to clinical and other indicators in older adults. J. Affect. Disord. 2006; 94:165–172. [PubMed: 16740318]

Wood JG, Joyce PR, Miller AL, Mulder RT, Kennedy MA. A polymorphism in the dopamine beta-hydroxylase gene is associated with "paranoid ideation" in patients with major depression. Biol. Psychiatry. 2002; 51:365–369. [PubMed: 11904130]

Studies	N	% F	Age, mean (SD)	Diagnostic interview
Study 1	41	68.3%	48.5 (13.0)	SCID
Study 2	101	100%	30.3 (6.0)	MINI
Study 3	350	69.2%	39.2 (12.2)	SCID
Study 4	87	69.0%	41.9 (11.7)	SCID

Table 2
Frequency of endorsement of items (bolded items reflecting DSM-IV criteria for a depressive episode).

Item	Item endorsemen
93. you felt guilty or remorseful	0.823
10. persistently sad or empty, blue or down in the dumps?	0.809
82. preoccupied with yourself and your own problems, thoughts and feelings	0.805
4. serious, introverted or gloomy	0.797
3. lonely	0.786
83. very vulnerable	0.772
84. disappointed in yourself	0.765
58. difficulty starting to do anything	0.752
2. nostalgic	0.751
13. purposeless, as if everything had lost its significance	0.749
21. lost pleasure in your social life	0.741
25. lost interest in hobbies or sport	0.741
63. trouble getting out of bed in the morning	0.740
1. frustrated and defeated	0.731
7. the littlest thing could make you sad?	0.725
99. gloomy future	0.725
11. crying very easily	0.724
139. repeatedly difficulty falling sleep	0.717
9. you found it unusually hard to take rejections, particularly those involving friendships or romantic relationships?	0.716
62. passive, sluggish	0.715
27. lost interest or pleasure in all or almost all the things you usually enjoyed	0.710
22. difficulty making new friends	0.704
8. lost your capacity to laugh, have fun, enjoy your life?	0.701
140. repeatedly wake up in the middle of the night and had difficulty falling sleep	0.701
65. fatigued weak, or tired for the smallest task	0.687
100. wishing to run away from your current life	0.682
6. deeply annoyed	0.672
101. using sleep as an escape	0.671
91. trouble thinking or concentrating	0.670
5. bored	0.669
138. you felt sleepy all the time	0.662
23. lost interest in your romantic life	0.643
141. repeatedly wake up much earlier	0.642
92. mentally dull or confused?	0.633
14. lost interest in how you looked	0.629
142. need much more sleep	0.617
90. difficulty making even minor decisions	0.615
88. problems with your memory	0.613
89. your housework/performance deteriorated	0.608

Cassano et al.

19. depressed when stopping any of these substances

17. depressed when taking medications

98. heard voices clearly

97. heard voices

Item Item endorsement 61. time as passing very slowly, hanging heavy 0.599 0.592 15. nothing you put on looked or felt right 59, physically "slowed down" 0.581 0.581 154. less sexually active 64, difficulty take to care yourself 0.576 0.575 155. difficulty becoming sexually aroused 102. life was not worth living 0.567 60. speech or thinking seemed slowed down 0.513 12. constantly complaining 0.510 0.508 151. craving sweets or carbohydrates 0.495 152. appetite/weight increased 132. difficult to work in the early morning 0.486 81. hypercritical or skeptical 0.461 26. indifferent about everything that happened to you or your family 0.456 0.454 104. want to die or hurt yourself 0.450 153. appetite/weight decrease 95 you felt surrounded by hostility, as if everybody was against you 0.448 103. wishing not to wake up in the morning 0.447 150. no food that appealed 0.416 0.380 66. difficulty to sit still or lie down 94.others were causing all of your problems 0.355 0.353 16. depressed during physical illnesses 96. everyone was talking about you 0.345 87. need to take refuge in religion or prayer? 0.337 105. specific plan to hurt or kill yourself 0.328 0.283 86. very preoccupied with money 0.282 85. body transformed 107. suicide attempt requiring medical attention 0.272 20. became depressed as a result of using alcohol, sleeping pills, anti-anxiety drugs, nicotine, caffeine, stimulants or 0.188 similar substances even though you took them in order to feel better 0.182 106. suicide attempt 18. depressed when drinking lots of alcohol or using substances 0.165

Page 19

0.133

0.113 0.090

0.063

Page 20

Table 3

Factor loadings derived from a 6-factor solution with varimax rotation (bolded items reflecting DSM-IV criteria for a depressive episode, and bolded italicized items reflecting those with a factor loading <0.40 in absolute value).

ITEM	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness-related depression	Psychotic features	Neurovegetative symptoms
10. persistently sad or empty, blue or down in the dumps	0.713	0.281	860.0	-0.075	0.089	0.023
4. serious, introverted or gloomy	0.707	0.137	0.146	-0.142	0.159	0.165
25. lost interest in hobbies or sport	0.701	0.264	0.104	-0.175	0.054	0.201
13. purposeless, as if everything had lost its significance	0.690	0.332	0.209	-0.152	0.041	0.028
3. lonely	0.663	0.171	0.087	0.100	0.147	0.203
6. deeply annoyed	0.624	0.149	0.053	-0.131	0.137	0.200
22. difficulty making new friends	0.624	0.166	0.141	-0.125	-0.001	0.236
7. the littlest thing could make you sad?	0.589	0.214	0.135	-0.068	0.243	0.174
8. lost your capacity to laugh, have fun, enjoy your life?	0.586	0.203	0.343	-0.179	0.158	-0.076
21. lost pleasure in your social life	0.583	0.310	0.229	-0.112	-0.011	0.290
27. lost interest or pleasure in all or almost all the things you usually enjoyed	0.573	0.399	0.281	-0.138	0.050	0.099
5. bored	0.572	0.134	0.108	-0.190	0.147	0.213
12. constantly complaining	0.567	0.118	-0.175	-0.185	0.310	0.028
15. nothing you put on looked or felt right	0.561	0.237	-0.033	-0.113	960.0	0900
26. indifferent about everything that happened to you or your family	0.557	0.260	0.007	-0.110	-0.057	0.192
1. frustrated and defeated	0.550	0.211	0.092	0.093	0.270	0.129
11. crying very easily	0.536	0.085	0.128	-0.136	0.114	-0.010
23. lost interest in your romantic life	0.510	0.197	0.125	-0.157	-0.057	0.247
9, you found it unusually hard to take rejections, particularly those involving friendships or romantic relationships?	0.479	0.144	0.046	-0.081	0.321	0.154
14. lost interest in how you looked	0.462	0.332	0.219	-0.169	-0.013	-0.038
2. nostalgic	0.457	0.082	0.117	0.080	0.223	0.062
84. disappointed in yourself	0.447	0.409	0.304	0.018	0.322	0.275
81. hypercritical or skeptical	0.316	0.145	0.090	0.122	0.294	0.205
59. physically "slowed down"	0.101	0.725	-0.040	-0.281	0.232	-0.062

ITEM	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness-related depression	Psychotic features	Neurovegetative symptoms
62. passive, sluggish	0.325	0.718	0.068	0.055	0.089	0.102
58. difficulty starting to do anything	0.275	0.717	-0.042	-0.095	0.083	0.138
60. speech or thinking seemed slowed down	0.250	0.688	0.015	-0.131	0.047	0.074
65. fatigued weak, or tired for the smallest task	0.288	0.679	0.211	-0.125	0.186	0.1111
63. trouble getting out of bed in the morning	0.190	0.630	0.183	0.087	0.022	0.236
89. your housework/performance deteriorated	0.241	0.612	0.162	0.001	0.125	0.229
61. time as passing very slowly, hanging heavy	0.217	0.594	0.083	-0.106	0.233	-0.006
64, difficulty take to care yourself	0.312	0.576	0.180	-0.053	0.048	0.079
90. difficulty making even minor decisions	0.334	0.574	0.039	-0.009	0.406	0.109
132. difficult to work in the early morning	0.180	0.524	0.113	-0.009	0.035	0.221
92. mentally dull or confused	0.163	0.505	0.147	-0.217	0.312	0.205
91. trouble thinking or concentrating	0.156	0.482	0.070	-0.117	0.431	0.220
101. using sleep as an escape	0.274	0.466	0.226	0.057	0.157	0.290
88. problems with your memory	0.169	0.393	0.089	-0.087	0.241	0.256
99. gloomy future	0.304	0.381	0.289	0.053	0.298	0.367
66. difficulty to sit still or lie down	0.054	0.322	-0.005	-0.043	0.322	0.152
106. suicide attempt	0.101	0.048	0.865	-0.004	0.107	-0.025
104, want to die or hurt yourself	0.276	0.177	0.783	-0.031	0.239	0.167
105. specific plan to hurt or kill yourself	0.207	0.092	0.756	0.035	0.132	0.029
107. suicide attempt requiring medical attention	0.134	0.100	0.730	-0.102	0.143	900.0-
103. wishing not to wake up in the morning	0.220	0.251	0.645	0.018	0.250	0.294
102. life was not worth living	0.360	0.320	0.578	-0.023	0.151	0.250
19. depressed when stopping any of these substances	0.235	0.098	0.039	-0.687	0.082	0.120
18. depressed when drinking lots of alcohol or using substances	0.330	-0.017	0.120	-0.635	-0.043	0.230
20. became depressed as a result of using alcohol, sleeping pills, anti-anxiety drugs, nicotine, caffeine, stimulants or similar substances even though you took them in order to feel better	0.210	0.089	0.164	-0.597	-0.015	0.182

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

ITEM	Depressive mood	Psychomotor retardation	Suicidality	Drug/illness-related depression	Psychotic features	Neurovegetative symptoms
17. depressed when taking medications	0.223	0.067	-0.216	-0.577	0.059	0.130
16. depressed during physical illnesses	0.237	0.117	-0.162	-0.466	0.095	0.040
95 you felt surrounded by hostility, as if everybody was against you	0.212	0.147	0.122	0.054	0.743	0.061
96. everyone was talking about you	0.204	0.142	0.064	-0.094	0.702	0.071
94.others were causing all of your problems	0.108	-0.007	0.065	0.031	0.610	-0.055
83. very vulnerable	0.233	0.373	0.211	0.085	0.568	0.133
97. heard voices	-0.190	0.118	0.243	-0.402	0.535	-0.190
93 you felt guilty or remorseful	0.218	0.246	0.237	0.085	0.523	0.309
85. body transformed	0.167	0.159	960.0	-0.196	0.386	-0.009
82. preoccupied with yourself and your own problems, thoughts and feelings	0.125	0.220	0.289	0.252	0.356	0.139
87. need to take refuge in religion or prayer	0.021	0.048	0.104	-0.081	0.348	0.137
98. heard voices clearly	-0.254	0.287	0.266	-0.466	0.299	-0.148
86. very preoccupied with money	0.229	0.151	0.092	-0.156	0.293	0.048
140. repeatedly wake up in the middle of the night and had difficulty falling sleep	-0.057	-0.061	0.018	-0.288	0.367	0.568
154. less sexually active	0.155	0.132	0.103	-0.166	0.028	0.524
155. difficulty becoming sexually aroused	0.156	0.210	-0.047	0.025	0.017	0.508
152. appetite/weight increased	0.213	0.192	0.126	-0.166	-0.003	0.500
153. appetite/weight decreased	0.299	0.155	090.0	0.031	-0.054	0.457
151. craving sweets or carbohydrates	0.279	0.123	-0.014	-0.037	0.082	0.453
139. repeated difficulty falling sleep	-0.011	0.090	-0.040	-0.108	0.379	0.446
141. repeatedly wake up much earlier	-0.032	-0.049	0.020	-0.254	0.303	0.442
142. need much more sleep	0.158	0.383	0.118	0.022	0.054	0.439
138. you felt sleepy all the time	0.184	0.390	0.045	0.036	0.178	0.434
150. no food that appealed	0.166	0.281	0.159	-0.177	0.015	0.305
100. wishing to run away from your current life	0.286	0.237	0.249	0.117	0.277	0.292