Published in final edited form as:
J Affect Disord. 2008 February ; 106(1-2): 83–89. doi:10.1016/j.jad.2007.05.024.

Assessment of Depressive Symptom Severity among Patients with Co-Occurring Bipolar Disorder and Substance Dependence

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Abstract

Background—We examined a modified version of the Hamilton Depression Rating Scale (HDRS) among treatment-seeking patients with co-occurring bipolar disorder and substance dependence in order to elucidate key features of depression in this specific population of patients.

Methods—Patients with current bipolar disorder and substance dependence who were prescribed mood stabilizers (n = 105) completed a 27-item version of the HDRS that was subjected to item and principal components analyses. Preliminary validity analysis consisted of comparing the derived total and component scores to the depressed mood indicators from the Addiction Severity Index (ASI).

Results—Eleven items representing two related components labeled “melancholia” and “anxiety” were retained. The 11-item HDRS total and component scores were higher for those who reported serious depression, serious anxiety, cognitive problems, and suicidal ideation on the ASI than for those who did not report these problems.

Limitations—We conducted the analyses with a relatively small sample of patients who were primarily white and were diagnosed with bipolar I disorder, thus limiting the generalizability of findings. Moreover, we obtained limited data regarding construct validity of the 11-item scale.

Conclusions—Our psychometric evaluation of the HDRS led us to retain 11 items representing primarily melancholic and neurovegetative symptoms of depression. These findings suggest that sample-specific item characteristics of the HDRS need to be evaluated prior to using this scale to assess depressive symptom severity among patients with complex diagnostic and treatment characteristics.

Keywords

depression; assessment; bipolar disorder; substance dependence

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Introduction

The Hamilton Depression Rating Scale (HDRS) has been used widely to assess depressive symptom severity since its development in the 1960s (Hamilton, 1960; 1967). Decades of research with the HDRS have resulted in many item modifications, and consequently have led to concerns about the scale's theoretical underpinnings, psychometric properties, and administration procedures. (e.g., Bagby et al., 2004; Ruhe et al., 2005; Santor and Coyne, 2001; Williams, 2001). Despite these concerns, various versions of the HDRS continue to be used in outcome-oriented investigations (e.g., Brown et al., 2006; Chengappa et al., 2000b; Gao and Calabrese, 2005; Nunes and Levin, 2004) that guide the development of pharmacotherapy and psychotherapy. This study aims to examine items that make up a modified version of the HDRS among treatment-seeking patients diagnosed with bipolar disorder and substance dependence.

Clinical and epidemiological studies consistently show that bipolar and substance use disorders co-occur at a high rate (Chengappa et al., 2000a; Grant et al., 2004; Sloan et al., 2000). To our knowledge there are no studies investigating how this combination of disorders may affect the reporting of specific HDRS depressive symptoms, even though examinations of depression among patients with bipolar disorder (Judd et al., 2002; Miller et al., 2004; Thase, 2005) and those with substance use disorders (Maremanni et al., 2006; Nunes and Levin, 2004; Sloan et al., 2000) show that manifestations of depressive symptoms in these specific populations differ from manifestations of depressive symptoms among patients with unipolar depression. Nonetheless, the HDRS total score has been used as one of the outcome measures in interventions conducted with patients diagnosed with bipolar and substance use disorders (e.g., Brown et al., 2006; Perugi et al., 2002; Salloum et al., 2005; Weiss et al., in press). Attention to depressive symptom assessment of this population is especially timely, since there is growing evidence showing that 1) the psychosocial impairments associated with bipolar depression are greater than are those associated with bipolar mania (Judd et al., 2002; Thase, 2005), 2) depressive symptoms are common among those in recovery from substance dependence (Hartka et al., 1991; Nunes & Levin, 2006), and 3) depressive symptoms pose a significant risk for relapse to substance use (Kolodziej & Weiss, 2000; Landheim et al., 2006).

Our goal then was to conduct a psychometric evaluation of a modified version of the HDRS among patients with co-occurring bipolar disorder and substance dependence who were participating in a study of outpatient group treatment for this combination of disorders (Weiss et al., in press), and who were prescribed mood stabilizers as one of the entry criteria into the study. The modified HDRS was comprised of 21 items originally developed by Hamilton (1960, 1967) as well as six additional items described below (see Methods). The psychometric evaluation of the HDRS included detailed item and principal components analyses, and comparison of derived total and component scores to the depressed mood indicators contained in the Addiction Severity Index (McLellan et al., 1992). Moreover, based on recent studies in this area, we examined the associations between days of substance use and HDRS scores.

Methods

Participants

Patients with current bipolar disorder and substance dependence were recruited for an outpatient group treatment study at a psychiatric hospital in the suburban Boston area. Each person gave written informed consent. Inclusion criteria were 1) diagnoses of bipolar disorder (any subtype) and substance dependence within the past year, established using the Structured Clinical Interview for DSM-IV, Research Version (SCID-IV; First et al., 1996), 2) substance use within 60 days prior to assessment, 3) ongoing pharmacotherapy with a mood stabilizer, and 4) permission to contact the treating psychopharmacologist. Exclusion criteria were 1)

presence of medical disorders or neurocognitive deficits that would preclude group study participation (e.g., traumatic brain injury), 2) severe psychotic symptoms defined by extensive hallucinations and/or delusions assessed via SCID-IV sections B and C, 3) residence in a setting in which substance use was controlled, and 4) danger to self or others. Participants who reported depressive symptoms on the first question of the HDRS were included in the current analyses (105 participants out of 163 recruited). The severity of participants' depressive symptoms during the week prior to the interview was categorized using the most commonly published version of the HDRS which is composed of the first 17 items.

The sample was made up of both men (n = 53, 50%) and women (n = 52 , 50%) with the mean age of 38 (SD = 10). The majority of participants were white (n = 96, 91%), unmarried (n = 73, 69%) and unemployed (n = 63, 60%). Approximately half of the participants had college or postgraduate education (n = 48, 46%). While most of the participants were diagnosed with bipolar disorder I (n = 79, 75%), some were diagnosed with bipolar disorder II (n = 19, 18%), and a minority were diagnosed with bipolar disorder NOS (n = 7, 7%). Sample mean for previous week's 17-item HDRS was 17 (SD=8) ("mild to moderate depression"). Ninety-five participants (90%) met DSM-IV criteria for at least one current (i.e., in the past 30 days) substance dependence: 72 participants (69%) had alcohol dependence, 23 (22%) had cocaine dependence, 22 (21%) had marijuana dependence, 15 (14%) had sedative/hypnotic/anxiolytic dependence, 8 (8%) had opioid dependence, four (4%) had amphetamine dependence, and one participant (1%) had polysubstance dependence. The remaining participants had substance dependence diagnoses in early remission, with substance use occurring in the 60 days prior to the assessment.

Measures

The current psychometric investigation of the HDRS is based on the administration of a 27-item version, which is comprised of the 21 items originally developed by Hamilton (1960; 1967) as well as six additional items (items 22 through 27). Items addressing helplessness (#22), hopelessness (#23), and worthlessness (#24) were added to the HDRS by Miller and colleagues (1985), who subsequently included these items in their study of the course of bipolar I disorder (Miller et al., 2004). Items addressing hypersomnia (#25), hyperphagia (#26), and weight gain (#27) have been added by many authors to investigate "reversed vegetative symptoms of depression" among various patient populations, including those with bipolar disorder (Chengappa et al., 2000b; Thase et al., 1992). All of the HDRS items are rated on a Likert scale ranging from 0 (not at all) to either 2, 3 or 4 (severe). The items and their maximum scores are listed in Table 1.

Validity analyses were conducted with participants' responses on relevant items from the Addiction Severity Index (ASI), Fifth Edition (McLellan et al., 1992). The ASI is a widely employed, empirically validated, structured interview designed to assess substance-related problems in five dimensions, including psychiatric problems. We used the ASI as one of the assessment tools in our longitudinal group studies (e.g., Weiss et al., 2007), and we extracted items from the "psychiatric problem" section of the ASI administered at baseline for this study's validity analyses. All of the items chosen for comparison to the HDRS are scored dichotomously (yes/no). Validity analyses were conducted with the following psychiatric problems occurring in the past 30 days: "serious depression," "serious anxiety or tension," cognitive problems defined by "trouble understanding, concentrating, or remembering," suicidal ideation defined by "serious thoughts of suicide," and any suicide attempts.

Procedures

A trained psychologist administered all of the SCID modules except module E, which inquires about substance use disorders. SCID Module E, the HDRS, and the ASI were administered by

a trained and supervised research assistant, who also administered other measures related to the treatment study. Following the original administration procedure guidelines provided by Hamilton (1960; 1967) and subsequently revised by Williams (1988), the full HDRS was administered only to participants who scored at least one on the first question concerning the experience of depressed mood. Assessment uncertainties were resolved during team meetings with the study's Principal Investigator (RDW).

Data Analysis

Data analyses were performed using SPSS for Windows, version 11 (SPSS, 2001). First, the 27-item version of the HDRS was subjected to a detailed item analysis, which consisted of examining each item's range of scores, mean (M), standard deviation (SD), and skew. According to Runyon and Haber (1984), the skew coefficient between plus or minus 0.50 indicates a non-significant deviation of normality, but values outside of this range show a more serious deviation. Alpha reliability coefficient was calculated for items that were retained for further analyses based on their satisfactory psychometric properties.

To determine whether the HDRS contained more than one dimension, the retained items were subjected to principal components analysis, with multiple correlation coefficients as communality estimates. The scree plot was examined to determine number of components to be extracted (Loehlin, 2004). A Promax rotation sequence was used because the components were expected to be correlated. Participants whose data were missing on individual questions (n=14) were incorporated into the analyses using mean values for these items and also removed from analyses altogether. These two different methods led to the same results; therefore, all the analyses are presented with missing item data incorporated into the analyses as the mean of the available item scores. Component scores were calculated by summing the items that loaded on each component. One-way analyses of variance (ANOVAs) were used to examine the HDRS total and component scores in relation to the dichotomous ASI variables.

Results

Item Analysis

Item characteristics consisting of each item's observed score range, mean (M), standard deviation (SD), and skew are presented in Table 1. Examination of these characteristics led to the retention of 13 items. Alpha reliability coefficient of the 13-item HDRS was .83.

Principal Components Analysis

Based on the examination of the scree plot, we decided to extract two components because a definite flattening of the slope was observed after the point representing the second component. These components, labeled melancholia (eigenvalue = 4.28) and anxiety (eigenvalue = 1.50), accounted for 44% of the total variance. Two items with weak component loadings were removed from further analyses: item 14 (loss of sexual desire) and item 18 (diurnal mood variation). Subsequently, the 11-item scale was subjected to principal components analysis with Promax rotation, which again resulted in the extraction of two components that explained 51% of the total variance: melancholia (eigenvalue = 4.20) and anxiety (eigenvalue = 1.46). The rotated component loadings of each item are presented in Table 2. The alpha reliability coefficient of the 11-item HDRS was .83 and the inter-component correlation was .37 showing that the components are related to each other.

Validity Comparisons

Table 3 shows HDRS total and component scores in relation to the following dichotomous ASI variables: serious depression, serious anxiety, cognitive problems, suicidal ideations, and

suicidal attempt. Participants with serious depression and those with suicidal ideations had higher HDRS total and melancholia component scores than those without serious depression or suicidal ideations. Participants with serious anxiety and those with cognitive problems had higher total HDRS scores as well as higher melancholia and anxiety component scores than those without serious anxiety or cognitive problems. There were no differences in HDRS scores between those who did and did not report a suicide attempt in the past month.

Discussion

The goal of this study was to conduct a psychometric evaluation of a modified HDRS administered to patients diagnosed with bipolar disorder and substance dependence who were seeking outpatient group treatment for this combination of disorders and who were prescribed mood stabilizers by their treating psychopharmacologists. Among the 27 items administered to individuals reporting depressive symptoms on the first question of the HDRS, 11 were chosen as the best depressive symptom indicators according to their conceptual and psychometric properties. Eight of these items, inquiring about depressed mood, guilt, early and middle insomnia, psychic and somatic anxiety, and energy loss, are from the original version of the HDRS (Hamilton, 1960; 1967). The remaining three items, addressing helplessness, hopelessness, and worthlessness, are derived from a modified version of the HDRS (Miller et al., 1985). The principal component analyses show that the 11-item scale is composed of two related dimensions which we labeled “melancholia” and “anxiety” on the basis of their item content.

The 11-item scale is distinguished by strong psychometric properties of individual items, but it is notable that 16 of the 27 items showed poor psychometric properties. For example, items representing the reversed vegetative symptoms of depression (e.g., hyperphagia, hypersomnia, and weight gain), which recently have been considered to be especially pertinent among patients with bipolar disorder (Thase, 2005) were eliminated because of poor item characteristics. Several items associated with somatic and neurovegatative symptoms (e.g., appetite decrease, hypochondriasis, and weight loss) also performed poorly, which is somewhat inconsistent with the common criticism that the HDRS is overly sensitive to these symptoms (e.g., Bagby et al., 2004; Ruhe et al., 2005). It is possible that the participants in this sample tended to attribute any physiologically-based experiences to their post-acute withdrawal symptoms stemming from recent substance use and/or to medication side effects rather than to depression per se (e.g., Gao and Calabrese, 2005; Maremmani et al., 2006; Perugi et al., 2002). Other sample characteristics, such as the study exclusion criterion of severe psychotic symptoms features are likely to have contributed to the relative low occurrence of symptoms associated with mood liability (e.g., agitation) and psychotic features (e.g., depersonalization and paranoid symptoms).

It is especially noteworthy that we removed the item related to suicidal ideation. The initial version of the manuscript had this item despite its poor psychometric item properties because a) suicidal ideation and behaviors are an important feature of depression, and b) it was expected that only a minority of participants would have a high score on this item. Nevertheless, we removed this item based on a compelling argument made by one of the anonymous reviewers as well as review of recent literature showing considerable fluctuations in the report of suicidal ideation among patients with bipolar disorder (Balazs et al., 2006; Valtonen et al., 2007). Removal of this item from our study was not associated with any significant changes in the factor analytic nor validity analyses.

The items that make up our study’s version of the HDRS overlap with depressive symptoms measured by other frequently administered scales of depression, including the 10-item Montgomery-Asberg Depression Scale (MADRS). The MADRS was developed specifically

to measure symptom changes in response to treatment (Montgomery and Asberg, 1979), and has been used in recent clinical studies conducted with patients diagnosed with bipolar disorder (Chengappa et al., 2000b; Williamson et al., 2006). The MADRS items are labeled apparent and reported sadness, tension, reduced sleep and appetite, concentration difficulties, lassitude, inability to feel, pessimistic and suicidal thoughts. The observed overlaps in item content between the MADRS and the 12-item HDRS suggest that the experience of depressive symptoms by our unique sample of patients diagnosed with the combination of bipolar disorder and substance dependence and prescribed mood stabilizers fits into a broader conceptual framework of the depression construct (cf. Iannuzo et al., 2006; Judd et al., 2002; Santor & Coyne, 2001).

The 11-item HDRS total and component scores were higher for those who reported serious depression, serious anxiety, cognitive problems, and suicidal ideation on the ASI than for those who did not report these problems. These results provide preliminary information about adequate construct validity of the 11-item scale. The paradoxical finding that suicide attempts in the past 30 days were not associated with higher scores on the 11-item HDRS is likely to be attributed to the very small number of persons who endorsed the suicide attempt item on the ASI.

Our results need to be interpreted in light of study limitations. Specifically, the degree to which our results generalize to other samples is limited by participant characteristics. In addition to the diagnostic features described above, it is important to note that this was a relatively small sample of participants who were mostly white, educated, and knowingly seeking treatment for both bipolar and substance use disorders. This last characteristic speaks to these patients' heightened awareness of these co-occurring diagnoses and may be one of the reasons why perceptions of worthlessness, helplessness, and hopelessness emerged as strong items in the psychometric examination of the HDRS. Another important limitation pertains to the fact that both the HDRS and the ASI were administered by the same person, whose ratings of symptoms on one scale may have biased the ratings on the other scale. While this limits broader interpretations of the finding showing strong associations between the HDRS and the ASI scores, it is important to keep in mind that the HDRS was administered first and that the interviewee chose the response categories (yes or no) on the ASI.

Despite these limitations, the results of this study have several useful clinical applications. For example, it is of interest that the mean scores of the frequently published 17-item version of the HDRS and our 11-item version were almost the same, yet the range of scores of the 11-item version was greater than that of the 17-item version. Moreover, the 11-item scale's maximum sample score of 33 was close to the scale maximum score of 37, whereas the highest score on the 17-item HDRS was 37 (with a maximum scale score of 52). This suggests that the 11-item version is more sensitive to depressive symptom fluctuations than the 17-item version when administered to patients with bipolar disorder and substance dependence who are prescribed mood stabilizers. Moreover, the items that showed strong psychometric properties in both item and principal components analyses were helplessness, hopelessness, and worthlessness. Although these items are not included in the typically used 17-item scale, they represent cognitive, belief-related aspects of depression (Miller et al., 1985) that are emphasized as amenable to cognitive-behavioral interventions for both mood and substance use disorders (Beck et al., 1993). Thus, the 11-item scale may show promise for the assessment of mood changes in relation to psychotherapeutic interventions with this population of patients.

In conclusion, our psychometric evaluation of a modified HDRS administered to patients diagnosed with bipolar disorder and substance dependence led us to identify 11 items that appear to measure key aspects of depression. Our findings emphasize the importance of a thorough psychometric evaluation prior to proceeding to use the HDRS in particular, and

symptom rating scales in general, with patients whose responses are likely to be biased by the given study's characteristics, including its inclusion (e.g., medication use) and exclusion (e.g., severe psychotic symptoms) criteria.

Acknowledgements

This work was supported by grants DA15968, DA00326, and DA09400 from the National Institute on Drug Abuse.

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Table 1

Item Analysis of the 27-item HDRS

HDRS Item	N	Observed Score Range	Item Maximum Score	M	SD	Skew
1 depressed mood	105	3	4	2.2	.9	.2
2 guilt	105	4	4	1.7	1.0	-.2
3 suicide	105	4	4	1.0	1.2	1.0
4 early insomnia	105	2	2	.8	.9	.4
5 middle insomnia	105	2	2	.8	.9	.3
6 late insomnia	105	2	2	.6	.9	.8
7 activity decrease	105	4	4	1.8	1.2	-.1
8 retardation	105	3	4	.5	.7	1.3
9 agitation	105	3	4	.3	.6	2.5
10 psychic anxiety	105	3	3	1.6	.8	-.2
11 somatic anxiety	105	4	4	1.4	1.2	.2
12 appetite decrease	105	2	2	.7	.8	.6
13 energy loss	105	2	2	1.1	.8	-.2
14 sexual desire loss	93	2	2	.8	.8	.5
15 hypochondriasis	103	3	4	.5	.8	1.4
16 weight loss	105	2	2	.4	.7	1.5
17 insight decrease	105	2	2	.1	.3	5.7
18 diurnal mood variation	105	2	2	.9	.8	.2
19 depersonalization	105	4	4	.7	1.0	1.3
20 paranoid symptoms	105	3	3	.3	.6	2.1
21 ocd symptoms	105	2	2	.3	.6	1.8
22 helplessness	105	4	4	1.3	1.2	.5
23 hopelessness	105	4	4	1.6	1.2	-.1
24 worthlessness	105	4	4	1.6	1.2	0
25 hypersomnia	105	2	4	.5	.8	1.0
26 hyperphagia	105	2	2	.3	.7	1.8
27 weight gain	105	2	2	.4	.7	1.7

Note: Items in **bold** made up the initial version of the HDRS that was then subjected to principal components analysis.

Table 2

Rotated Component Loadings of the 11-Item HDRS.

Item	Component 1: Melancholia	Component 2: Anxiety
22 helplessness	**.78**	.34
7 activity decrease	**.76**	.32
23 hopelessness	**.76**	.14
1 depressed mood	**.73**	.16
24 worthlessness	**.72**	.28
13 energy loss	**.70**	.37
2 guilt	**.64**	.30
11 somatic anxiety	.12	**.72**
5 middle insomnia	.28	**.69**
10 psychic anxiety	.42	**.66**
4 early insomnia	.24	**.64**

Note: Components loadings shown in **bold** correspond to specific dimensions labeled “melancholia” and “anxiety.”

Table 3

11-Item HDRS Factor Scores in Relation to Selective ASI Variables.

ASI Variable	n	11-item HDRS		
		Total 16 (7)	Depression 11 (5)	Anxiety 5 (3)
Serious Depression				
Yes	77	17 (6)[a]	12 (5)[b]	5 (3)
No	28	13 (7)	9 (6)	4 (3)
Serious Anxiety				
yes	76	17 (7)[c]	12 (5)[d]	5 (3)[e]
No	29	13 (6)	10 (6)	3 (2)
Cognitive Problems				
yes	80	17 (7)[f]	12 (5)[g]	5 (3)[h]
No	25	12 (6)	9 (6)	3 (2)
Suicidal Ideations				
yes	44	18 (7)[i]	13 (6)[j]	5 (3)
No	61	14 (6)	10 (5)	4 (2)
Suicidal Attempt				
yes	12	18 (8)	12 (6)	6 (3)
No	93	16 (7)	11 (5)	5 (2)

Note: All the score means are accompanied by standard deviations in brackets, M (SD).

[a] $F(1, 103) = 6.85$, $p = .010$;

[b] $F(1, 103) = 8.66$, $p = .004$;

[c] $F(1, 103) = 9.28$, $p = .003$;

[d] $F(1, 103) = 4.03$, $p = .047$;

[e] $F(1, 103) = 14.85$, $p = .0001$;

[f] $F(1, 103) = 10.40$, $p = .002$;

[g] $F(1, 103) = 7.32$, $p = .008$;

[h] $F(1, 103) = 7.45$, $p = .007$;

[i] $F(1, 103) = 7.78$, $p = .006$;

[j] $F(1, 103) = 9.00$, $p = .003$.