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The structure of depressive symptoms and characteristics and their relation to overall severity in major depressive disorder

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ABSTRACT

Although many investigators have examined symptoms of major depressive disorder (MDD), the multivariate relations among these features of depression and their relative associations with overall severity of depression are not well understood. The present study is the first to examine the underlying factor structure of depression across a broad set of constructs and to model the multivariate association of these factors with the overall severity of depression. We conducted a large-scale factor analysis and multiple regression in a sample of participants diagnosed with MDD (N = 233) and healthy controls (N = 235). We obtained a five-factor solution composed of the following factors: (1) anxiety; (2) behavioral activation; (3) core symptoms; (4) rumination; and (5) emotional intensity. The *core symptoms factor*, composed primarily of DSM-5 diagnostic criteria for MDD, was the only factor that showed a consistent, significant association with overall severity of depression and functional impairment. Rumination combined with behavioral inhibition and positive and negative affect combined with each other to form coherent constructs that may be useful in examining differences among depressed individuals. These findings provide an important data-driven framework for the multidimensional symptom structure of depression and suggest several actionable ways for improving clinical assessment and treatment for individuals with MDD.

1. Introduction

Major depressive disorder (MDD) is the most burdensome disease and the leading cause of disability worldwide (WHO, 2008). Researchers have extensively studied the cardinal symptoms of MDD – sadness and anhedonia – as well as other psychological characteristics, such as rumination, behavioral inhibition, difficulty concentrating, blunted affect, and anxiety, in depressed individuals. Studies of depressive symptoms, however, have typically used small sample sizes and have each examined a limited number of depression-related characteristics; there are few comprehensive investigations that have integrated multiple features of MDD. The present study was designed to provide an integrative framework of depressive symptoms and characteristics by addressing three important issues that have not been well examined in the existing literature.

First, we designed this study to examine the underlying structure and multivariate relations among a broad set of key features of depression. Although investigators have studied specific symptoms of depression examined in isolation, we know little about the relations among these symptoms and their components. In several cases, when investigators have analyzed selected relations among symptoms, these symptoms have been shown to either conflate distinct characteristics into a single construct or artificially separate a unitary characteristic into multiple components. For example, many studies of depressive *rumination* have treated this construct as a unitary characteristic; recently, however, researchers have demonstrated that rumination is composed of a pathological *brooding* component and an adaptive *reflective pondering* (Treynor et al., 2003) or *intentional rumination* component (Whitmer and Gotlib, 2011). Similarly, investigations of the cardinal depressive symptom of *anhedonia* have demonstrated that this

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construct can be separated into *anticipatory* and *consummatory* components (Knutson et al., 2008; Pizzagalli et al., 2009; Treadway and Zald, 2011). Conversely, several studies indicate that *depression* and *anxiety*, which are currently regarded as co-morbid but separable constructs, may be better conceptualized as a single coherent characteristic (Watson et al., 2005; Oathes et al., 2015). These findings underscore the importance of examining systematically and comprehensively the multivariate relations among symptoms and characteristics of MDD.

Clinically, the current edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) requires the presence of five of nine symptoms of depression in order for an individual to meet criteria for a formal diagnosis of MDD. There is little empirical basis, however, for this formulation of nine symptoms or the required combination of five symptoms (Lilienfeld and Treadway, 2016; Hyman, 2010); moreover, the multivariate relations among these symptoms are poorly understood beyond the limited framework of melancholic, atypical, and psychotic subtypes (Baumeister et al., 2012; Foti et al., 2014). The present study was designed to examine the structure of MDD by conducting a factor analysis on a broad range of depression-related symptoms and constructs, thereby providing an empirically driven framework to organize a range of characteristics associated with MDD.

Second, this study examined the relative association of each of these empirically derived factors with the overall severity of MDD, operationalized as the sum of depression symptoms as well as the degree of impairment and subjective distress. Although severity of depression is often used as a primary outcome measure in clinical trials, the relative contribution of various depression-related characteristics to severity ratings is not well understood. Clinically, DSM-5 distinguishes among the cardinal symptoms (i.e., sadness and anhedonia), diagnostic symptoms (e.g., psychomotor retardation, excessive guilt, abnormal appetite), and other depression-related characteristics (e.g., rumination, behavioral inhibition); the empirical basis for making these distinctions, however, is not clear. Developing an evidence-based framework for understanding the relative importance of depression-related characteristics in tracking overall severity of depression will provide researchers and clinicians with important information that can be used in the assessment and treatment of depressed individuals.

Finally, this study compared the derived factor structures of individuals diagnosed with MDD and healthy controls. Typically, existing studies comparing depressed individuals with non-disordered controls examine group differences in the *magnitude* of scores on constructs of interest, rather than differences in underlying symptom *structures* or *networks* (e.g., Mandell et al., 2014; Kasch et al., 2002; Kumar et al., 2015;). Thus, it is not clear whether depressed and nondepressed individuals differ in the multivariate relations among measures of symptoms and characteristics of MDD (Guillion and Rush, 1998; Huang and Chen, 2015). Examining the multivariate structure of depressive characteristics will yield important information concerning underlying patterns of clinical symptoms of depression and more precise knowledge about specific differences between depressed and nondepressed individuals.

2. Methods

2.1. Overview

We conducted a factor analysis on data collected from a large sample of participants ($N = 468$) who completed a battery of self-report questionnaires and structured clinical interviews assessing depressive symptoms and related psychological constructs. After deriving the factor structure for participants diagnosed with MDD, we used multiple regression to examine the relative impact of each factor on overall severity of depression. Finally, we derived the factor structure separately for nondepressed participants and compared this factor structure with that obtained with depressed participants.

2.2. Participants

The sample assessed in this study consisted of age- and gender-matched adults diagnosed with MDD ($N = 233$) and healthy controls (HCs; $N = 235$) recruited from the local community between January 2006 and December 2015, who completed at least four of six questionnaires examined in this study. Participants who were excluded from analysis during the matching process did not differ significantly from included participants on any of the measures examined in this study, including the HAMD and the 15 self-report subscales (see "Measures" section), within either the MDD group (included: $N = 233$; excluded: $N = 5$; $p > 0.05$; FDR-corrected) or the HC group (included: $N = 235$; excluded: $N = 73$; $p > 0.05$; FDR-corrected).

Participants were administered the Structured Clinical Interview for DSM-IV (SCID-I; First et al., 2001) by trained interviewers and were included in the MDD group if they met DSM criteria for current MDD or in the HC group if they did not meet diagnostic criteria for any current or past DSM Axis I disorder. Individuals were excluded from further study if they reported either psychosis or symptoms of substance abuse in the last 6 months or a history of major head trauma. The Stanford University Institutional Review Board approved the studies that contributed data to the present sample, and all participants signed written informed consent.

2.3. Measures

We administered the SCID-I to all participants to establish psychiatric diagnoses as well as the Hamilton Depression Rating Scale (HAMD), the Global Assessment of Functioning (GAF), and an individual severity item from the SCID-I (SCID-Sev) to participants diagnosed with MDD to assess clinical severity. In addition, all participants completed six self-report questionnaires, which collectively include 15 subscales that assess a range of affective, cognitive, and behavioral characteristics associated with MDD. See Table 1 for a summary of these subscales and their abbreviations and eAppendix for a more detailed description of their composition and scoring.

2.4. Statistical analyses

2.4.1. Overview

We conducted a factor analysis followed by multiple regression to

Table 1
The 6 self-report scales and their 15 subscales included in the factor analysis. Subscales for which higher or lower scores reflect greater severity of depression-related characteristics are labeled as *direct* or *inverse* associations, respectively. .

Scale	Subscales	Abbreviation	Association with MDD
Beck Depression Inventory (BDI)	Cognitive	BDI-Cog	Positive
	Somatic-affective	BDI-SomAff	Positive
Beck Anxiety Inventory (BAI)	Subjective	BAI-Subj	Positive
	Neurophysiological	BAI-Phys	Positive
	Autonomic	BAI-Autonom	Positive
	Panic	BAI-Panic	Positive
Positive and Negative Affect Schedule (PANAS)	Positive affect	PAS	Negative
	Negative affect	NAS	Positive
Snaith-Hamilton Pleasure Scale (SHPS)	n/a	n/a	Negative
Ruminative Response Scale (RRS)	Brooding	RRS-Brood	Positive
	Reflective pondering	RRS-Pond	Positive
Behavioral Inhibition and Activation System Scales (BIS/BAS)	Sensitivity to punishment	BIS	Positive
	Sensitivity to reward	BAS-Rew	Negative
	Drive	BAS-Drive	Negative
	Fun-seeking	BAS-Fun	Negative

identify the factors that underlie symptoms and psychological characteristics of MDD and to elucidate the relations among these empirically derived constructs and their relative impact on overall symptom severity in MDD. Statistical analyses were conducted using SPSS-23's (IBM Corp., 2015) *factor analysis* and *multiple regression* functions as well as MATLAB 2015b's (The MathWorks, Inc., 2015) *PCA* routine and R's *lavaan* package.

2.4.2. Examining the factor structure of MDD

"We first conducted a factor analysis to examine the factor structure of these scales in the full sample of MDD participants (N = 233). Participants' scores on each of the 15 subscales (see Table 1) were included as observed variables. Factors with eigenvalues ≥1.00, which corresponds to the contribution from each observed variable to variance explained, were extracted from the correlation matrix using the principal components method, which also standardizes each observed variable to remove confounds from differences in scoring… The number of factors extracted based on the eigenvalue threshold of ≥1.00 was cross-checked with a visual inspection of the inflection point of the scree plot (Costello and Osborne, 2005; Fabrigar et al., 1999). Missing data for subscale scores were imputed from the relevant group mean, and missing data for individual items were imputed from the mean of the corresponding subscale for each participant.

2.4.3. Modeling relations between factors and overall severity of MDD

We computed factor scores for each participant using the obtained factor loadings and conducted a multiple regression of these five factor scores predicting severity of MDD, as measured by the HAMD. Because of the overlap in content between the HAMD and BDI, we conducted two additional analyses in which we regressed the five factor scores on SCID-Sev and GAF, which do not share content with the BDI and provide alternative ways of measuring overall severity of MDD. The resulting models provide estimates of overall fit, or the extent to which the overall factor solution explains variance in depressive severity; in addition, standardized coefficients for each factor can be used to compare the relative association of each obtained factor with depressive severity, while controlling for effects of the other included factors.

2.4.4. Comparison of factor structures of MDD vs HCs

We then modeled the factor structure of the measures for non-depressed participants (N = 235) separately, using the same procedures described above, and compared the resulting factor structure to that of depressed participants using Tucker's congruence coefficient (TCC; see eAppendix), which serves as a quantitative index of the overall similarity of factor structures observed for two groups (Lorenzo-Seva and Berge, 2006). In addition, we conducted a formal test of measurement (composition) invariance (Hirschfeld and Von Brachel, 2014; Vanderberg and Lance, 2000) to further quantify the overall difference in factor structures between MDD and HC participants.

3. Results

3.1. Participant characteristics

Demographic information for the MDD and HC participants and clinical information for the MDD participants are presented in Table 2. Descriptive statistics for each of the 15 included subscales and results of t-tests comparing participants with MDD and HCs are presented in Table 3. As expected, participants with MDD obtained scores indicating significantly ($p < 0.05$, FDR-corrected) more pathological functioning than did HC participants on each of the 15 subscales.

3.2. Factor structure of MDD

The EFA conducted on the 233 participants diagnosed with MDD yielded a five-factor solution (see Fig. 1) that explained 66.82% of the total variance across the 15 subscales (see Fig. 2). Based on their subscale composition, we labeled these factors *anxiety, behavioral activation, core symptoms, rumination*, and *emotional intensity*. These five factors each had an eigenvalue ≥1.00 (see Table 4) and corresponded to a nearby inflection point in the resulting scree plot (see Fig. 3), which supports the choice of this five-factor model as the optimal solution.

Table 2
Demographic and Clinical Information for MDD (N = 233) and HC Participants (N = 235) and T-Test Results.

	MDD Participants	HC Participants	p-value[a]
Sample Size	233	235	n/a
Age[b] (in years)	39.72 (11.65)	38.48 (11.45)	0.25
Gender (female)	0.69	0.68	0.89
HAMD[b]	25.81 (10.05)	n/a	n/a
Duration of current MDE[b] (years)	1.93 (4.21)	n/a	n/a
Number of lifetime MDEs[b]	6.83 (9.62)	n/a	n/a
Age at first onset of MDD[b] (years)	20.80 (12.53)	n/a	n/a
Comorbidity[c,d]	125 (0.54)	n/a	n/a
Dysthymia	24 (0.10)		
GAD	16 (0.07)		
PTSD	20 (0.09)		
OCD	7 (0.03)		
Panic	14 (0.06)		
Agoraphobia	5 (0.02)		
Specific Phobia	33 (0.14)		
Social Phobia	12 (0.05)		
Anorexia	1 (0.00)		
Bulimia	2 (0.01)		
Binge Eating	15 (0.06)		

Abbreviations: MDD: major depressive disorder; HC: healthy control; MDE: major depressive episode.

[a] Uncorrected values listed here; statistical significance determined with FDR-correction.

[b] These statistics are reported as *mean (standard deviation)*.

[c] These statistics are reported as *raw number (proportion)*.

[d] Comorbid diagnosis of any other DSM-IV Axis I disorder.

Table 3
Descriptive Statistics and T-Test Results for 15 Depression-Related Subscales .

	MDD Participants		HC Participants		T-Test	
	Mean	St Dev	Mean	St Dev	t-stat	p-value[a]
BDI-Cog	8.91	4.04	0.52	1.37	29.98	< 0.001*
BDI-SomAff	13.19	5.24	1.00	1.68	33.79	< 0.001*
BAI-Subj	13.23	4.76	6.96	2.39	13.34	< 0.001*
BAI-Phys	10.92	4.12	7.32	1.32	9.80	< 0.001*
BAI-Autonom	7.54	2.77	4.72	1.32	10.51	< 0.001*
BAI-Panic	5.89	2.46	4.19	0.82	7.70	< 0.001*
PAS	21.57	5.87	25.02	5.40	−6.60	< 0.001*
NAS	20.68	6.88	19.36	4.79	2.38	= 0.018*
SHPS	49.14	9.54	63.36	5.73	−19.41	< 0.001*
RRS-Brood	13.07	3.00	8.14	2.38	19.70	< 0.001*
RRS-Pond	11.39	2.47	8.52	2.40	12.75	< 0.001*
BIS	23.83	3.51	19.31	3.62	13.68	< 0.001*
BAS-Rew	16.18	2.54	17.33	2.03	−5.38	< 0.001*
BAS-Drive	9.70	2.57	11.67	2.07	−9.09	< 0.001*
BAS-Fun	10.64	2.49	12.15	2.17	−7.00	< 0.001*

Abbreviations: MDD: major depressive disorder; HC: healthy control; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; PAS: Positive Affect Scale; NAS: Negative Affect Scale; SHPS: Snaith-Hamilton Pleasure Scale; RRS: Ruminative Response Scale; BIS: Behavioral Inhibition Scale; BAS: Behavioral Activation Scale; Cog: Cognitive Subscale; SomAff: Somatic-Affective Subscale; Subj: Subjective Subscale; Phys: Neurophysiological Subscale; Autonom: Autonomic Subscale; Brood: Brooding Subscale; Pond: Reflective Pondering Subscale; Rew: Reward Responsiveness Subscale.

[a] Uncorrected values listed here; statistical significance determined with FDR-correction.

* Indicates variable reached statistical significance ($p \leq 0.05$; FDR-corrected).

	Factor				
	1	2	3	4	5
	"Anxiety"	"Behavioral Activation"	"Core Symptoms"	"Rumination"	"Emotional Intensity"
Variance Explained	24.03%	16.78%	10.36%	8.56%	7.09%
Subscale					
BAI-Phys	0.85	0.05	0.01	0.08	-0.06
BAI-Panic	0.83	0.04	0.08	0.05	0.07
BAI-Subj	0.73	0.03	0.32	0.17	0.10
BAI-Autonom	0.71	-0.01	0.15	0.09	0.06
BAS-Fun	-0.09	0.83	-0.01	-0.03	0.01
BAS-Rew	0.09	0.82	-0.21	0.15	0.12
BAS-Drive	0.11	0.76	0.03	-0.19	0.06
BDI-SomAff	0.20	0.06	0.82	0.20	-0.04
BDI-Cog	0.19	0.00	0.81	0.21	0.09
SHPS	-0.07	0.35	-0.66	0.02	0.12
RRS-Brood	0.07	0.05	0.15	0.81	0.03
RRS-Pond	0.09	0.01	0.06	0.74	0.17
BIS	0.12	-0.12	0.10	0.57	-0.06
PAS	-0.04	0.27	-0.17	-0.06	0.84
NAS	0.17	-0.05	0.11	0.20	0.84

Fig. 1. The 5-factor solution and 15 subscale loadings for participants diagnosed with MDD. Factors are ordered by decreasing percent variance explained. Subscale loadings with an absolute value ≥ 0.40 are indicated in color and reflect a significant contribution to a given factor.
Abbreviations: MDD: major depressive disorder; BAI: Beck Anxiety Inventory; BAS: Behavioral Activation Scale; BDI: Beck Depression Inventory; SHPS: Snaith-Hamilton Pleasure Scale; RRS: Ruminative Response Scale; BIS: Behavioral Inhibition Scale; PAS: Positive Affect Scale; NAS: Negative Affect Scale; Phys: Neurophysiological Subscale; Subj: Subjective Subscale; Autonom: Autonomic Subscale; Rew: Reward Responsiveness Subscale; SomAff: Somatic-Affective Subscale; Cog: Cognitive Subscale; Brood: Brooding Subscale; Pond: Reflective Pondering Subscale.

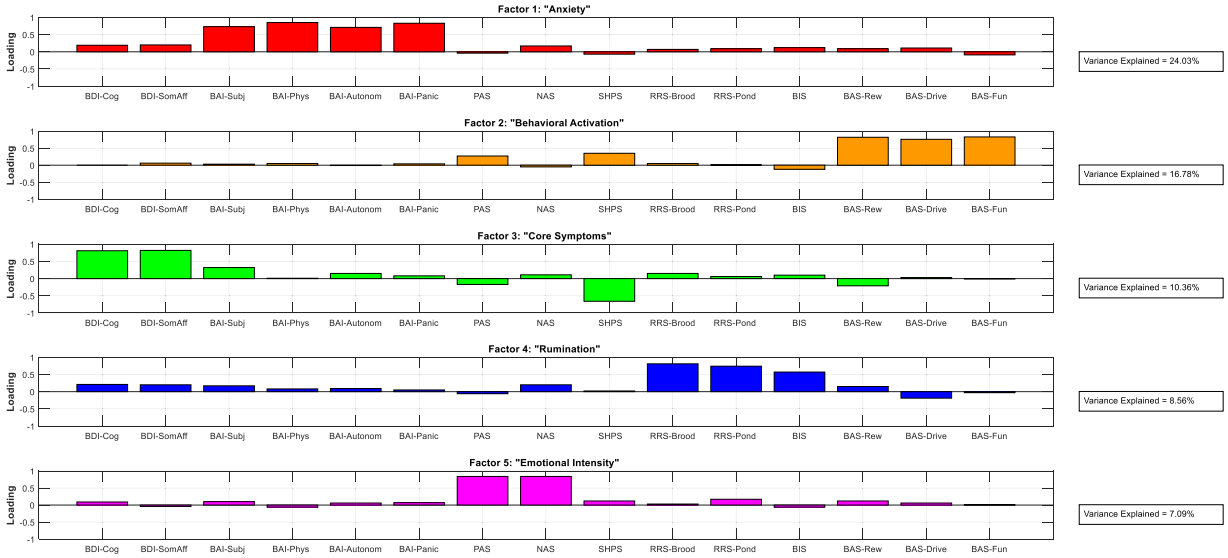

Fig. 2. The 5-factor solution and 15 subscale loadings for participants diagnosed with MDD. Factors are ordered by decreasing percent variance explained.
Abbreviations: MDD: major depressive disorder; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; PAS: Positive Affect Scale; NAS: Negative Affect Scale; SHPS: Snaith-Hamilton Pleasure Scale; RRS: Ruminative Response Scale; BIS: Behavioral Inhibition Scale; BAS: Behavioral Activation Scale; Cog: Cognitive Subscale; SomAff: Somatic-Affective Subscale; Subj: Subjective Subscale; Phys: Neurophysiological Subscale; Autonom: Autonomic Subscale; Brood: Brooding Subscale; Pond: Reflective Pondering Subscale; Rew: Reward Responsiveness Subscale.

3.3. Regression of derived factors with severity of MDD

We first conducted a multiple regression analysis that modeled the relations between each of these five factors and severity of depression, as measured by the HAMD. This model (see Table 5) yielded a statistically significant, moderate overall fit [$p < 0.001$; R^2-adjusted = 0.31; $F(5238) = 22.60$]. Three factors reached statistical significance in this analysis ($p < 0.05$): anxiety, core symptoms, and rumination. We also conducted two similar analyses in which we used the SCID-Sev (see eTable 1) and GAF (see eTable 2) as alternative measures of severity of depression. These two models yielded a statistically significant ($p < 0.05$) but modest overall fit (R^2-adjusted = 0.11 and 0.04,

Table 4
Total Variance Explained by Number of Factors for Participants Diagnosed with MDD (N = 233).

Factor	Initial Eigen-values	% Variance Explained	Cumulative%	Extracted & Rotated Eigen-values	% Variance Explained	Cumulative%
1	3.604	24.028	24.028	2.625	17.503	17.503
2	2.517	16.780	40.808	2.138	14.254	31.757
3	1.554	10.361	51.169	2.002	13.343	45.100
4	1.284	8.561	59.730	1.763	11.752	56.852
5	1.063	7.087	66.817	1.495	9.965	66.817
6	.925	6.166	72.983			
7	.768	5.121	78.104			
8	.596	3.972	82.076			
9	.536	3.570	85.646			
10	.489	3.259	88.905			
11	.426	2.843	91.748			
12	.387	2.579	94.327			
13	.331	2.207	96.534			
14	.305	2.033	98.568			
15	.215	1.432	100.000			

Abbreviations. MDD: major depressive disorder.

respectively), and both identified core symptoms as a statistically significant ($p < 0.05$) factor.

3.4. Comparison of factor structures of MDD vs HCs

Overall, participants diagnosed with MDD and HCs had qualitatively similar factor structures (see Figs. 1-2 and eFigs. 1-2); however, tests directly comparing the models revealed some statistically significant differences (TCC = 0.89; $\chi 2$ [160] = 298.19, $p < 0.001$). In particular, both groups are best characterized by a five-factor solution characterized by the same factor loading pattern ($\lambda \geq 0.40$) for a majority of variables (11/15) and equivalent loadings on factor 1 (TCC = 0.96). However, factors 2–5 showed some substantial between-group differences in the variables that reached the threshold for factor loading values ($\lambda \geq 0.40$). In participants with MDD, BIS loaded positively with RRS-Brood and RRS-Pond ($\lambda = 0.57$), and SHPS loaded negatively with BDI-SomAff and BDI-Cog ($\lambda = -0.66$); in contrast, in the HCs, BIS loaded negatively ($\lambda = -0.68$) with PAS and NAS, and SHPS loaded positively ($\lambda = 0.54$) with BAS-Fun, BAS-Rew, and BAS-Drive.

4. Discussion

The results of this study highlight the significance of five discrete factors in explaining variation in the symptomatology and characteristics of MDD. Our findings also indicate that these five factors have different relations with the overall severity of depression. Finally, our findings identify key differences between depressed participants and healthy controls in the magnitude and structure of these factors.

4.1. Factor structure of MDD

We obtained a five-factor solution for adults diagnosed with MDD, with the following factors: (1) anxiety; (2) behavioral activation; (3) core symptoms; (4) rumination; and (5) emotional intensity. This factor structure provides an empirically based framework of depression-related constructs that are individually measurable with a coherent set of subscales. The estimate of the amount of variance explained by each of these factors and the contribution of each subscale to individual factor scores described here can be used to help researchers systematically increase statistical power, decrease degrees of freedom, and better manage the advantages and disadvantages of various data reduction procedures.

Interestingly, the *anxiety factor* (factor 1), which includes neurophysiological, panic, subjective, and autonomic aspects of anxiety, appears to be largely independent of other depression-related constructs and explains nearly twice as much of the total variance (24.07%) as any other factor. In addition, separation of an anxiety factor from the remaining depression-related variables provides empirical validation and a data-driven method for distinguishing between depression and anxiety, despite their high levels of comorbidity (Blanco et al., 2014; Hasin et al., 2005; Kessler et al., 2005). In cases where depression and anxiety do co-occur, researchers have proposed an anxious subtype of depression (Baumeister and Parker, 2012). This formulation has important implications for prognosis and treatment: depressed individuals with high levels of anxiety have a more chronic course, greater functional impairment, increased incidence of suicidality, and poorer response to antidepressant treatments; they may also require lower starting doses, more gradual dose increases, higher end-point doses, longer treatment regimens, and early augmentation with benzodiazepines in order to achieve adequate treatment response (Rao et al., 2009). Given the importance of the presence of anxiety in explaining variance among depressed individuals in this study and in predicting treatment response in other clinical trials, future research should continue to explore the utility of using measures of anxiety to help inform treatment decisions.

In addition, the emergence of the *core symptoms factor* (factor 3) indicates that somatic, affective, cognitive, and anhedonic symptoms form a single, cohesive construct that meaningfully separates from other variables. Importantly, these subscales closely correspond to the diagnostic criteria for MDD listed in DSM-5 (2013), including the

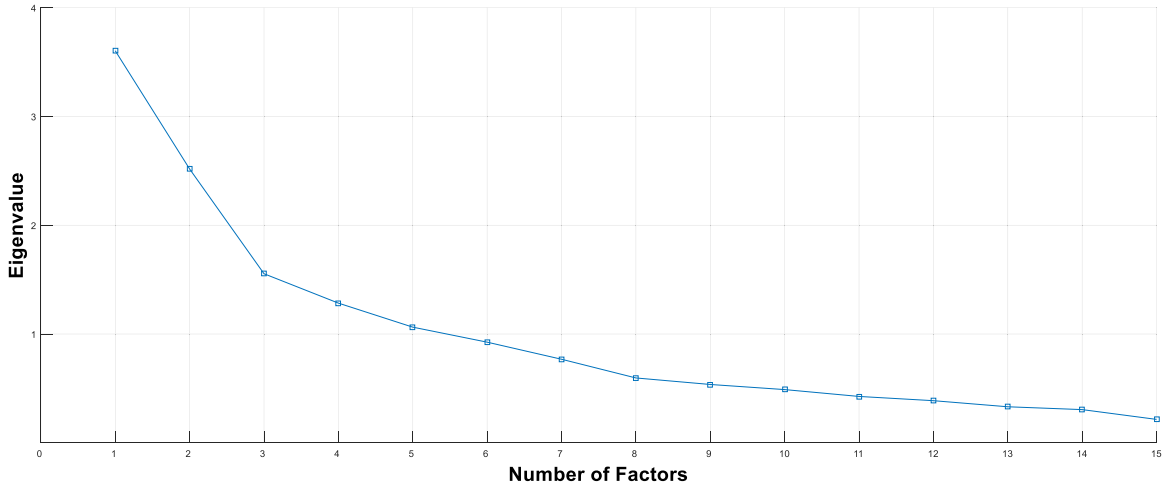

Fig. 3. Initial eigenvalues for factors 1–15. The first 5 factors possessed eigenvalues ≥ 1.00 and were selected as the optimal solution. .

Table 5
Multiple Regression of Derived Factors with Severity of Depression (HAMD).

Model Summary							
Model	R	R-Square	Adjusted R-Square	Std. Error of the Estimate			
1	.568[a]	.323	.308	8.360			
Coefficients							
Model	Unstandardized Coefficients		Standardized Coefficients	t	p-value	95.0% Confidence Interval for Beta	
	Beta	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	25.84	0.54		47.98	0.000	24.78	26.90
*Anxiety (Factor 1)	2.03	0.54	0.20	3.77	0.000	0.97	3.10
Behavioral Activation (Factor 2)	−0.86	0.54	−0.09	−1.60	0.110	−1.92	0.20
*Core Symptoms (Factor 3)	5.08	0.54	0.51	9.46	0.000	4.02	6.14
*Rumination (Factor 4)	1.08	0.54	0.11	2.01	0.046	0.02	2.14
Emotional Intensity (Factor 5)	0.69	0.54	0.07	1.27	0.206	−0.38	1.75

Abbreviations. HAMD: Hamilton Depression Rating Scale.
* Indicates variable reached statistical significance ($p \leq 0.05$).

cardinal symptoms of depression—sadness and anhedonia—as well as altered weight/appetite, hypersomnia/insomnia, psychomotor agitation/retardation, feelings of worthlessness, excessive guilt, impaired concentration, and suicidal ideation. Although DSM has been criticized frequently for its definition of depression as a variable combination of these nine specific symptoms (Lilienfeld and Treadway, 2016; Hyman, 2010), their emergence as a single factor in this analysis suggests that this particular constellation of symptoms does indeed form a broader, cohesive depression construct, or syndrome, that is separate from other related variables. Future research should examine differences among depressed individuals in the expression of these core symptoms as well as other symptoms, which may develop secondarily, to help inform the diagnostic criteria and subtyping approaches used in MDD.

The *rumination factor* (factor 4), composed of brooding/reflective pondering/behavioral inhibition, demonstrates a strong link between rumination and behavioral inhibition. Thus, rumination, which is measured predominantly as a cognitive phenomenon on the RRS, and behavioral inhibition, which is assessed as overt behaviors on the BIS, may be complementary ways of conceptualizing the same underlying factor. Interestingly, rumination and behavioral inhibition have each been linked independently with neural abnormalities in the default-mode network (DMN). Interestingly, investigators have also recently described a plausible neural mechanism involving the DMN that links these two constructs. According to this model increased DMN *activity* is associated with high levels of maladaptive rumination (Hamilton et al., 2011) and decreased DMN *connectivity* with the ventral striatum and motor cortex may underlie behavioral inhibition (Bellgowan et al., 2015). Future research should investigate the reliability and specificity of these neural abnormalities in depression and the intriguing possibility of discovering an integrative neural mechanism responsible for the close relation between these cognitive and behavioral constructs of depression.

Finally, the *emotional intensity factor* (factor 5) includes both positive and negative affect subscales. Importantly, both variables loaded strongly and positively onto this factor, suggesting that this construct reflects the *degree* of emotional intensity, independent of *valence*. This finding underscores the importance of assessing overall magnitude of both positive and negative emotions when attempting to understand individual differences among depressed individuals. Indeed, in emotion reactivity paradigms, investigators have found reduced levels of responses to both positive and negative stimuli in depressed individuals compared to healthy controls (Bylsma et al., 2008), which appears to be driven by emotion context insensitivity (Rottenberg et al., 2005); that is, depressed participants do not respond differently to positive and negative stimuli. Interestingly, other researchers have suggested that two subtypes of MDD might reflect differences in this emotional intensity factor: a *melancholic* subtype, characterized by a nonreactive mood and blunted emotional responses, and an *atypical* subtype, characterized by mood reactivity and increased levels of certain somatic behaviors (Baumeister and Parker, 2012). These two putative subtypes appear to follow different clinical courses and may respond differentially to certain pharmacological treatments (e.g., tricyclic antidepressants vs. monoamine oxidase inhibitors). Future research should investigate the relation between this emotionality factor and emotional reactivity to specific stimuli as well as neurobiological abnormalities associated with melancholic vs. atypical subtypes and the clinical utility of using these variables to inform treatment and predict outcome.

4.2. Association of factors with severity

The results of our multiple regression analyses indicate that these five factors differentially predict overall severity, as measured by multiple instruments. In particular, the core symptoms factor was associated more strongly and significantly with overall severity of MDD, as measured by three severity scales (i.e., HAMD, SCID-Sev, and GAF), than were all of the other factors. In addition, higher levels of anxiety and rumination corresponded to significantly higher levels in one or more measures of overall severity, after controlling for other factors, although these associations were not as strong or consistent as was the association between the core symptoms factor and overall severity. In contrast, levels of behavioral activation and emotional intensity were not significantly associated with overall severity, after controlling for other factors. These findings raise the possibility that developing clinical interventions that specifically target core symptoms may produce the largest improvements in overall severity. The finding that some factors are significantly associated with overall severity only before controlling for other factors also suggests that treatments that target some symptoms may actually exert their influence on overall severity through improvement in the core symptoms of depression. It will be important in future research to examine these possibilities more directly and systematically in treatment outcome research and to include mediation analyses in these studies.

4.3. Comparison of factor structures in MDD vs HC participants

Although we found a high degree of overall similarity between participants with MDD and healthy controls in their respective factor structures, there were some notable group differences in the relations among some depression-related constructs. In particular, depressed participants exhibited a strong, positive coupling of behavioral inhibition with rumination, whereas nondepressed participants showed a strong, negative coupling of behavioral inhibition with positive/negative affect. This finding might be explained in terms of increased cognitive load from depressive rumination, failed attempts at mood repair, or emotion context insensitivity, each of which might be expected to weaken an adaptive link between behavioral engagement and normal affective experiences. For example, some investigators have suggested a possible association between ruminative processes and increased cognitive load (Schiller et al., 2013); taken together with our findings, this

raises the possibility that behavioral inhibition develops to cope with the increased cognitive demands associated with rumination in depressed individuals. Also, in depressed individuals, adaptive attempts to repair mood that require behavioral disinhibition may repeatedly fail (Foland-Ross et al., 2013), leading to the gradual decoupling of affective processes and behavioral responses. Alternatively, poor discrimination between positive and negative emotional stimuli in depressed individuals (Rottenberg et al., 2005) may similarly break what is normally an adaptive link between affective processes and behavioral responses. Future research should examine these three hypotheses as possible mechanisms through which depressed individuals develop characteristics such as behavioral inhibition as well as characteristic relations between constructs such as behavioral inhibition and rumination.

4.4. Limitations and future directions

We should note the following limitations of this study. First, the factor analyses were conducted on self-report data, which are susceptible to response bias and depend on participants' self-awareness. Nevertheless, these data were obtained using well-established self-report scales with strong psychometric properties, and scores for each subscale were created by summing several items. Second, the factor analyses presented in this paper were conducted at the subscale level analysis. This provides a useful view of symptom structure in MDD, but does not provide a hierarchical view of factors across multiple levels or a granular view of individual item-level responses. This latter approach would require a much larger sample size in order to satisfy conventional criteria for factor analysis Costello and Osbourne, 2005) and would likely present a complex pattern of many factor loadings that would be difficult to interpret parsimoniously. Future investigations examining the factor structure of depression may provide complementary views at other levels of analyses, such as more specific depressive symptoms or broader domains of depressive characteristics.

Third, we chose to examine the multivariate relations among depressive symptoms and characteristics by using a factor analytic approach to identify a reduced set of variables that are orthogonal to each other and that appear to underlie the larger set of observed variables from commonly used self-report scales. Other investigators have taken a different approach that involves using network analytic methods (Beard et al., 2016; Cramer et al., 2017) to elucidate the centrality and density of numerous depressive symptoms based on observed associations among them (Borkulo et al., 2015; Wigman et al., 2015). These data-driven approaches reflect different conceptualizations of mental disorders and address different research questions but may provide complementary findings that increase our understanding of the factors underlying these dynamic networks of interacting symptoms.

Fourth, although the subscales represent a broad array of depression-related constructs, there is some degree of overlap among the constructs assessed in these measures. In particular, the multiple regression analysis included the HAMD and BDI, both of which are often used to measure severity of depression and include several items that appear to overlap considerably. To address this limitation, we included two additional measures, SCID-Sev and GAF, which independently assess severity of depression. Similarly, although the resulting factor structures tended to include subscales belonging to the same questionnaire, we also found several factors that included significant loadings from multiple scales, suggesting that the obtained factor structures do not merely reflect the composition of the original questionnaires. Finally, because we did not include a nondepressed clinical group in this study, we cannot determine the extent to which the obtained factor structures are specific to MDD or are common across different psychiatric disorders. Nevertheless, the approach taken in the present study reflects the structure of depression-related symptoms and psychological constructs in a heterogeneous and clinically representative population of patients with MDD. Future research should address this issue by conducting comparisons with individuals diagnosed with other disorders.

4.5. Conclusions

This study is the first to examine the factor structure of MDD across a broad set of constructs and to model the multivariate association of these factors with the overall severity of MDD. We found that a five-factor model composed of (1) anxiety; (2) behavioral inhibition; (3) core symptoms; (4) rumination; and (5) emotional intensity best explained variation in depressive symptoms and characteristics. Among these five factors, the *anxiety factor* accounted for the largest portion of variance in depressive symptoms and characteristics, highlighting the importance of assessing anxiety when investigating differences among depressed individuals; furthermore, the separation of the anxiety factor from other depression-related constructs provides further empirical validation for the distinction between anxiety and depression, despite their high levels of comorbidity. In addition, the *core symptoms factor*, which closely corresponds to DSM-5 diagnostic criteria for MDD, formed a coherent factor separable from other depression-related constructs and was the only factor that showed a consistent, significant association with overall severity of depression and functional impairment; this raises the possibility that developing clinical interventions that specifically target this factor may produce the largest improvements in overall severity and general functioning. The *rumination factor*, which was composed of measures of both rumination and behavioral inhibition, demonstrated a strong link between these two constructs and suggests that they provide complementary ways of conceptualizing the same underlying variable. The *emotional intensity factor* consisted of a positive coupling of both positive and negative affect, underscoring the importance of assessing the overall magnitude of emotions, independent of valence, in depressed individuals. Finally, we found that participants diagnosed with MDD differed from healthy controls not only in the *magnitude* of depression-related characteristics, but also in the *relations* among these characteristics; in particular, depressed participants showed a positive coupling of behavioral inhibition with rumination and, unlike in healthy controls, a decoupling of these symptoms with positive and negative affect. Taken together, these findings provide an important data-driven framework for the multidimensional symptom structure of depression and suggest several actionable ways for improving clinical assessment as well as treatment development for individuals with MDD.

CreditAuthorStatement

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Declaration of Competing Interest

All authors declare no conflict of interest.

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Supplementary materials

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