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The factor structure of depressive symptoms in patients with obesity enrolled in the RAINBOW clinical trial

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Abstract

Background: Examining variability in the presenting symptoms of depression may be particularly important in characterizing depression in patients with comorbid conditions such as

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Declaration of Competing Interest

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obesity. Identifying the underlying constructs of depression in such patients may produce phenotypic information to aid diagnosis and treatment decisions.

Objective: To examine the latent factors of symptoms using the depression Symptom Checklist (SCL-20) and the Patient Health Questionnaire (PHQ-9), separately, in patients with obesity and elevated depressive symptoms.

Methods: Exploratory factor analysis (EFA) was performed on baseline data from 409 patients with obesity and elevated depressive symptoms recruited in primary care. Bootstrap analysis was performed to estimate the precision and potential replicability of identified latent factors.

Results: Participants (70% women, mean age of 51.0 ± 12.1 years) had moderate depression. EFA of the SCL-20 suggested two reliable factors: dysphoric mood (71% of the variance) and anhedonia (15% of the variance). EFA of the PHQ-9 yielded one factor: dysphoric mood (87% of the variance). Bootstrapped results supported the replicability of these results. The top most endorsed symptoms were feeling low energy, overeating and disturbed sleep.

Limitations: The generalizability of these findings to severe depression may be limited.

Conclusions: Patients with elevated depressive symptoms and obesity present with heterogeneous symptoms. The SCL-20 seems more sensitive than the PHQ-9 for differentiating symptom profiles in this population. Some possible reasons include: 1) differences in number of scale items, and 2) differences in the aspects of depression they tap into; the SCL-20 measures the severity of symptoms, whereas the PHQ-9 measures the frequency of symptoms.

Keywords

Depression; obesity; PHQ-9; SCL-20; Exploratory factor analysis

Introduction

Unipolar depression is predicted to be the number one leading cause of burden of disease globally by 2030 (World Health Organization, 2008). A wide range of physical conditions are associated with depression, including metabolic syndrome, cardiovascular disease, rheumatoid arthritis, chronic pain, and neurodegenerative disease (Slavich and Irwin, 2014). Obesity, defined as a body mass index (BMI) ≥30 kg/m^2, often coexists with depression. Indeed, a bidirectional association between depression and obesity has been noted (Luppino et al., 2010). The prevalence of obesity among adults with depression was reported at 53% in 2005-2010 (Pratt and Brody, 2014). In addition, individuals with obesity (BMI ≥30 kg/m^2) had a higher lifetime prevalence of major depressive disorder (MDD) than normal weight individuals (Petry et al., 2008).

Commonly used terms in clinical practice, including depression, often reflect a combination of constructs, rather than a single construct (Smith et al., 2010). Based on Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria, MDD is defined by a constellation of signs and symptoms, including affective (e.g., depressed mood), cognitive (e.g., concentration difficulty), and neurovegetative symptoms (e.g., fatigue) (American Psychiatric Association, 2013). Importantly, these constructs may differ in their underlying etiology, prognoses, and medical comorbidities as well as in responsiveness to treatment

(Vares et al., 2015). Therefore, there has been a call to identify more homogenous constructs within depressive symptomatology rather than only relying on a single score of a multidimensional construct given that the former may provide insight into the underlying neurobiology as well as inform diagnoses and treatment decisions (Smith et al., 2010).

Importantly, the presentation of depression varies greatly across patients. Clinical, behavioral, and sociodemographic factors, including weight status, help account for such variation. For example, higher BMI was associated with higher neurovegetative/somatic symptoms of depression (Udo et al., 2015). Consistently, patients seeking bariatric surgery reported higher neurovegetative/somatic symptoms of depression relative to affective/cognitive symptoms (Munoz et al., 2007). In spite of the high comorbidity of depression with obesity, little research has focused on the effect of obesity on symptom profiles of depression. Indeed, understanding the structure of depression in the context of obesity might help identify those constructs that are more prototypical to the concept of depression in this population.

Given that a single scale is typically comprised of limited items which cannot accurately assess all dimensions of depression, extensive item pools are needed to capture all components of depressive symptoms (Shafer, 2006). However, there is value in exploring the factor structure of existing depression scales because it will add to our understanding of the components of depression that are being measured by each scale. Research findings regarding the underlying constructs or factor structures of commonly used depression scales vary by setting and population.

The depression Symptom Checklist (SCL-20) has been used in different medical settings, including patients with obesity, chronic illness, epilepsy, and primary care patients (Chaytor et al., 2011; Ciechanowski et al., 2010; Katon et al., 1996; Katon et al., 2010; Linde et al., 2011; Simon et al., 2000). In spite of its widespread use, however, evidence regarding the factor structure of the SCL-20 is scarce. The underlying structure of the Patient Health Questionnaire (PHQ-9) has been explored in broader populations, including patients with cardiovascular disease (de Jonge et al., 2009), spinal cord injury (Kalpakjian et al., 2009; Krause et al., 2008, 2010, 2011; Richardson & Richards, 2008), persistent major depressive disorder (Guo et al., 2017), substance abuse (Dum et al., 2008), and primary care patients (Baas et al., 2011; Cameron et al., 2008; Elhai et al., 2012; Huang et al., 2006; Petersen et al., 2015). The majority of these studies supported a 2-factor model (de Jonge et al., 2007; Elhai et al., 2012; Guo et al., 2017; Kalpakjian et al., 2009; Krause et al., 2008, 2010, 2011; Richardson & Richards, 2008; Petersen et al., 2015); the two factors that emerged included “somatic” items (e.g., appetite changes, sleep disturbance) and “non-somatic” items (e.g., loss of interest, depressed mood). In contrast, however, a few studies yielded a 1-factor structure (Baas et al., 2011; Cameron et al., 2008; Dum et al., 2008; Huang et al., 2006), indicating more unidimensional depression. Although the 2-factor structure of the PHQ-9 was relatively prevalent and consistent across studies, there have been inconsistencies in terms of items that loaded on each factor. These inconsistencies could be explained in part by differences in study sample. Although both the SCL-20 and PHQ-9 have been used in a population of individuals with comorbid depression and obesity (Cassin et al., 2013; Linde

et al., 2011; Simon, Ludman, Linde, Belinda, & Jeffery, 2008), no study to our knowledge has explored the underlying structure of these scales in this specific population.

Much of the existing literature in individuals with obesity has examined the factor structure of depressive symptomatology using the Beck depression inventory (BDI). Of five studies that we are aware of, four found a three-factor structure (Hall et al., 2013; Hayden et al., 2010; Hayes et al., 2015; Udo et al., 2015), and one found a 2-factor model (Munoz et al., 2007). It is not clear whether the identified 3-factor structure is a function of the BDI scale or a feature of depression in this specific population. Hence, it is important to explore the factor structure of other depression scales to help answer this important question.

Additional considerations to developing more precise phenotypic definitions of depression include that presenting symptoms of depression often vary across sex and age; we posit that this may further differ across profiles of depressive symptoms. For example, women were more likely to present neurovegetative symptoms of depression (e.g., increased appetite, weight gain, leaden paralysis) than men (Łojko et al., 2015). In addition, greater age was associated with higher neurovegetative/somatic symptoms of depression (Hegeman et al., 2012; Schaakxs et al., 2018; Udo et al., 2015). This evidence highlights the importance of exploring the effects of sex and age on the symptom profiles of depression, which in turn may provide insight into assessment and evaluation of intervention effects for specific subgroups of patients.

The present study aimed to understand the symptom profiles of depression in patients with obesity and elevated depressive symptoms. To accomplish this, we had two specific aims. The first aim was to examine the factor structure of depression as assessed by the SCL-20 and PHQ-9 in patients with obesity and elevated depressive symptoms using exploratory factor analysis. The factor structure of the SCL-20 and PHQ-9 might be different due to (1) differences in number of scale items, and (2) differences in the aspects of depression they tap into. The SCL-20 items are intended to measure the "*intensity*" of symptoms, whereas the PHQ-9 items are intended to measure the "*frequency*" of symptoms. Therefore, exploratory factor analysis (EFA) was conducted separately on the SCL-20 and PHQ-9 to explore whether the factor structures differ across these two scales. Although evidence on the factor structure of the SCL-20 is lacking, given that the items on the SCL-20 are similar to the BDI items, and that both scales measure the same aspect of symptoms (i.e., the intensity of symptoms), we hypothesized that a 3-factor model will emerge from the SCL-20. Given that a 2-factor model of the PHQ-9 was observed in the majority of prior studies, we hypothesized that a 2-factor model will emerge from this scale, with one factor containing neurovegetative items and the other containing affective items. It would be ideal to parse out the cognitive factor from the affective factor given that these two reflect distinct constructs according to the Research Domain Criteria (RDoC) framework. However, commonly used depression rating scales include only a limited number of items, if any, that capture core cognitive elements of depression (e.g., difficulty concentrating). Therefore, we did not expect the affective and cognitive items to diverge. The second aim of this study was to examine whether the severity of the identified factors varies across sex, age groups (18-<45, 45- <65, ≥65), and BMI category (27-<35, 35-<40, ≥40). Given the lack of evidence on

the moderating effects of these variables on symptom profiles of depression to inform a priori hypotheses, this aim was exploratory.

Methods

Participants

This study reports a post-hoc analysis of baseline data from the RAINBOW trial, a 2-arm randomized clinical trial that evaluated an integrated, collaborative care intervention to treat adults with obesity and elevated depressive symptoms in primary care. A detailed description of the trial protocol can be found elsewhere (Ma et al., 2015). Inclusion criteria included men and women ≥18 years of age, residing in the Bay Area, California, with BMI ≥30.0 kg/m^2 (≥27 if of Asian descent), and clinically significant depression reflected by PHQ-9 ≥10. The World Health Organization (2004) has suggested a BMI value of 27.5 kg/m^2 or greater as representing high health risks (e.g., cardiovascular disease) in Asian populations. Given the ethnic differences in BMI and disease risk, in the present study participants from Asian descent were included if they had a BMI value ≥27.0 kg/m^2. Participants were excluded if they had active suicidal ideation, any psychiatric disorders other than minor/major depressive disorder, dysthymia, and/or comorbid anxiety disorder, active bulimia nervosa within the past three months, bariatric surgery within the past 12 months, current alcohol/substance use disorder, pre-existing diabetes or cardiovascular disease, or a diagnosis of cancer (for a complete and detailed list of inclusion and exclusion criteria see Ma et al., 2015). This resulted in a sample of 409 participants.

Assessment and measures

Participants completed a self-reported questionnaire assessing sociodemographic characteristics including age, sex, race, ethnicity, education, income, marital status, and household size. BMI was calculated based on height and weight measured by trained study coordinators. Depressive symptoms were assessed by the SCL-20 and PHQ-9. The SCL-20 is a self-report questionnaire with 20 items that were drawn from the SCL-90. Respondents answered questions regarding *how much* they were distressed by a symptom over the last two weeks. Each item is rated on a 5-point scale (0 = *not at all*, 1 = *a little bit*, 2 = *moderately*, 3 = *quite a bit*, 4 = *extremely*). Based on previous research, the SCL-20 has high reliability and validity (Derogatis et al., 1974). The SCL-20 has shown a Cronbach's alpha of 0.86 (Derogatis et al., 1974; Williams et al., 2004). In the present sample, the total SCL-20 scale showed a Cronbach's alpha of 0.85. Cronbach's alpha values for the dysphoric mood factor, anhedonia factor and sleep disturbance factor were 0.87, 0.67 and 0.64, respectively. The PHQ-9 is a self-report questionnaire with 9 items that corresponds to DSM-IV criteria for diagnosis of MDD. Respondents answered questions regarding how often a symptom has bothered them over the last two weeks. Each item is rated on a 4-point scale (0 = *not at all*, 1 = *several days*, 2 = *more than half the days*, 3 = *nearly every day*). The PHQ-9 has shown a Cronbach's alpha of 0.89 in primary care patients (Kroenke, et al., 2001). In the present sample, Cronbach's alpha values for the total PHQ-9 scale and the dysphoric mood factor were 0.40 and 0.58 respectively. In previous studies, a PHQ-9 score of 10 or greater had a sensitivity of 77% to 88% and a specificity of 88% to 94% for detecting major depressive disorder (a systematic review by Kroenke, et al., 2010). In the

present study, the PHQ-9 was used to screen participants online or by phone. Participants with a PHQ-9 score of 10 or greater were scheduled for baseline visits, at which time the SCL-20 was administered.

Statistical analysis

Exploratory factor analyses with oblique rotations (Osborne & Banjanovic, 2016) were conducted to examine the factor structure of the SCL-20 and PHQ-9, separately. The unweighted least squares method was used to extract factors because of the non-normal distribution of data (Fabrigar et al., 1999; Nunnally, 1994). Bootstrap resampling method was performed to estimate the precision and potential replicability of identified factors (Diciccio and Efron, 1996). Factor loadings of 0.30 or greater was used to represent that the item loaded onto the factor (Brown, 2014). The number of factors were determined based on three criteria: (1) the Kaiser criterion based on eigenvalues >1.0 (Braeken and van Assen, 2017), (2) inclusion of at least three items for each factor, and (3) interpretability of the identified factors and loaded items in the context of theoretical concepts and empirical evidence. Communalities, which are estimates of the amount of variance in the given indicator explained by the latent factors, were calculated as a function of both the factor loadings and the factor correlations (for more details see Brown, 2014). Standardized scoring coefficients were estimated for each scale item with salient loadings on the factor (Osborne & Banjanovic, 2016) and used to compute weighted factor scores. The mean score on each identified factor was estimated by multiplying the raw values of items with salient loadings on the factor by the standardized scoring coefficients and then averaged. Analysis of variance was conducted to compare overall depression scores and scores of the identified factors across age groups, sex, and BMI categories. All analyses were conducted using SAS, version 9.4 (SAS Institute Inc., Cary, North Carolina). $P < 0.05$ (2-sided) was considered statistically significant.

Results

Subject characteristics

Subject characteristics are shown in Table 1. The study sample consisted of 409 individuals (70% women) with obesity and elevated depressive symptoms with a mean age of 51.0 ± 12.1 years. The mean SCL-20 and PHQ-9 scores were 1.5 ± 0.5 and 13.8 ± 3.1 respectively, representing moderate depressive symptoms. The mean BMI score was 36.7 ± 6.4, indicating moderate obesity. No significant differences were observed between men and women in BMI or in age (*ps* > 0.5).

Most endorsed depressive symptoms

The top most endorsed symptoms with a mean value of greater than 2 on the SCL-20 were feeling low energy/slowed down, overeating, disturbed sleep, and worrying too much, indicating that on average the intensity of these symptoms was rated as moderate or greater during the past two weeks (see Supplemental Table 1 [S1]). The top most endorsed symptoms with a mean value of 2 or greater on the PHQ-9 were low energy/feeling tired, overeating/poor appetite, and sleep disturbance, indicating that on average they were present more than half the days or nearly every day over the past two weeks (see Table S2).

Exploratory Factor Analysis

SCL-20—The eigenvalues, factor patterns and communalities from EFA on the SCL-20 are shown in Tables 2 and 3. Two factors met all of the three pre-specified criteria. The first factor accounted for 71% of the total variance and it was labeled “dysphoric mood” based on the loaded items. Ten items- reflecting “negative mood”, “negative bias” and “worry and rumination”-were retained in factor 1, including blaming yourself (coefficients=0.83), feelings of worthlessness (0.82), guilt (0.78), hopeless (0.72), blue (0.61), being trapped (0.60) and lonely (0.55), worrying too much about things (0.54), crying easily (0.43), and thoughts of death (0.34). The second factor accounted for 15% of the total variance and it was labeled “anhedonia.” Four items were retained in factor 2, including feelings everything is an effort (0.74), no interest in things (0.62), low energy or slowed down (0.51), and loss of sexual interest or pleasure (0.39). The third factor had an eigenvalue < 1.0 and thus could be unreliable, but it met the three loaded item and interpretability criteria. Factor 3 accounted for 10% of the total variance and was labeled “sleep disturbance” based on the three items loaded onto it, which included restless or disturbed sleep (0.86), trouble falling asleep (0.57), and awakening early in the morning (0.42). The item “thoughts of ending life” did not load significantly on any of the factors. The communalities for the SCL-20 items, with salient loadings on the three factors, ranged from 0.14 to 0.73.

The “dysphoric mood” factor correlated moderately with the “anhedonia” factor ($r = 0.52$, $p < 0.001$) and correlated weakly with the “sleep disturbance” factor ($r = 0.18$, $p < 0.001$). In addition, the “anhedonia” factor also correlated weakly with the “sleep disturbance” factor ($r = 0.18$, $p < 0.001$). Inter-factor correlations are shown in Table S3. Total SCL-20 scores correlated strongly with the “dysphoric mood” factor ($r = 0.88$, $p < 0.001$) and moderately with the “anhedonia” factor ($r = 0.71$, $p < 0.001$) and the “sleep disturbance” factor ($r = 0.46$, $p < 0.001$). No significant correlations were observed between BMI and either total SCL-20 score or the three factors. Among the SCL-20 items, “overeating” correlated weakly with BMI ($r = 0.11$, $p < 0.05$).

The mean score on the “dysphoric mood” factor (0.17 ± 0.10) was significantly lower than the mean score on the “anhedonia” factor (0.49 ± 0.20; $t(408) = -36.83$, $p < 0.0001$) and the mean score on the “sleep disturbance” factor (0.64 ± 0.33; $t(408) = -28.66$, $p < 0.0001$). The mean score on the “anhedonia” factor was significantly lower than the mean score on the “sleep disturbance” factor ($t(408) = -8.47$, $p < 0.0001$). The mean factor scores are shown at the top of Table 5.

PHQ-9—The eigenvalues, factor patterns and communalities of the PHQ-9 are shown in Tables 2 and 4. Only the first factor met the three pre-specified criteria. It accounted for 87% of the total variance and was labeled “dysphoric mood.” Three items were retained in factor 1, including feeling down, depressed or hopeless (coefficients= 0.64), little interest or pleasure in doing things (0.48), and feeling bad about yourself (0.46). For these three items, the communalities ranged from 0.21 to 0.42. Six items including sleep disturbance, fatigue or low energy, changes in appetite, difficulty concentrating, psychomotor retardation or agitation, and thoughts of death did not load on this factor. The mean score on the dysphoric mood factor is presented at the top of Table 6. Total PHQ-9 scores correlated significantly

with the "dysphoric mood" factor ($r = 0.68$, $p < 0.001$). No significant correlations were observed between BMI and either total PHQ-9 score or factor 1. Among the PHQ-9 items, two items of "difficulty concentrating" and "psychomotor retardation/agitation" negatively correlated with BMI, although the strength of correlations was weak ($r = -0.11$, $p < 0.05$ and $r = -0.11$, $p < 0.05$, respectively).

Bootstrap results to test internal validation—The bootstrapped mean eigenvalues for the first four factors of the SCL-20 and two factors of the PHQ-9 are presented in Table 2. Regarding the SCL-20, the mean values for the first four eigenvalues, across 2000 resamples, were consistent with our initial EFA analysis, supporting a two-factor structure. Regarding the PHQ-9, the mean value for the first factor, across 2000 resamples, was greater than 1, supporting a one-factor structure. The average bootstrapped factor loadings are shown in Tables S4-S5. Based on the bootstrapped statistics, the same items were retained in the factors as they were identified in the initial analysis, suggesting the stability of the initial results across 2000 resamples.

Depression scores across groups:

SCL-20—Women scored significantly higher on the SCL-20 total score ($F = 4.32$, $p = 0.038$) and the "sleep disturbance" factor score ($F = 8.99$, $p = 0.003$) compared to men. No significant differences were found between men and women in two other factor scores ($p > 0.7$). No significant differences were found in the SCL-20 total score or the three factor scores across BMI categories or age groups (all p's > 0.4). Results are presented at the bottom of Table 5.

PHQ-9

No significant differences were found between men and women in the PHQ-9 total score ($F = 3.39$, $p = 0.07$) or the "dysphoric mood" factor score ($p = 0.7$). No significant differences were found in the PHQ-9 total score or the "dysphoric mood" factor score across BMI categories or age groups (All p's > 0.3). Results are presented at the bottom of Table 6.

Discussion

This study is the first to examine the factor structure of the PHQ-9 and the SCL-20 in patients with obesity and elevated depressive symptoms. Our results suggest that both scales capture the "dysphoric mood" construct in these patients. However, the SCL-20 seems more sensitive than the PHQ-9 to capture other depression-related constructs (e.g., anhedonia). Some possible reasons for this observation include: (1) differences in number of scale items, and (2) differences in the aspects of depression they tap into; the SCL-20 measures the severity of depressive symptoms, whereas the PHQ-9 measures the frequency of symptoms. These findings provide important information regarding the clinical utility of these scales. Given that the PHQ-9 (or PHQ-2) has increasingly been adopted as a depression screening tool in primary care, our findings suggest that this practice may need to be re-examined in patients with comorbid depression and obesity; that is, insofar as this scale may largely capture only the negative mood dimension of depression, studies that need to screen on other

aspects of depression or those seeking to determine sub-types of depression may be better served by considering additional items and/or alternative scales.

In contrast to our findings, most prior studies supported a 2-factor model of the PHQ-9 in other samples (e.g., cardiovascular disease, MDD, substance abuse) (de Jonge et al., 2007; Elhai et al., 2012; Guo et al., 2017; Kalpakjian et al., 2009; Krause et al., 2008, 2010, 2011; Richardson & Richards, 2008; Petersen et al., 2015). Relatively few studies yielded a 1-factor structure including all nine items (Baas et al., 2011; Cameron et al., 2008; Dum et al., 2008; Huang et al., 2006). Interestingly, in the present study the items related to neurovegetative symptoms (e.g., fatigue, sleep) on the PHQ-9 did not load on the dysphoric mood factor, suggesting that these symptoms may represent a distinct underlying construct. More factors may have been identified if more indicators of this potential construct were included on the PHQ-9. Considered together, these data are consistent with the notion that the factor structure of the PHQ-9 may differ across patient populations.

Evidence on the factor structure of the SCL-20 in individuals with obesity is lacking. However, some prior findings in these individuals revealed a three-factor structure on the BDI scale using factor analysis (Hall et al., 2013; Hayden et al., 2010; Hayes et al., 2015; Udo et al., 2015). In one study, these factors consisted of the “negative perceptions”, “diminished vigor” and “cognitive dysregulation” factors (Hayes et al., 2015). The first two factors as well as the loaded items on these factors were similar to our results on the SCL-20; the “negative perception” factor included items that represented negative mood and negative bias, and the “diminished vigor” factor included the items “loss of energy”, “fatigue” and “loss of interest in sex”. In other three studies, a three-factor structure represented “negative mood or affective”, “negative self-attitudes or cognitive”, and “somatic” items (Hall et al., 2013; Hayden et al., 2010; Udo et al., 2015). In these studies, items relevant to depressed mood (e.g., sadness) and negative bias (e.g., guilty feeling) consistently form two distinct clusters. Conversely, in the present study, depressed mood symptoms (i.e., feeling blue, hopeless, crying easily, thoughts of death), negative bias symptoms (i.e., feeling worthless, guilty, lonely, self-blame), and worry and rumination symptoms (worrying too much, feeling trapped) as measured by the SCL-20 shared the same latent factor (i.e., loaded on the same factor). Of note, self-blame, worthlessness and guilty feeling had the highest factor loadings on the dysphoric mood factor, suggesting that negative self-perception plays a major role in the experience of depressed mood in our sample. Because our study is the first to examine the factor structure of the SCL-20 and the PHQ-9 in patients with obesity and elevated depressive symptoms, future studies need to evaluate the replicability of factors emerged from our study in this specific sample.

Although the eigenvalue for the sleep disturbance factor was less than one, there may be potential value in reporting the results for this factor as it may provide additional information about other symptom manifestations of depression in this population. In the present study, the item “sleep disturbance” on the SCL-20 did not cluster with the items” loss of energy/fatigue” and tended to form a distinct factor, suggesting that these symptoms may have a different underlying construct and/or cause. In contrast, in prior studies among individuals with obesity and depression, the items “sleep changes”, “fatigue and loss of energy” on the BDI loaded together and form a separate somatic factor (Hall et al., 2013;

Hayden et al., 2010; Udo et al., 2015). The weak correlation between the sleep factor and the dysphoric mood factor in the present study suggests that sleep problems may not be mainly driven by the underlying construct of depression. There is evidence indicating that sleep and obesity are related. Sleep disturbance may contribute to the development and progression of obesity via several biological and behavioral mechanisms (reviewed by Cooper et al., 2018). For example, sleep deprivation has been associated with increased ghrelin levels (a hormone that stimulates appetite) and decreased leptin (a hormone that inhibits appetite) levels, which in turn contribute to increased appetite and weight gain. Importantly, sleep disturbance may occur secondary to obesity. Indeed, obesity has been linked to the development and severity of obstructive sleep apnea (reviewed by Hargens et al., 2013). However, there is evidence indicating the obesity-sleep association exists independent of sleep apnea (Vgontzas et al., 2006).

We found that the loss of interest item on the SCL-20 did not load on the affective factor. This is in line with the notion from early research suggesting that positive affect and negative affect are two main dimensions of emotional experience (Clark & Watson, 1991; Watson & Tellegen, 1985). The loss of interest item shared the same latent factor as loss of energy and fatigue symptoms. The item “feeling everything is an effort” had the strongest factor loading on the anhedonia factor. Conceptually, this item can reflect physical fatigue and mental fatigue or reduced motivation features of depression. In addition, the anhedonia factor correlated with the dysphoric mood factor and did not correlate with BMI. This suggests that the experience of fatigue and low energy in this sample is a feature of depression and not merely driven by physical problems due to obesity. Examining whether symptoms of anhedonia, low energy and fatigue share a common underlying neurobiology in patients with comorbid depression and obesity would be a fruitful avenue of future research. Existing evidence indicates that inflammation can play a role in the pathophysiology of depression (Dowlati et al., 2010; Hiles et al., 2012; Howren et al., 2009). In addition, evidence suggests that inflammation can alter dopamine in the basal ganglia, resulting in anhedonia, fatigue and psychomotor retardation (reviewed by Felger & Miller, 2012). Given that obesity is characterized by low-grade inflammation (Shelton and Miller, 2010), we speculate based on our preliminary findings that loss of energy, fatigue and loss of interest lumped together partly because they are interrelated in an inflammatory network. Exploring homogenous constructs within depression with a particular biosignature is an important next step in advancing translational research in the context of comorbid depression and obesity.

We found that patients scored higher on the anhedonia and the sleep disturbance factors compared to the dysphoric mood factor. The factor scores showed consistent patterns across sex, age and BMI categories with one exception; women scored higher in the potential sleep disturbance factor compared to men. Prior studies suggest that clinical presentation of depression may differ across sex, with women more likely to exhibit neurovegetative symptoms (e.g., sleep, fatigue) (Delisle et al., 2012; Silverstein, 2002, 1999). In addition, the most endorsed symptoms on both the SCL-20 and the PHQ-9 were low energy/fatigue, sleep disturbance and overeating/changes in appetite. Studies in obesity yielded similar patterns of results. For example, loss of energy, fatigue, changes in sleep patterns or appetite were among the most endorsed depressive symptoms in a sample of obese subjects seeking bariatric surgery (Hall et al., 2013; Hayden et al., 2010; Munoz et al., 2007). These findings,

combined with our results, support the notion that neurovegetative symptoms of depression may be more prevalent and/or severe compared to affective/cognitive symptoms in patients with obesity and elevated depressive symptoms.

These findings on the symptom domains of depression are constrained by the nature of the scales we examined. Given that the obtained factors are influenced by the number of indicators included in the factor analysis, and that a single scale has a limited number of items, the observed factors likely do not fully capture the heterogeneity of depression. For example, two items (overeating and poor appetite) hinted at the potential presence of a fourth factor on the SCL-20 related to the impact of depression on consumptive behavior. However, with only two items this factor may not have been adequately measured. Overeating, and perhaps associated feelings of shame and guilt, might be a feature of depression in this specific population (Goss and Allan, 2009). Another important example is cognition. Commonly used depression rating scales assess cognitive symptoms using only one or two items, which does not allow for a full representation of this construct (Majd et al., 2020). Indeed, core cognitive elements of depression (indecisiveness or difficulty concentrating) were assessed by only one item on the PHQ-9 and no items on the SCL-20. Therefore, use of additional assessment tools that more fully capture cognitive function may be important.

Identifying the factor structure of depressive symptoms in the context of obesity may help identify those constructs that are more central to the concept of depression in this population. More generally, this view is in line with the need to identify moderators of treatment response. There is substantial variability in response to treatment across depressed patients (Nierenberg, 2003). Comorbid psychiatric and medical conditions, prolonged depressive episodes, older age, and severity of illness have been identified as potential negative predictors of treatment response (reviewed by Kornstein & Schneider, 2001; Nierenberg, 2003). In addition, there is some evidence suggesting that obesity or higher BMI predicted poor treatment outcomes in patients with depression (Dennehy et al., 2015; Khan et al., 2007; Kloiber et al., 2007; Papakostas et al., 2005; Uher et al., 2009). Interestingly, it has been found that the effects of higher BMI/obesity on response to antidepressants may be treatment and/or symptom-specific (Green et al., 2017; Jha et al., 2018; Uher et al., 2009). For example, depressed patients with higher BMI were more responsive to venlafaxine than escitalopram, and this improvement was particularly evident on neurovegetative symptoms (Green et al., 2017). Hence, understanding depressive symptomology in the context of obesity will provide insight into more comprehensive assessment tools that capture the heterogeneity of depression. Importantly, this information may inform future efficacy/effectiveness studies to explore whether components of depression respond differentially to treatment. Eventually, these data may help tailor treatment to individual based on presenting symptoms and could improve treatment outcome. This notion is in line with precision medicine approaches that aim for improving outcomes for patients.

Limitations

The results of this preliminary analysis need to be interpreted with caution until replicated. This sample represented moderate depressive symptoms, which may limit generalizability to

severe levels of depression. In addition, this study was (albeit by intent) limited to individuals with BMI ≥ 30.0 kg/m^2 (≥27 if of Asian descent), therefore our findings reported here may not generalize to a broader range of BMI values.

Conclusions

This study supports the idea that depression is not a unidimensional construct and relying only on depression sum-scores (i.e. total score) may mask important information in depressed patients with obesity. In addition, these findings highlight that the aspects of depression that are being measured by depression measures may vary across patient populations. Importantly, the clinical utility of depression measures should consider the capacity of the scales to discern the underlying constructs (or symptom profiles) of depression given that the latter may inform treatment decisions in patients presenting with varying symptom profiles. Finally, a comprehensive assessment tool that measures various aspects of depression, particularly cognitive symptoms, fatigue, anhedonia, sleep, and overeating, in addition to negative emotions/affect, may be needed to better characterize the nature of depression in patients with comorbid obesity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- In patients with depression and obesity the SCL-20 captures two reliable factors: dysphoric mood and anhedonia
- In patients with depression and obesity the PHQ-9 only captures one reliable factor: dysphoric mood
- In these patients, low energy/fatigue, sleep disturbance and overeating were endorsed most
- Neurovegetative symptoms may be more prevalent and/or severe relative to affective/cognitive symptoms in patients with comorbid depression and obesity

Table 1

Subject characteristics

	Total sample
N	409
Sex: N (%) Women Men	287 (70) 122 (30)
Age [years]: Mean (SD)	51.0 (12.1)
BMI [kg/m^2]: Mean (SD)	36.7 (6.4)
Ethnicity/ Race: N (%) Non-Hispanic white Black Asian/Pacific islander Hispanic Other	289 (71) 6 (1) 40 (10) 56 (14) 18 (4)
Annual family income: N/total (%) <$75,000 $75,000– <$150,000 ≥$150,000	93/365 (26) 117/365 (32) 155/365 (42)
Marital status: N/total (%) Married or living with partner Single/divorced/separated/widowed	247/406 (61) 159/406 (39)
Education: N (%) ≤ High school graduate or GED Some college Undergraduate degree Graduate-level work or degree	27 (7) 98 (24) 151 (37) 133 (32)

Table 2.

Eigenvalues for the correlation matrix

	Original results			*Bootstrap results across 2000 resamples*		
	Eigenvalue	**Variance**	**Cumulative variance**	**Mean Eigenvalue (Min, Max)**	**95% CI**	**SD**
SCL-20						
Factor 1	**5.32**	0.71	0.71	**5.38**(4.57, 6.15)	5.37, 5.39	0.24
Factor 2	**1.15**	0.15	0.86	**1.26**(0.93, 1.72)	1.25, 1.26	0.11
Factor 3	0.77	0.10	0.96	0.86 (0.86, 1.20)	0.85, 0.86	0.08
Factor 4	0.54	0.07	1.04	0.63(0.63, 0.88)	0.63, 0.64	0.06
PHQ-9						
Factor 1	**1.28**	0.87	0.87	**1.33** (1.32, 1.33)	1.25, 1.41	0.12
Factor 2	0.45	0.30	1.18	0.55 (0.31, 0.87)	0.55, 0.56	0.07

Table 3.

Rotated Factor Pattern (Standardized Regression Coefficients) of the SCL-20

		Communalities[1]	Factor 1*	Factor 2*	Factor 3*	Factor 4
SCL1	Feeling low energy or slowed down	0.25	−0.09	0.51	0.06	0.10
SCL2	Thoughts of ending your life	0.07	0.26	0.03	−0.06	−0.01
SCL3	Poor appetite	0.21	0.12	0.17	0.21	−0.32
SCL4	Crying easily	0.23	0.43	−0.06	0.17	0.06
SCL5	Feeling of being caught or trapped	0.37	0.60	0.02	0.00	0.04
SCL6	Blaming yourself for things	0.60	0.83	−0.12	−0.00	0.05
SCL7	Feeling lonely	0.34	0.55	0.03	0.02	0.06
SCL8	Feeling blue	0.54	0.61	0.20	0.02	−0.01
SCL9	Worrying too much about things	0.40	0.54	0.04	0.19	−0.06
SCL10	Feeling no interest in things	0.49	0.17	0.62	−0.07	−0.09
SCL11	Loss of sexual interest or pleasure	0.19	0.01	0.39	0.12	−0.02
SCL12	Trouble falling asleep	0.33	0.04	−0.02	0.57	−0.08
SCL13	Feeling hopeless about the future	0.60	0.72	0.08	−0.02	−0.09
SCL14	Thoughts of death or dying	0.14	0.34	0.07	−0.05	0.04
SCL15	Overeating	1.00	0.08	0.09	0.03	0.97
SCL16	Awakening early in the morning	0.19	−0.05	0.07	0.42	0.06
SCL17	Sleep that is restless or disturbed	0.73	−0.01	0.01	0.86	−0.02
SCL18	Feeling everything is an effort	0.63	0.09	0.74	−0.02	0.03
SCL19	Feelings of worthlessness	0.67	0.82	0.02	−0.12	−0.05
SCL20	Feelings of guilt	0.55	0.78	−0.09	0.00	0.039

[1]The estimate of the amount of variance in the indicator explained by the factors. Communalities were calculated as a function of both the factor loadings and the factor correlations, give that an oblique rotation was used.

*Factor 1 was labeled "*dysphoric mood*", Factor 2 was labeled "*anhedonia*" and factor 3 was labeled "*sleep disturbance*"

Table 4.

Factor Pattern of the PHQ-9

		Communalities[1]	Factor 1*
PHQ1	Little interest or pleasure in doing things	0.24	0.48
PHQ2	Feeling down, depressed or hopeless	0.42	0.64
PHQ3	Trouble falling or staying asleep, or sleeping too much	0.008	0.089
PHQ4	Feeling tired or having little energy	0.03	0.17
PHQ5	Poor appetite or overeating	0.003	0.05
PHQ6	Feeling bad about yourself - or that you are a failure or have let yourself or your family down	0.21	0.46
PHQ7	Trouble concentrating on things, such as reading the newspaper or watching television	0.07	0.27
PHQ8	Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0.02	0.15
PHQ9	Thoughts that you would be better off dead, or of hurting yourself	0.03	0.17

[1]The estimate of the amount of variance in the indicator explained by the factor. The communalities are the factor loading squared, given that one factor was extracted.

*Factor 1 was labeled "*dysphoric mood*"

Table 5.

Mean total SCL-20 and factor scores in the entire sample and across groups

	Sample Size	Total score Mean[a] (SD)	Score on *dysphoric mood* Mean[b] (SD)	Score on *anhedonia* Mean[b] (SD)	Score on *sleep disturbance* Mean[b] (SD)
Total sample	409	1.5 (0.5)	**0.17**[1,2] (0.10)	**0.49**[1,3] (0.20)	**0.64**[2,3] (0.33)
Women Men	287 122	**1.5**[4] (0.5) **1.4**[4] (0.5)	0.17 (0.10) 0.17 (0.10)	0.49 (0.21) 0.48 (0.19)	**0.67**[4] **(0.33) 0.56**[4] **(0.33)**
BMI 27- <35 35 - <40 ≥ 40	209 111 89	1.5 (0.6) 1.5 (0.5) 1.5 (0.5)	0.17 (0.10) 0.18 (0.10) 0.16 (0.10)	0.48 (0.20) 0.51 (0.22) 0.49 (0.20)	0.63 (0.35) 0.67 (0.34) 0.64 (0.29)
Age 18- <45 45- <65 ≥ 65	115 248 46	1.6 (0.5) 1.5 (0.6) 1.4 (0.5)	0.19 (0.10) 0.17 (0.10) 0.16 (0.09)	0.52 (0.20) 0.47 (0.20) 0.52 (0.21)	0.62 (0.35) 0.66 (0.33)0.61 (0.34)

[a] the SCL-20 total scores are the average values for the 20 items, ranging from 0 (not depressed at all) to 4 (extremely depressed)

[b] the mean score on each identified factor was estimated by taking the mean of the raw values of items with salient loadings on the factor multiplied by the standardized scoring coefficients

[1] indicates a significant difference between the mean score on the dysphoric mood factor and anhedonia factor (p <0.0001, Cohen's d=1.82)

[2] indicates a significant difference between the mean score on the dysphoric mood factor and sleep disturbance factor (p <0.0001, Cohen's d=1.42)

[3] indicates a significant difference between the mean score on the anhedonia and sleep disturbance factor (p <0.0001, Cohen's d=0.42)

[4] indicates a significant difference across men and women (p <0.05, Cohen's d=0.22 for total score and 0.32 for sleep disturbance factor)

Table 6.

Mean total PHQ-9 and factor score in the entire sample and across groups

	Sample Size	**Total score[1] Mean (SD)**	**Score on *dysphoric mood*[1]**
Mean (SD)			
Total sample	409	13.8 (3.1)	0.40 (0.17)
Women Men	287 122	14.0 (3.1) 13.4 (3.2)	0.41 (0.17) 0.40 (0.16)
BMI 27- <35 35 - <40 ≥ 40	209 111 89	13.9 (3.2) 13.6 (2.8) 13.8 (3.2)	0.41 (0.18) 0.38 (0.15) 0.42 (0.16)
Age 18- <45 45- <65≥ 65	115, 248, 46	14.0 (3.3) 13.6 (3.0) 14.1 (3.3)	0.41 (0.18) 0.40 (0.16) 0.44 (0.16)

[a] the PHQ-9 total score is the sum of all 9 items, ranging from 0 to 27

[b] the mean score on the identified factor was estimated by taking the mean of the raw values of items with salient loadings on the factor multiplied by the standardized scoring coefficients

[1] no significant differences were found in the PHQ-9 total score or the dysphoric mood factor score across sex, BMI categories or age groups (All *p's* > 0.05)