See commentary by McElroy



# Depression, Obesity, and Metabolic Syndrome:
## Prevalence and Risks of Comorbidity in a Population-Based Representative Sample of Mexican Americans

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**ABSTRACT**

***Introduction:*** We examined the prevalence of depression, obesity, and metabolic syndrome and associations between them in a population-based representative cohort of Mexican Americans living on the United States–Mexico border.

***Method:*** The sample in this cross-sectional analysis consisted of 1,768 Mexican American adults (≥ 18 years of age) assessed between the years 2004 and 2010, with whom we tested our central hypothesis of a significant relationship between obesity and depression. Depression was measured using the Center for Epidemiologic Studies-Depression scale (CES-D) with a cutoff score of ≥ 16 for depression and a cutoff score of ≥ 27 for severe depression. We categorized body mass index (BMI) values as obese (≥ 30kg/m$^2$) and later subdivided the obese subjects into obese (30–39 kg/m$^2$[inclusive]) and morbidly obese (≥ 40 kg/m$^2$). Metabolic syndrome was defined using the American Heart Association definition requiring at least 3 of the following: increased waist circumference, elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, elevated blood pressure, and elevated fasting glucose. Weighted data were analyzed to establish prevalence of depression, obesity, and metabolic syndrome. Univariate and multivariable weighted regression models were used to test potential associations between these disorders.

***Results:*** Using weighted prevalence, we observed high rates of depression (30%), obesity (52%), and metabolic syndrome (45%). Univariate models revealed female gender ($P$ = .0004), low education ($P$ = .003), low HDL level ($P$ = .009), and increased waist circumference ($P$ = .03) were associated with depression. Female gender ($P$ = .01), low education ($P$ = .003), and morbid obesity ($P$ = .002) were risk factors for severe depression and remained significant in multivariable models.

***Conclusions:*** In this large cohort of Mexican Americans, obesity, female gender, and low education were identified risk factors for depression. These indicators may serve as targets for early detection, prevention, and intervention in this population.

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The prevalence of obesity in the United States has reached epidemic proportions, affecting over 30% of the adult population over the age of 18 years.[1,2] Worldwide, obesity has a tremendous economic burden,[3,4] with roughly $147 billion dollars in costs attributed to obesity and related health conditions annually in the United States.[5] In addition to the economic burden to society, there is extensive evidence linking obesity to poor physical outcomes, including cardiovascular disease, hypertension, stroke, obstructive sleep apnea, and type 2 diabetes.[3] Obesity is also a contributor to metabolic syndrome,[6] which is a clustering of major cardiovascular risk factors that include a constellation of atherogenic dyslipidemias, elevated blood pressure, increased waist circumference, and elevated glucose.[7] In terms of mental health, obesity and metabolic syndrome have been associated with poorer outcomes, particularly in regard to depression.[3,8–10]

The significant but modest association between obesity and depression has been replicated in many studies.[9,11] A meta-analysis[11] of cross-sectional community studies revealed an elevated odds ratio (OR) of 1.18 (95% CI, 1.01–1.37) for depression in subjects who were obese compared to those who were not, and a meta-analysis[12] of longitudinal studies estimated depression increased the OR of developing obesity to 1.58 (95% CI, 1.33–1.87). The mechanisms for the co-occurrence of these disorders is complex, with proposed biological components such as adipose-induced inflammation,[13,14] hypothalamic-pituitary-adrenal (HPA) axis alterations,[15] and psychosocial factors such as stigma and low self-esteem[16] identified as potential contributors.

Hispanics now comprise the largest ethnic minority group residing in the United States, accounting for 15% of the population and over 46 million people.[17] Interestingly, depression has been identified as the most common mental illness in this ethnic group,[18–20] and studies have suggested that obesity and depression are highly prevalent among Hispanic and Latino populations.[21–23] Within Hispanic and Latino populations, Mexican Americans, who number over 31 million, are the largest single subgroup and the fastest growing ethnic group in the United States, with a 54% increase between 2000 and 2010.[17] Alarmingly, studies that specifically report on Mexican American populations estimate the prevalence of obesity to be between 50% and 70%.[1,24,25] With the increased prevalence of obesity, it is not surprising that obesity-related sequelae such as cardiovascular disease,[26–28] diabetes,[29–31] and metabolic syndrome[32] have also been shown to be significantly more prevalent in Mexican American populations. Given that depression has been associated separately with obesity[9] and metabolic syndrome,[10] examining the

**Clinical Points**

- Our data highlight the association between obesity and depression in Mexican Americans.
- Female patients and those with low education status are particularly vulnerable to obesity and depression.
- Clinician awareness of these risk factors can assist in early identification and treatment.

link between depression, obesity, and metabolic syndrome in Mexican Americans may have significant public health implications and may identify potential targets for future intervention strategies in this vulnerable population.

Herein, we examine the prevalence of depression, obesity, and metabolic syndrome in a randomly selected, population-based cohort of 1,768 Mexican Americans living on the United States–Mexico border as part of a larger Cameron County Hispanic Cohort.[25]

## METHOD

### Study Population

Participants were recruited between the years 2004 and 2010 as part of the Cameron County Hispanic Cohort.[25] Subjects were selected with stratified 2-stage random sampling based on the 2000 US Census tract data (http://www.census.gov/main/www/cen2000.html) in the city of Brownsville, Texas, situated on the United States–Mexico border. Our sample consisted of 1,768 Mexican American adult participants (≥ 18 years of age) who completed a comprehensive questionnaire regarding basic demographic information, medical history, medication use, and social and family history, as described previously.[25] Our sample was predominantly female (n = 1,181 [66%]) with a mean age of 43.3 years (standard error [SE] = 0.69), which did not differ between genders.

In order to test our a priori hypothesis regarding the association between obesity and depression, we included the Center for Epidemiologic Studies-Depression scale (CES-D).[33] This instrument is a 20-item scale developed for epidemiologic studies of depressive symptoms in the general population, with a cutoff score of ≥ 16 suggestive of depression and with established reliability and validity.[33–35] Consistent with prior studies,[35] we further classified individuals as mildly depressed if their CES-D score was 16–26 (inclusive) and severely depressed if their score was ≥ 27. As described previously,[25] body mass index (BMI [kg/m$^2$]) for each subject was calculated based on measured height and weight of each subject with shoes removed by using a portable electronic scale for weight, which was recorded to the nearest 0.2 kg, and a stadiometer for height, which was measured to the nearest 0.2 cm. We categorized BMI values as obese (≥ 30 kg/m$^2$) and later subdivided the obese subjects into obese (30–39 kg/m$^2$ [inclusive]) and morbidly obese (BMI ≥ 40 kg/m$^2$). Metabolic syndrome was defined using the American Heart Association definition,[7] which requires the presence of at least 3 of the following: (1) increased waist circumference of ≥ 102 cm or 40 inches for men, or ≥ 88 cm or 35 inches for women, (2) elevated triglycerides of ≥ 150 mg/dL, (3) reduced high-density lipoprotein (HDL) cholesterol level ≤ 40 mg/dL for men or ≤ 50 mg/dL for women, and (4) elevated blood pressure of ≥ 130/85 mm Hg or use of medication for hypertension, and (5) elevated fasting glucose ≥ 100 mg/dL. Blood samples were taken and aliquots immediately stored at −70°C for a range of clinical and experimental assays. Blood glucose measurement was performed on site, and stored specimens were sent in batches to a CLIA-approved (Clinical Laboratory Improvement Amendments–approved) clinical laboratory for clinical chemistries. All participants provided written informed consent, and this study was approved by the institutional review board of the University of Texas Health Science Center at Houston.

### Statistical Analysis

From the original cohort of 2,583 subjects, 1,768 had complete data and were included in this study. These 1,768 subjects did not differ from the original cohort in terms of age and gender status. To correct the imbalance of the sampling ratios of genders and age groups, and to adjust the sample to population scale, we incorporated age- and gender-adjusted sampling weights into our analysis, as fully described previously.[25] In addition to the sampling weight adjustments, we took into account the potential clustering (correlated data) among subjects within the same household and subjects within the same census blocks. All analyses were performed using SAS version 9.1 (SAS Institute, Inc; Cary, North Carolina) and Stata 10 SE (StataCorp LP; College Station, Texas). For descriptive purposes, demographic and clinical characteristics were analyzed using $\chi^2$ and $F$ tests for categorical and continuous variables across the depression strata. Data are presented as weighted means with standard errors (SEs) for continuous variables and as frequencies and unweighted and weighted percentages for categorical variables. Univariate analysis with weighted logistic regression was performed in order to examine obesity, cholesterol, and metabolic syndrome and demographic characteristics and estimate the odds ratios (ORs) for depression. The variables that had a statistically significant effect at < .05 level in the univariate analyses were examined in multivariable logistic regression models. Given that prior work has noted gender differences for depression[36] and metabolic outcomes,[32,37] we explored the potential effects of these variables separately for men and women. In addition, we focused on cases with severe depression and morbid obesity as this strategy may reduce heterogeneity.[38–40]

## RESULTS

On the basis of the weighted prevalence estimates, we observed that 30% of the sample had CES-D scores in the clinically significant range (≥ 16), with 15% classified as mildly depressed (CES-D scores 16–26 [inclusive]) and 14% severely depressed (CES-D scores ≥ 27). Approximately half of our sample (52%) was obese, with 44% classified as

**Table 1. Demographic and Clinical Variables by Gender**

| Variable | Women (n = 1,163) n (%) (unweighted) | Women (n = 1,163) % (weighted) | Men (n = 605) n (%) (unweighted) | Men (n = 605) % (weighted) | Total (%) n = 1,768 n (%) (unweighted) | Total (%) n = 1,768 % (weighted) |
|---|---|---|---|---|---|---|
| Age, y | 44.32 (0.75)[a] | | 41.46 (1.24)[a] | | 43.33 (0.69)[a] | |
| Spanish preference | 904 (77.7) | 76.7*** | 409 (67.6) | 64.0 | 1,313 (74.3) | 72.2 |
| English preference | 259 (22.3) | 23.3*** | 196 (32.4) | 36.0 | 455 (25.7) | 27.8 |
| Less than high school education | 685 (59.0) | 60.8*** | 288 (47.7) | 45.7 | 973 (55.1) | 55.6 |
| Married | 680 (58.5) | 56.8*** | 447 (73.9) | 72.9 | 1,127 (63.7) | 62.4 |
| Unemployed | 700 (60.2) | 59.0*** | 185 (30.6) | 27.4 | 885 (50.1) | 48.0 |
| BMI | 30.91 (0.36)[a] | | 31.17 (0.32)[a] | | 31.00 (0.27)[a] | |
| CES-D total score | 14.05 (0.68)[a],*** | | 8.80 (0.77)[a] | | 12.22 (0.53)[a] | |
| Obese (BMI ≥ 30) | 624 (53.7) | 49.7 | 298 (49.3) | 54.9 | 922 (51.7) | 52.2 |
| Mild obesity (BMI 30–39) | 513 (44.1) | 40.9* | 256 (42.3) | 50.0 | 769 (43.5) | 44.0 |
| Morbid obesity (BMI ≥ 40) | 111 (9.4) | 9.4* | 42 (6.9) | 5.0 | 153 (8.5) | 8.7 |
| Metabolic syndrome | 546 (47.0) | 47.3 | 257 (42.5) | 42.8 | 803 (45.2) | 45.4 |
| Hypertension | 257 (22.1) | 21.5 | 153 (25.3) | 27.3 | 410 (23.2) | 23.5 |
| Elevated triglycerides | 414 (35.6) | 38.1 | 304 (50.3) | 51.2** | 718 (40.6) | 42.6 |
| Elevated glucose | 480 (41.3) | 39.2 | 310 (51.2) | 50.9** | 790 (44.7) | 43.3 |
| Low HDL | 696 (59.9) | 60.7*** | 248 (41.0) | 41.7 | 944 (53.4) | 54.1 |
| Increased waist circumference | 946 (81.0) | 81.3*** | 336 (55.4) | 58.3 | 1,282 (72.5) | 72.0 |
| Depression (CES-D score ≥ 16) | 410 (35.3) | 34.1*** | 115 (19.0) | 18.8 | 525 (29.0) | 29.7 |
| Mild depression (CES-D score 16–26) | 214 (18.4) | 16.6** | 79 (13.1) | 11.7 | 293 (16.6) | 14.9 |
| Severe depression (CES-D score ≥ 27) | 196 (16.9) | 17.8** | 36 (5.6) | 7.2 | 232 (13.1) | 14.2 |

[a]Values are weighted estimate (standard error).
*≤ .05. **≤ .01. ***≤ .001.
Abbreviations: BMI = body mass index, CES-D = Center for Epidemiologic Studies-Depression scale, HDL = high-density lipoprotein.

**Table 2. Weighted Odds Ratios (ORs)[a] and 95% CIs for Depression (CES-D score ≥ 16) and Selected Risk Factors[b]**

| Risk Factor | Unadjusted OR (95% CI) | Model 1, OR (95% CI)[c] |
|---|---|---|
| Age | 1.01 (0.99–1.02) | |
| Female gender | **2.26 (1.44–3.52)** | **1.93 (1.26–2.96)** |
| Language preference | 1.24 (0.82–1.88) | |
| Less than high school education | **1.63 (1.18–2.26)** | **1.47 (1.05–2.07)** |
| Marital status | 1.37 (0.98–1.92) | |
| Unemployment | 1.39 (0.97–1.98) | |
| Obesity | 1.02 (0.72–1.44) | |
| Cholesterol | 0.99 (0.99–1.00) | |
| Metabolic syndrome | 1.22 (0.87–1.74) | |
| Metabolic syndrome components | | |
| Hypertension | 0.98 (0.67–1.43) | |
| Elevated triglycerides | 0.88 (0.62–1.25) | |
| Elevated glucose | 1.02 (0.72–1.43) | |
| Low HDL | **1.63 (1.13–2.37)** | 1.39 (0.96–2.02) |
| Increased waist circumference | **1.63 (1.04–2.55)** | 1.30 (0.81–2.08) |

[a]Odds ratios reflect risk for depression.
[b]Values in bold are statistically significant.
[c]Simultaneously modeling gender, education, low HDL, and increased waist circumference. Risk factors that were statistically significant in the unadjusted analysis were included in model 1.
Abbreviations: CES-D = Center for Epidemiologic Studies-Depression scale, HDL = high-density lipoprotein.

obese (BMI = 30–39 [inclusive]) and 9% as morbidly obese (BMI ≥ 40). In addition, 45% of the cohort met criteria for metabolic syndrome (Table 1).

Examining the effect of gender, we observed significantly higher mean CES-D depression scores in women compared to men (14.1 ± 0.7 vs 8.8 ± 0.8) ($F_{1,\ 1043} = 27.61$, $P < .0001$). On sociodemographic variables, women compared to men were more likely to report a Spanish language preference (76.7% vs 64.0%) ($F_{1,\ 1043} = 11.30$, $P = .0008$), were more likely to have less than a high school education (60.8% vs 45.7%) ($F_{1,\ 1043} = 13.49$, $P = .0003$), were less likely to be married (56.8% vs 72.9%) ($F_{1,\ 1043} = 13.95$, $P = .0002$), and were more likely to be unemployed (59.0% vs 27.4%) ($F_{1,\ 1043} = 73.50$, $P < .0001$). There was no difference in BMI or prevalence of metabolic syndrome between women and men; however, more men had elevated triglycerides (51.2% vs 38.1%) ($F_{1,\ 1043} = 8.43$, $P = .0038$) and elevated glucose levels (50.9% vs 39.2%) ($F_{1,\ 1043} = 8.37$, $P = .0039$), while more women had lower HDL levels (60.7% vs 41.7%) ($F_{1,\ 1043} = 19.5$, $P < .0001$) and increased waist circumferences (81.3% vs 58.3%) ($F_{1,\ 1043} = 25.6$, $P < .0001$) (see Table 1).

Using weighted univariate logistic regression, we examined the broad CES-D cutoff for depression (CES-D score ≥ 16) for age, gender, obesity, cholesterol, and metabolic syndrome and its subcomponents. Consistent with the raw CES-D scores described above, we found that higher risk for depression was associated with female gender (OR = 2.26; 95% CI, 1.44–3.52; $P < .001$). Our sociodemographic variables included language preference, education, marital status, and employment status; however, only having less than a high school education (OR = 1.63; 95% CI, 1.18–2.26; $P = .003$) was predictive of depression (Table 2). When we examined the subcomponents of metabolic syndrome separately, low HDL level (OR = 1.63; 95% CI, 1.13–2.37; $P = .009$) and increased waist circumference (OR = 1.63; 95% CI, 1.04–2.55; $P = .03$) were associated with a higher risk of depression (Table 2).

In a multivariable analysis including gender, education, low HDL level, and waist circumference, only female gender (OR = 1.93; 95% CI, 1.26–2.96; $P = .001$) and low education status (OR = 1.47; 95% CI, 1.05–2.07; $P = .03$) remained significant (Table 2). No statistically significant result was seen for depression when data were adjusted for age, and age did not alter the association between any of the other variables and depression.

Using a similar strategy, we further classified the CES-D depression scores into mild (CES-D score 16–27) and severe

**Table 3. Weighted Odds Ratios (ORs)[a] and 95% CIs for Depression and Selected Risk Factors[b]**

| Risk Factor | Unadjusted OR (95% CI) | Adjusted OR (95% CI)[c] |
|---|---|---|
| Age | | |
| Mild depression | 1.01 (0.99–1.02) | |
| Severe depression | 1.00 (0.99–1.02) | |
| Female gender | | |
| Mild depression | **1.76 (1.15–2.69)** | 1.32 (0.83–2.24) |
| Severe depression | **3.06 (1.28–7.30)** | **2.73 (1.31–5.69)** |
| Language preference | | |
| Mild depression | 1.57 (0.96–2.55) | |
| Severe depression | 1.00 (0.54–1.82) | |
| Less than high school education | | |
| Mild depression | 1.39 (0.95–2.04) | 1.41 (0.96–2.06) |
| Severe depression | **1.94 (1.25–3.02)** | **1.74 (1.14–2.71)** |
| Marital status | | |
| Mild depression | 1.43 (0.97–2.12) | |
| Severe depression | 1.31 (0.82–2.09) | |
| Unemployment | | |
| Mild depression | 1.20 (0.82–1.75) | |
| Severe depression | 1.62 (0.92–2.83) | |
| Morbid obesity (BMI ≥ 40) | | |
| Mild depression | **2.32 (1.34–4.02)** | **2.02 (1.15–3.54)** |
| Severe depression | **2.65 (1.45–4.85)** | **2.37 (1.28–4.38)** |
| Cholesterol | | |
| Mild depression | 1.00 (0.99–1.002) | |
| Severe depression | 1.00 (0.99–1.004) | |
| Metabolic syndrome | | |
| Mild depression | 1.14 (0.79–1.66) | |
| Severe depression | 1.33 (0.79–2.25) | |
| Metabolic syndrome components | | |
| Hypertension | | |
| Mild depression | 1.17 (0.76–1.78) | |
| Severe depression | 0.80 (0.47–1.37) | |
| Elevated triglycerides | | |
| Mild depression | **0.68 (0.47–0.99)** | **0.61 (0.40–0.91)** |
| Severe depression | 1.13 (0.68–1.87) | 1.13 (0.65–1.98) |
| Elevated glucose | | |
| Mild depression | 1.03 (0.71–1.49) | |
| Severe depression | 1.01 (0.61–1.67) | |
| Low HDL | | |
| Mild depression | **1.66 (1.11–2.46)** | **1.53 (1.03–2.26)** |
| Severe depression | 1.61 (0.91–2.86) | 1.29 (0.72–2.29) |
| Increased waist circumference | | |
| Mild depression | **1.73 (1.13–2.67)** | 1.47 (0.89–2.44) |
| Severe depression | 1.54 (0.75–3.14) | 1.02 (0.50–2.11) |

[a]Reference category compared to nondepressed.
[b]Values in bold are statistically significant.
[c]Simultaneously modeling the effects of gender, education, obesity, triglycerides, HDL, and waist circumference. Risk factors that were statistically significant in the unadjusted analysis were included in adjusted analysis.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein.

(CES-D score ≥ 27) depression as well as obese (BMI = 30–40) and morbid obesity (BMI ≥ 40). In the univariate analyses, we found significant associations for female gender as a predictor of mild (OR = 1.76; 95% CI, 1.15–2.69; $P = .009$) and severe (OR = 3.06; 95% CI, 1.28–7.30; $P = .012$) depression (Table 3). Lacking a high school education (OR = 1.94; 95% CI, 1.25–3.02; $P = .003$) was predictive of severe depression. Morbid obesity was also a significant predictor of both mild (OR = 2.32; 95% CI, 1.34–4.02; $P = .003$) and severe (OR = 2.65; 95% CI, 1.45–4.85; $P = .002$) depression (see Table 3).

Although metabolic syndrome was not a predictor of depression, when we examined its subcomponents separately, a low HDL level (OR = 1.66; 95% CI, 1.11–2.46; $P = .01$) and increased waist circumference (OR = 1.73; 95% CI, 1.13–2.67; $P = .01$) had significantly elevated ORs for mild depression (Table 3). In this model, high triglycerides were protective for mild depression (OR = 0.68; 95% CI, 0.47–0.99; $P = .046$).

We then included the significant risk factors in a multivariable model, which revealed that being morbidly obese (OR = 2.02; 95% CI, 1.15–3.54; $P = .01$) and having low HDL level (OR = 1.53; 95% CI, 1.03–2.26; $P = .03$) were significantly associated with increased risk for mild depression, whereas high triglycerides were protective for mild depression (OR = 0.61; 95% CI, 0.40–0.91; $P = .01$). Using this strategy, female gender (OR = 2.73; 95% CI, 1.31–5.69; $P = .002$), low education status (OR = 1.74; 95% CI, 1.14–2.71; $P = .01$), and morbid obesity (OR = 2.37; 95% CI, 1.28–4.38; $P = .02$) were associated with severe depression (see Table 3). No statistically significant result was seen for depression when data were adjusted for age, and age did not alter the association between any of the other variables and depression.

Examining significant factors separately by gender revealed that morbid obesity was statistically significant for women as a predictor of mild (OR = 2.93; 95% CI, 1.54–5.57; $P = .001$) and severe (OR = 2.77; 95% CI, 1.39–5.51; $P = .004$) depression. Furthermore, low HDL level was a significant predictor for mild depression (OR = 1.67; 95% CI, 1.08–2.61; $P = .02$) only in women. For men, no single variable significantly predicted mild or severe depression.

## DISCUSSION

In this large, randomly selected, population-based sample of Mexican Americans, we observed an alarmingly high prevalence of depression (30%) and putative depression risk factors, obesity (51%), and metabolic syndrome (45%). These prevalence rates are all considerably greater than national estimates of current depression (9%),[41] obesity (33%),[1] and metabolic syndrome (22%),[42] underscoring the epidemic status of these syndromes in the Mexican American population in South Texas.

Our most consistent finding that women were observed to have higher levels of depression, regardless of the cutoff used, is in line with a large body of depression literature.[36,43,44] Prior research has identified puberty and associated sex hormone changes[45] as well as stress reactivity, thyroid hormones, preexisting anxiety, response styles, and stress associated with gender roles[36] as potential risk factors contributing to the increased risk for depression observed among women.

As noted by earlier studies,[46–49] obesity and increased waist circumference were also noted as risk factors for depression. In our cohort, these anthropomorphic findings were especially noteworthy when we examined severe depression and were largely driven by morbidly obese women. Our findings mirror other studies that note women[11,21,50] with morbid obesity[21,50] are at particularly high risk for depression. Although not significant in our sample, the

relationship between metabolic syndrome and depression has also been reported to be stronger in women.[51,52]

Given the common co-occurrence of depression and obesity, a causal relationship between these disorders can be difficult to untangle.[11,53] In a study[48] of the temporal relationship between depression and obesity, obesity at baseline was associated with future depression; however, depressed subjects who were not obese at baseline were not more likely to become obese than were nondepressed subjects. However, a recent meta-analysis[12] of longitudinal studies highlighted the bidirectional relationship between depression and obesity, with 9 studies showing depression increased the odds for developing obesity (OR = 1.58; 95% CI, 1.33–1.87) and 8 studies showing obesity at baseline increased the risk of onset of depression at follow-up (OR = 1.55; 95% CI, 1.22–1.98).[12] One putative mechanism for the relationship between obesity and depression is the secretion by adipocytes of adipocytokines such as interleukins (ILs) (eg, IL-1β, IL-6, IL-8, tumor necrosis factor-α, transforming growth factor-β,) resulting in a state of chronic low-level inflammation in obese subjects.[13] These proinflammatory cytokines cross the blood-brain barrier and can directly influence brain physiology, which may contribute directly to the development of depressive symptoms.[13,14,54] Conversely, the HPA axis activation seen in depression is marked by increased cortisol,[55] which may induce abdominal obesity.[56] Additionally, a recent report found significant but negative genetic correlations between BMI and multiple cortical and subcortical regions, suggesting the same genetic factors that increase BMI could lead to decreases in brain anatomy[57] that in turn could underlie the risk to develop depression.

Although metabolic syndrome was not a significant predictor of depression in our sample, 2 subcomponents of metabolic syndrome, low HDL level and increased waist circumference, were. Low HDL level is known for its associated cardiovascular risk,[58,59] and it has also been linked with depression.[60,61] Of interest, the purported cardiovascular risk effects of low HDL level are believed to be due to a loss of the anti-inflammatory and antioxidative properties of HDL cholesterol.[59,62] This mechanism is consistent with the previously noted hypothesis linking increased inflammatory markers to depression,[13,54,63] and it may account for our findings associating depression with a low HDL level. Our finding of a protective effect of elevated triglycerides is paradoxical given that elevated triglycerides have been found to be predictive of depression in women[51] and older adults.[64] Of note, this finding was only marginally significant for mild depression, and for severe depression the odds ratio was in the expected direction, suggesting an increased risk that was not statistically significant.

There are several limitations to the current study that should be considered when interpreting the results. This study was cross-sectional in nature and therefore cannot address the issues of causality or directionality. In addition, while the CES-D is a well-accepted measure of depressive symptoms,[33,65] it cannot establish chronicity and number of episodes, and it does not account for confounding or comorbid psychiatric conditions. Furthermore, the CES-D does not follow strict *DSM* criteria; however it, has shown a high level of agreement with the *DSM-III* diagnosis of depression, especially when using a more stringent cutoff (CES-D score ≥ 27)[35] as done in our study. Despite these limitations, the breadth and representativeness of the sample allow for an initial exploration of the risk factors associated with severe depression in a Mexican American population and suggest that obesity and related risk factors are playing a central role in this debilitating disease, especially among women.

Depression and obesity are major public health issues in the United States. Lifestyle changes such a healthy diet and increased physical activity are the accepted interventions for addressing obesity[66] and are reported to have beneficial effects in decreasing depressive symptoms.[67] However, promoting a healthy diet and increased physical activity is challenging[68,69] and will require a concerted effort across multiple domains.

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