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Social anxiety symptoms moderate the link between obesity and metabolic function

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ABSTRACT

Background: Obesity is a well-known risk factor for elevated inflammation and insulin resistance. Social anxiety may moderate this relationship, such that individuals who are*both* obese *and* socially anxious may have an even greater risk for elevated inflammation and insulin resistance than those who are obese but not socially anxious; the combination of obesity and social anxiety is markedly stressful.

Methods: The current paper reports secondary analyses from the Biomarker wave of the Mid-Life in the United States (MIDUS) study (N = 1255), a publicly available dataset of American adults. Participants completed a standard scale measuring social anxiety symptoms and had their waist circumference, height, and weight measured by a staff member. They also provided a fasting blood sample that was assayed for CRP, IL-6, HOMA-IR, glucose, and insulin.

Results: The interaction between obesity and social anxiety symptoms was significant. People with a larger waist circumference and more social anxiety symptoms had greater inflammation and insulin resistance relative to those with a larger waist circumference but less social anxiety symptoms. These results were similar for both measures of inflammation and were robust across both the unadjusted and adjusted models. The results were also largely replicated in models using body mass index (BMI) rather than waist circumference as the measure of obesity.

Conclusions: The current findings build on existing work about the health risks of obesity, extending it in an important new direction by demonstrating that these health risks are stronger among those who are also socially anxious. In fact, the magnitude of the relationship between obesity and metabolic function is 1.5 times stronger among those with more social anxiety symptoms. Thus, knowing whether a person is obese only provides one piece of the puzzle; knowing information about both obesity and social anxiety symptoms is critical for understanding who is most at risk for obesity-related health problems. Thus, a critical next step is for intervention scientists to examine health programs tailored to people who are both obese and socially anxious.

1. Introduction

Obesity is a worldwide epidemic; obesity rates have increased globally from 3% to 11% among men and 6% to 15% among women over the past 40 years (Flegal et al., 2012). Moreover, over a half billion people were obese as of 2016 (World Health Organization, 2018). The obesity epidemic is particularly problematic in the U.S.; around 35% of adults in the U.S. were obese as of 2010 (Flegal et al., 2012), and these numbers continue to rise. In fact, researchers have estimated that anywhere between 42–51% of the U.S. population will be obese by 2030 (Finkelstein et al., 2012).

Obesity is also a pressing public health concern; obesity increases risk for a host of medical problems, including Type 2 diabetes mellitus, metabolic syndrome, and atherosclerosis (Dandona et al., 2004; Grundy, 2004; Must et al., 1999; Ritchie and Connell, 2007; Rocha and Libby, 2009). Thus, researchers are keenly interested in understanding physiological correlates of both obesity and obesity-related health problems, like Type 2 diabetes. Inflammation and insulin resistance are two well-studied physiological correlates in this context. For example, Type 2 diabetes, which is highly comorbid with obesity, is characterized as an insulin-resistant state and an inflammatory condition because both inflammation and insulin-resistance are so central to the disease (Dandona et al., 2004; Wellen and Hotamisligil, 2005). In addition, obesity is related to both inflammation and insulin-resistance (Bastard

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et al., 2006; Shoelson et al., 2007; Xu et al., 2003; Zeyda and Stulnig, 2009). For example, people who are obese have higher inflammation relative to those who are not obese, in part because adipose tissue is one source of proinflammatory cytokines (Bastard et al., 2006). Elevated inflammation can also trigger insulin resistance; proinflammatory cytokines alter insulin action by inhibiting downstream signaling of the insulin receptor (Shoelson et al., 2007; Wellen and Hotamisligil, 2005).

The links among obesity, inflammation, and insulin resistance are highly robust (Bastard et al., 2006; Shoelson et al., 2007; Xu et al., 2003; Zeyda and Stulnig, 2009). However, there is also heterogeneity in the strength of these relationships. For instance, although a larger waist circumference is linked to higher inflammation and greater insulin resistance, there is considerable variability in inflammation and insulin resistance among people with an identical waist circumference (Park et al., 2005; Reaven, 2005). Similarly, a higher body mass index (BMI) is correlated with higher inflammation and greater insulin resistance, but there is variability in inflammation and insulin resistance among people with the same BMI (Park et al., 2005; Reaven, 2005). A critical next step is to investigate potential psychological moderators that could explain the heterogeneity in these relationships. Understanding which people with obesity have particularly high inflammation and insulin-resistance would allow intervention scientists an opportunity to tailor health programs for individuals with the greatest need.

This paper explores social anxiety, an anxious state people experience when they anticipate negative evaluations in interpersonally evaluative situations (Leary, 1983; Schlenker and Leary, 1982), as one potential moderator. Social anxiety symptoms vary along a continuum, ranging from little or no symptoms, to subclinical symptoms, to clinically diagnosable social anxiety disorder (Baker et al., 2002; Fresco et al., 2001). People who experience more social anxiety symptoms worry about social situations, fearing they will embarrass themselves and that people won't accept or value them (Stein and Stein, 2008). Although they desire to make a positive impression, they are concerned that they won't be able to, either because they are unsure how to create one, they don't have the ability to do so, or for other reasons (Schlenker and Leary, 1982). Thus, social anxiety represents a potent form of social stress that interferes with a person's basic need to belong and feel connected to other people (Baumeister and Leary, 1995).

Social stressors and other threats to belonging increase risk for elevated inflammation, which consequently increases risk for insulin resistance (Black, 2003; Jaremka and Sunami, 2017). Individuals who are both obese and socially anxious may be particularly at risk for elevated inflammation and insulin resistance, relative to those who are obese but not socially anxious, because the combination of obesity and social anxiety is markedly stressful. Specifically, people with more social anxiety symptoms fear negative social evaluation, and these fears are likely to be realized among those who are also obese. Individuals with obesity frequently experience weight discrimination and weight stigma (Puhl et al., 2008; Puhl and Heuer, 2010), two powerful social stressors. In fact, weight discrimination is one of the most commonly reported forms of discrimination by U.S. adults (Puhl et al., 2008). In addition, some people think it is okay to publicly criticize people who are obese, leading researchers to label weight stigma as the last socially "acceptable" form of bias (Puhl and Brownell, 2001). Because socially anxious people are very reactive to negative evaluation (Clark, 2005), and weight-related bias is highly prevalent (and even accepted) (Puhl et al., 2008; Puhl and Heuer, 2010), experiencing weight-related bias would be especially difficult for obese people who are also socially anxious. On the other hand, a person who is obese but not socially anxious would not react as strongly to weight-related bias because they are not as fearful of negative evaluation. Thus, the combination of both obesity and social anxiety symptoms is particularly socially stressful relative to either obesity or social anxiety on their own, and thus the combination should be linked to elevated inflammation and insulin resistance.

2. Study overview

This paper explores whether social anxiety symptoms moderate the relationship between (a) obesity and inflammation and (b) obesity and insulin resistance. We hypothesize that people who are obese and experiencing more social anxiety symptoms will have higher inflammation and greater insulin resistance relative to those who are obese and experiencing less social anxiety symptoms. To test this hypothesis, we conducted secondary analyses on data from the Biomarker wave of the Mid-Life in the United States (MIDUS) study, a publicly available dataset of American adults. MIDUS included two obesity measures: waist circumference and body mass index (BMI). We used waist circumference as the obesity measure in the primary paper and conducted all analyses both without and with covariates, allowing us to test whether the results were robust to the inclusion of covariates.

We conducted a series of additional analyses, reported in the supplemental material because they are not the primary focus of the paper but they provide additional context for interpreting the primary analyses. First, we repeated the primary analyses using BMI as the obesity measure rather than waist circumference; BMI is heavily influenced by muscle mass and is thus less precise (Rothman, 2008). These analyses investigated whether the results were robust to the operational definition of obesity. We also tested whether general anxiety moderated the link between obesity and metabolic function in a similar fashion as social anxiety symptoms, examining whether the effects were specific to social anxiety. Finally, we tested depressive symptoms as a potential mediator explaining how the combination of social anxiety symptoms and obesity might affect metabolic function, as described further in the supplemental material.

3. Methods

3.1. Procedure

MIDUS is a publicly available series of studies assessing age-related changes in mental and physical health among American adults. The Biomarker Study, conducted between 2004–2009, was one of four subprojects for the MIDUS II parent study (Dienberg Love et al., 2010). Data for the Biomarker Study was collected during a 24 -h overnight visit at the UCLA, University of Wisconsin, and Georgetown University General Clinical Research Centers (GCRC). On Day 1, participants completed questionnaires assessing their medical history, health behaviors, and psychosocial characteristics. On Day 2, they provided a fasting blood sample, used to assess inflammation and metabolic function. Additional information about the inter-relations between the Biomarker study and other MIDUS projects, along with the Biomarker study protocols and codebooks can be found at http://midus.wisc.edu/.

3.2. Participants

A detailed description of the recruitment techniques used to for the Biomarker study can be found in existing published paper (Dienberg Love et al., 2010). People who completed the MIDUS II phone interview and self-administered questionnaire and who lived in the U.S. were invited to participate in the Biomarker study. After excluding people who were unable to be located or contacted, 43.1% (N = 1255) of eligible people participated in the Biomarker study. Participants' average age was 57.32 years (SD = 11.55), and the majority of participants were White (n = 985, 78.5%). The average BMI was 29.77 kg/m^2 with a standard deviation of 6.63; 0.4% of the sample was underweight, 23.4% was normal weight, 35.1% was overweight, and 41.1% were obese (defined as a BMI < 18.00 kg/m^2, between 18.00–24.99, between 25.00–29.99, and > 30.00 respectively). Additional sample characteristics are listed in Table 1.

Table 1
Sample Characteristics.

Characteristic	Category/Description	Frequency(%)	Mean(*SD*)
Race	White	985 (78.5)	–
	Black/African American	215 (17.1)	–
	Other	51 (4.1)	–
	Missing/Refused	4 (0.3)	–
Ethnicity	Hispanic	42 (3.3)	–
	Not Hispanic	1208 (96.3)	–
	Missing/Refused	5 (0.4)	–
Education	Eighth grade or below	14 (1.1)	–
	Some high school/high school graduate	336 (26.8)	–
	Some college/College graduate	629 (50.1)	–
	Graduate/Professional training	273 (21.8)	–
	Missing/Refused	3 (0.2)	–
Marital Status	Married	789 (62.9)	–
	Separated/Divorced/Widowed	305 (24.3)	–
	Living with Someone	23 (1.8)	–
	Never Married	138 (11.0)	–
	Missing/Refused	0 (0)	–
Gender*	Male	542 (43.2)	–
	Female	713 (56.8)	–
Age	Age in years	–	57.32 (11.55)
Social anxiety symptoms	Possible range 1 - 4	–	1.83 (0.55)
Waist circumference	Measured in centimeters	–	97.61 (17.02)
BMI	Measured in kg/m^2	–	29.77 (6.63)

Note. Non-binary options for gender were not provided to participants at the time this data was collected.

3.3. Measures

Participants completed an abbreviated version of the Liebowitz Social Anxiety Scale (LSAS) (Baker et al., 2002; Fresco et al., 2001). Specifically, participants indicated how much anxiety or fear they would experience in 9 different social situations. For example, participants indicated how anxious or fearful they would feel "going to a party" or "being the center of attention". All ratings were made on a scale of 1 "none", 2 "mild", 3 "moderate", and 4 "severe". Responses were averaged to create a composite, with higher numbers reflecting more social anxiety symptoms ($\alpha = 0.852$). Out of a range of 1–4 for the composite score, the average score in this sample was 1.83, with a standard deviation of 0.55. Thus, participants were experiencing mild levels of social anxiety on average, reflecting subclinical social anxiety symptoms.

Participants stood with their feet shoulder width apart while a staff member measured their waist circumference, defined as the narrowest point between the ribs and iliac crest (measured in centimeters to 1 decimal point). Participants provided information about their age, race, and gender. They also indicated whether they had any medical conditions including diabetes, a history of smoking cigarettes (no history versus former or current smoker), or if they were currently on an anti-inflammatory medication (no versus yes).

A staff member collected fasting blood samples between 6:30-7:00am on Day 2 of their GCRC visit. Participants were instructed to avoid strenuous exercise prior to the blood draw. Within 30–120 minutes after collection, a staff member centrifuged the samples and created aliquots. The aliquots were stored in a -60–-80^{0}C freezer until being shipped on dry ice to the MIDUS Biomarker Core Lab. Samples were then stored at -65^{0}C until being assayed. A trained technician assayed the blood samples for C-reactive protein (CRP), interleukin-6 (IL-6), glucose, and insulin. Details of the assay procedures can be found in the supplemental material.

3.4. Analytic strategy

Outliers > 4 *SD* above the sample mean were excluded from analyses (< 0.05% of all data), following prior research from the first author's lab (Jaremka et al., 2013). The distributions of the remaining samples were positively skewed and were thus square root transformed, with the exception of the glucose data that did not require transformation.

We conducted all of the analyses in SPSS 25.0 (IBM, New York) using linear regression. For each outcome, we report coefficients from 2 linear regressions using the main effect of waist circumference, the main effect of social anxiety symptoms, and the waist circumference by social anxiety symptoms interaction as predictors. Specifically, we repeat each analysis, first without and then with covariates, allowing us to test if the results were robust to the inclusion of covariates.

The unadjusted analyses had no covariates except for height, which was included because a person's height heavily contributes to their weight (in addition, including height kept the analyses similar to those reported in the supplemental material, since BMI accounts for height by definition; kg/m^2). The adjusted analyses included covariates that were selected based on their relationships to obesity, inflammation, and insulin resistance. Specifically, we adjusted for gender, age, race (white vs non-white), total number of medical conditions, history of diabetes (no vs. yes), cigarette smoking history (no vs. yes), and current anti-inflammatory medication use (no vs. yes) (Barnes, 2006; Chapman et al., 2009; Cossrow and Falkner, 2004; Geer and Shen, 2009; Gonçalves et al., 2011; Wellen and Hotamisligil, 2005; Yang and Kozloski, 2011).

Significant waist circumference by social anxiety symptom interactions were decomposed in two ways, consistent with recommendations (Aiken and West, 1991). First, we examined the simple slope of waist circumference predicting each dependent measure for lower (-1 SD) and higher (+1 SD) social anxiety symptoms (corresponding to the tests of the slope of each line in the supplemental figures). Second, we tested the simple slope of social anxiety symptoms predicting each dependent measure at smaller (-1 SD) and larger (+1 SD) waist circumference (corresponding to the test of the difference between the end point of each line in the supplemental figures). Conducting both sets of follow-up analyses allowed us to isolate where the effects of interest were occurring.

We conducted three sets of ancillary analyses, reported exclusively in the supplemental material. First, we repeated the primary analyses, but replaced waist circumference with BMI in all analyses, providing a way to test whether the results were consistent across operational definitions of obesity. Second, we tested whether *general* anxiety moderated the link between obesity and either inflammation or insulin resistance. This allowed us to test whether an overall tendency to be

Table 2
Social anxiety symptoms by waist circumference predicting inflammation.

		CRP – unadjusted model	CRP – adjusted model	IL-6 – unadjusted model	IL-6 – adjusted model
	Predictor ↓	*b*	*b*	*b*	*b*
Analytic Model	Age	–	-.005*	–	.007***
	Race	–	.168**	–	.200***
	Gender (0 = male, 1 = female)	–	.298***	–	.204***
	Total number of medical conditions	–	-.026	–	.003
	History of diabetes (0 = no, 1 = yes)	–	.027	–	.006
	History of smoking (0 = no, 1 = yes)	–	.061	–	.087**
	Anti-inflammatory medication (0 = no, 1 = yes)	–	-.026	–	.039
	Height	-.025***	-.014***	-.009***	.0004
	Waist circumference (WC)	.020***	.021***	.013***	.012***
	Social anxiety symptoms	-.017	-.037	-.005	-.00006
	WC x social anxiety symptoms	.008***	.008***	.005**	.004**
Follow-up tests	Simple slope of WC at less social anxiety symptoms	.015***	.016***	.010***	.010***
	Simple slope of WC at more social anxiety symptoms	.025***	.025***	.016***	.015***
	Simple slope of social anxiety symptoms at smaller WC	-.161**	-.181***	-.086*	-.076*
	Simple slope of social anxiety symptoms at larger WC	.127*	.107*	.077*	.076*

Note: Summary of regression analyses reported in the primary results. Waist circumference (WC) and social anxiety symptoms were mean centered. *b* = unstandardized beta coefficient, †$p < .10$, *p < .05, **p < .01, ***p < .001. Lower and higher WC and social anxiety symptoms are defined as +/- 1 standard deviation from the sample mean.

anxious would also moderate the relationship between obesity and either inflammation or insulin resistance, or whether the results were exclusive to social anxiety symptoms. Next, we explored depressive symptoms as a potential mediator that could explain the process through which both obesity and social anxiety symptoms might drive elevated inflammation and insulin resistance.

4. Results

4.1. The combination of waist circumference and social anxiety symptoms predicting inflammation

In unadjusted analyses, people with a larger waist circumference had higher CRP and IL-6 than people with a smaller waist circumference [CRP: $b = 0.020$, $t(1211) = 15.392$, $p < 0.001$; IL-6: $b = 0.013$, $t(1213) = 13.800$, $p < 0.001$]. These effects were qualified by a significant social anxiety symptoms by waist circumference interaction predicting CRP and IL-6 [CRP: $F(1, 1211) = 15.225$, $p < 0.001$; IL-6: $F(1, 1213) = 9.308$, $p = 0.002$; see Table 2 and supplemental Figures 1 and 2]. Follow-up tests revealed that people with a larger waist circumference had higher CRP and IL-6 than people with a smaller waist circumference, both among those with less [CRP: $b = 0.015$, $t(1211) = 9.807$, $p < 0.001$; IL-6: $b = 0.010$, $t(1213) = 9.001$, $p < 0.001$] and more [CRP: $b = 0.025$, $t(1211) = 12.716$, $p < 0.001$; IL-6: $b = 0.016$, $t(1213) = 11.188$, $p < 0.001$] social anxiety symptoms. However, the magnitude of the relationship between waist circumference and inflammation was over 1.5 times stronger among those with more social anxiety symptoms. In addition, among people with a larger waist circumference, those with more social anxiety symptoms had higher CRP and IL-6 than people with less social anxiety symptoms [CRP: $b = 0.127$, $t(1211) = 2.366$, $p = 0.018$; IL-6: $b = 0.077$, $t(1213) = 1.977$, $p = 0.048$]. Interestingly, among people with a smaller waist circumference, those with more social anxiety symptoms had lower CRP and IL-6 than those with less social anxiety symptoms [CRP: $b = -0.161$, $t(1211) = -3.105$, $p = 0.002$; IL-6: $b = -0.086$, $t(1213) = -2.271$, $p = 0.023$]. The interaction of social anxiety symptoms and waist circumference predicting CRP and IL-6, along with all of the simple slopes, remained significant in the adjusted models (see Table 2).

4.2. The combination of waist circumference and social anxiety symptoms predicting insulin resistance

In unadjusted analyses, people with a larger waist circumference had higher HOMA-IR, insulin, and glucose than people with a smaller waist circumference [HOMA-IR: $b = 0.022$, $t(1217) = 21.931$, $p < 0.001$; Insulin: $b = 0.039$, $t(1217) = 22.081$, $p < 0.001$; Glucose: $b = 0.356$, $t(1214) = 11.684$, $p < 0.001$]. These effects were qualified by a significant social anxiety symptoms by waist circumference interaction predicting HOMA-IR and insulin, but not glucose [HOMA-IR: $F(1, 1217) = 12.000$, $p = 0.001$; Insulin: $F(1, 1217) = 15.430$, $p < 0.001$; Glucose: $F(1, 1214) = 0.728$, $p = 0.394$; see Table 3 and supplemental Figures 3–4]. Follow-up tests revealed that people with a larger waist circumference had higher HOMA-IR and insulin than people with a smaller waist circumference, both among those with less [HOMA-IR: $b = 0.019$, $t(1217) = 15.313$, $p < 0.001$; Insulin: $b = 0.033$, $t(1217) = 15.068$, $p < 0.001$] and more [HOMA-IR: $b = 0.026$, $t(1217) = 16.877$, $p < 0.001$; Insulin: $b = 0.046$, $t(1217) = 17.267$, $p < 0.001$] social anxiety symptoms. However, the magnitude of the relationship between waist circumference and both outcomes was around 1.5 times stronger among those with more social anxiety symptoms. Furthermore, among those with a larger waist circumference, people with more social anxiety symptoms had higher HOMA-IR and insulin than people with less social anxiety symptoms [HOMA-IR: $b = 0.122$, $t(1217) = 2.852$, $p = 0.004$; Insulin: $b = 0.298$, $t(1217) = 4.008$, $p < 0.001$]. Among people with a smaller waist circumference, social anxiety symptoms were not significantly related to HOMA-IR or insulin [HOMA-IR: $b = -0.081$, $t(1217) = -1.955$, $p = 0.051$; Insulin: $b = -0.102$, $t(1217) = -1.415$, $p = 0.157$].

The interaction between social anxiety symptoms and waist circumference predicting HOMA-IR and insulin remained significant in the adjusted models. The simple slopes were also consistent with those reported in the unadjusted models (see Table 3).

5. Discussion

Consistent with prior research, people with a larger waist circumference had higher inflammation (CRP and IL-6) and greater insulin resistance (HOMA-IR) than those with a smaller waist circumference. Importantly, social anxiety symptoms moderated the relationship between waist circumference and both inflammation and insulin resistance. Specifically, people with a larger waist circumference had higher inflammation and greater insulin resistance than people with a smaller waist circumference, both among those with less and more social anxiety symptoms. However, the magnitude of the relationship between obesity and both outcomes was around 1.5 times stronger among those with more social anxiety symptoms. In addition, people with a larger waist circumference and more social anxiety symptoms

Table 3
Social anxiety symptoms by waist circumference predicting insulin resistance.

		HOMA-IR – unadjusted model	HOMA-IR – adjusted model	Glucose – unadjusted model	Glucose – adjusted model	Insulin – unadjusted model	Insulin – adjusted model
	Predictor ↓	*b*	*b*	*b*	*b*	*b*	*b*
Analytic Model	Age	–	-.005**	–	.028	–	-.009**
	Race	–	.064	–	1.754	–	.101
	Gender (0 = male, 1 = female)	–	.017	–	−3.177*	–	.110
	Total number of medical conditions	–	-.019	–	-.383	–	-.032
	History of diabetes (0 = no, 1= yes)	–	.390***	–	23.166***	–	.270**
	History of smoking (0 = no, 1 = yes)	–	-.009	–	-.441	–	-.024
	Anti-inflammatory medication (0 = no, 1 = yes)	–	-.044	–	−1.535	–	-.040
	Height	-.006**	-.005*	-.059	-.093	-.012***	-.008†
	Waist circumference (WC)	.022***	.021***	.356***	.239***	.039***	.039***
	Social anxiety symptoms	.021	-.023	-.967	-.320	.098†	.084
	WC x social anxiety symptoms	.006**	.006***	.044	.019	.012***	.012***
Follow-up tests	Simple slope of WC at less social anxiety symptoms	.019***	.018***	—	—	.033***	.032***
	Simple slope of WC at more social anxiety symptoms	.026***	.024***	—	—	.046***	.046***
	Simple slope of social anxiety symptoms at smaller WC	-.081†	-.080*	—	—	-.101	-.125†
	Simple slope of social anxiety symptoms at larger WC	.122**	.125**	—	—	.298***	.29***

Note: Summary of regression analyses reported in the primary results. Wait circumference (WC) and social anxiety symptoms were mean centered. *b* = unstandardized beta coefficient, †$p < .10$, *$p < .05$, **$p < .01$, ***$p < .001$. Lower and higher WC and social anxiety symptoms are defined as +/- 1 standard deviation from the sample mean.

had greater inflammation and insulin resistance relative to those with a larger waist circumference but less social anxiety symptoms. These relationships were identical for both measures of inflammation and were robust to the inclusion of covariates.

The current results extend prior work in an important new direction by demonstrating that knowledge about obesity status is not sufficient for determining a person's risk for elevated inflammation and insulin resistance; knowing about *both* obesity and social anxiety symptoms is critical to understanding health risk. These results support the hypothesis that the combination of obesity and social anxiety is markedly stressful. Specifically, socially anxious people are particularly reactive to negative evaluation (Clark, 2005), and weight-related bias is highly prevalent (Puhl et al., 2008; Puhl and Heuer, 2010). Thus, experiencing weight-related bias as a person with obesity should be especially difficult for those who are also socially anxious.

The HOMA-IR composite uses both glucose and insulin data (Matthews et al., 1985). Thus, we examined the waist circumference by social anxiety symptoms interaction predicting glucose and insulin separately to see which was driving the results. Among those with a larger waist circumference, people with more social anxiety symptoms had higher insulin, but not higher glucose, than those with less social anxiety symptoms. Accordingly, the HOMA-IR results appear to be driven by differences in insulin. A critical next step is to follow-up on these results either with a longitudinal or intervention study, allowing researchers to determine the direction of the effects and whether glucose would also become elevated over time among those who are chronically socially anxious and obese.

Of note, social anxiety scores were relatively low in this sample, with the average score reflecting mild social anxiety symptoms. In addition, the variance of scores around the average was relatively small; the estimated score one standard deviation above the mean was still below moderate levels of social anxiety symptoms. Since the estimates of lower and higher social anxiety symptoms in the analyses were based on +/- 1 SD around the sample mean (as per published recommendations; Aiken and West, 1991), the results largely describe people who have subclinical social anxiety. Thus, it is possible that the difference between people with lower and higher obesity would be even stronger among people with diagnosable levels of social anxiety. Investigating the moderating role of social anxiety symptoms among a clinical sample is an exciting direction for future research.

Interestingly, among people with *a smaller* waist circumference, those with more social anxiety symptoms had lower inflammation than those with fewer social anxiety symptoms. On the other hand, these results did not replicate with insulin resistance as the outcome; social anxiety and insulin resistance were unrelated among those with a smaller waist circumference. Thus, readers should be cautious in interpreting the results for those with a smaller waist circumference. One possible explanation for the inflammation findings is that social anxiety may be experienced differently among people who are not obese relative to those who are obese. Specifically, people with more social anxiety symptoms fear negative social evaluation, and these fears are likely to be realized among those who are also obese. Weight discrimination is one of the most commonly reported forms of discrimination by U.S. adults (Puhl et al., 2008) and leading researchers have labeled weight stigma as the last socially "acceptable" form of bias (Puhl and Brownell, 2001). People with more social anxiety symptoms who are not obese also fear negative social evaluation. However, those fears may not be realized in the context of weight discrimination and weight stigma, if they are realized at all. This difference raises the interesting possibility that there is something psychologically unique to the combination of social anxiety symptoms and obesity. Perhaps social anxiety symptoms centered around weight and weight stigma increases risk for health problems, whereas social anxiety symptoms centered around another topic may be protective with specific health-related outcomes (in this case, inflammation). Due to the nature of the MIDUS data, there is no way to determine the source of people's social anxiety symptoms. However, these interesting data patterns suggest an important need for a study focused on different sources of social anxiety symptoms (e.g., weight, other appearance concerns, personality, social identities).

Waist circumference and BMI, the obesity measures reported in the primary and supplemental analyses respectively, are common and convenient ways to assess obesity. Although they are reasonable operational definitions of obesity, they also have their limitations, notably that neither directly measures percentage of fat or visceral fat. Thus, an important next step would be to replicate these analyses using a sample where obesity was measured with a Dual X-ray Absorptiometry (DXA) scan, a highly accurate but more resource and time-intensive way to assess obesity.

The current finding have potential clinical implications; these data support the theoretical argument that the combination of obesity and social anxiety places people at elevated risk for obesity-related health problems. However, the cross-sectional nature of these data preclude a definitive statement about causality and the direction of the effects. Thus, a critical next step is to examine these links longitudinally. In addition, researchers could consider tailoring health interventions towards people who are both obese and socially anxious to determine whether these effects are causal.

Examining potential mediators that explain how the combination of obesity and social anxiety symptoms might lead to inflammation and insulin resistance is another direction for future research. Depressive symptoms are one promising target because obesity and social anxiety predict changes in depressive symptoms over time, and depressive symptoms predict changes in inflammation over time (Luppino et al., 2010; Stein et al., 2001; Stewart et al., 2009). However, as discussed in the supplemental material, the current paper did not find support for depressive symptoms as a mediator, although caution is warranted in interpreting those results, given their cross-sectional nature. Another potential mechanistic target for future research is activation of the hypothalamic–pituitary–adrenal (HPA) and sympathetic-adrenal-medullary (SAM) axes. The combination of obesity and social anxiety is particularly stressful because weight-stigma is prevalent and socially accepted by many people, as described above (Puhl and Brownell, 2001; Puhl et al., 2008). Stress influences inflammation via the HPA and SAM axes. Specifically, stress activates the HPA and SAM axes, which causes the release of epinephrine and norephinephrine. In turn, these hormones stimulate the release of proinflammatory cytokines. Finally, health behaviors like smoking, diet, and sleep, represent promising potential mechanisms; obesity is linked to a variety of poor health behaviors that may also promote inflammation (Irwin et al., 2016; Yang et al., 2017).

In conclusion, obesity is a worldwide epidemic that has important health consequences (Dandona et al., 2004; Flegal et al., 2012; Grundy, 2004; Must et al., 1999; Ritchie and Connell, 2007; Rocha and Libby, 2009). Inflammation and insulin resistance are two physiological correlates of obesity and obesity-related health problems (Bastard et al., 2006; Shoelson et al., 2007; Xu et al., 2003; Zeyda and Stulnig, 2009). The current research demonstrated that knowing whether a person is obese only provides one piece of the puzzle; knowing information about both obesity and social anxiety symptoms is critical for understanding who is most at risk for obesity-related health problems. Thus, intervention scientists should explore health programs tailored to people who are both obese and socially anxious.

Declaration of Competing Interest

All authors declare that there are no financial conflicts of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.104425.

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