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## Does Co-Morbid Depression Alter the Inverse Relationship between Obesity and Substance Use Disorders?

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### Abstract

**Background**—Substance use disorders and obesity are often inversely related to one another, hypothetically due to competition over shared neurobiological reward circuitry. However, obesity and substance use disorders share common risk factors, such as other psychiatric disorders. It is unknown whether the inverse relationship between obesity and substance use disorders continues to exist in the presence of shared risk factors.

**Methods**—For the current study, we examined the associations between major depression, alcohol and drug use disorders, and overweight/obesity status in a nationally representative sample of U.S. adults (n=40,715).

**Results**—Our findings demonstrated that adults with major depression were more likely to be obese, whereas adults with alcohol or drug use disorders were less likely to be obese. However, the inverse relationship between substance use and obesity continued to exist in adults with co-morbid depression. Adults with depression disorders co-morbid with alcohol (Relative Risk [RR]=0.63, 95%CI=0.47-0.84) or drug (RR=0.54, 95%CI=0.36-0.81) use disorders were less likely to be obese vs. normal weight.

**Conclusions**—Our findings provide support for the proposal that excess food consumption and excess drug use appear to compete over shared neurobiology even when the motivation to self-medicate with either food or substances might be elevated.

### Keywords

Obesity; Addiction; Mood; Depression; Substance Use Disorders

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**Contributors** All authors developed the study hypothesis. Ms. Gearhardt managed the literature searches and took the lead role in writing the manuscript. Dr. Harrison and Dr. McKee undertook the statistical analyses. All authors edited the paper and approved the final manuscript.

**Conflict of Interest** All authors declare they have no conflicts of interests.

## 1. Introduction

Excess food consumption and substance use disorders continue to be major public health challenges. Obesity and use of substances are leading causes of preventable death in the United States (Mokdad et al., 2004). Psychiatric disorders also contribute significantly to worldwide disease burden (Kessler et al., 2005; Greenberg et al., 1999), and are highly comorbid with both obesity (Simon et al., 2006) and substance use disorders (Grant et al., 2004).

Despite the shared comorbidity with psychiatric disorders, obesity and substance use exhibit an inverse relation with each other (Gruchow et al., 1985; Lahti-Koski et al., 2002; Liu et al., 1994; Kleiner et al., 2004; Rohrer et al., 2005; Gearhardt and Corbin, 2009; Warren et al., 2005; Pickering et al., in press). In other words, greater substance consumption is associated with lower body mass indexes (BMI). Substance use disorder diagnoses are also inversely related to obesity (Simon et al., 2006; Pickering et al., 2007; Desai et al., 2009). Although some studies have found either no association (Petry et al., 2008; Mather et al., 2009) or a positive relation (McLaren et al., 2008) between BMI and substance use, a recent longitudinal study found that overweight/obese individuals were less likely to receive a diagnoses of substance or alcohol use disorders at a three-year follow up (Pickering et al., in press).

This inverse relation has led to the hypothesis that palatable foods and addictive substances may compete for the same neural receptors (Kleiner et al., 2004; Pickering et al., in press), as consumption of both food and addictive substances activate the mesolimbic dopaminergic system (Volkow et al., 2008) and endogenous opioid system (Smith and Berridge, 2007). Thus, when the reward system is activated by excess consumption of one substance (e.g., food), desire for and use of the other substance (e.g., alcohol) may be reduced or blocked.

Little research has explored the association between obesity and substance use disorders in the presence of co-occurring psychiatric disorders. We chose to examine this question with major depression, as major depression is prevalent in the population and is associated with an increased likelihood for both obesity and substance use disorders (Grant et al., 2004; Simon et al., 2006). To our knowledge no previous studies have examined the link between obesity and substance use in the presence of a mood disorder. Exploring this question may be especially important, because a mood disorder may encourage self-medication through the excess consumption of both palatable food and addictive substances. Thus, the inverse relation between obesity and substance use disorders may be negated when a mood disorder is present. In contrast, depression may increase the likelihood of either obesity or a substance use disorder, but excess consumption would be isolated to either food or substances potentially due to the proposed reward-related neural competition.

In the current study, we examined the associations between major depression, alcohol and drug use disorders, and overweight/obesity in a nationally representative United States sample. Given the shared neurobiology between food and substance use, we predicted substance use disorders and obesity would more likely co-occur with depression, but that these co-morbidities would be mutually exclusive (i.e., depression would not co-occur simultaneously with both substance use disorders and obesity).

## 2. Methods and Procedures

### 2.1 Participants and procedures

Data for these analyses were taken from the National Institute on Alcohol Abuse and Alcoholism's NESARC study (Wave 1, 2001-2002). Face-to-face personal interviews were

conducted with 43093 non-institutionalized civilians aged 18 and older. All potential respondents were informed about the nature of the NESARC and only participants who consented to participate were included in the study. The NESARC protocol received full ethical approval from the U.S. Census Bureau and the U.S. Office of Management and Budget (Grant et al., 2002). The response rate was 81% and African-Americans, Hispanics, and young adults (age = 18-24) were over-sampled. See Grant (2006) for more details about the sampling, purpose, and weight procedures for the NESARC. The current analyses were conducted for the subsample of NESARC participants with reported height and weight and whose Body Mass Index (BMI) scores indicated normal weight (18.5 BMI) or greater (n = 40715). Underweight participants were omitted from the current analyses due to the relatively small size of this weight class (n=864).

## 2.2 Measures

**Demographics and Body Mass Index information**—Participants provided demographic information including gender, age, race, education, and marital status. Using National Heart, Lung, and Blood Institute standards, Body Mass Index (BMI) scores were calculated using self-reported height and weight (National Institutes of Health, 2004). BMI categories were defined as *normal weight* (18.5-24.9), *overweight* (25.0-29.9), and *obese* (30.0 and higher).

**Psychiatric diagnoses**—Current psychiatric diagnoses (past 12 months) were determined using the Alcohol Use Disorders and Associated Disabilities Interview Schedule – Version for the DSM-IV (AUDADIS-IV), (Grant et al., 2001) which has demonstrated adequate reliability (Grant et al., 2003).

Alcohol use disorders were defined as any DSM-IV Alcohol Abuse or Dependence diagnoses. Drug use disorders were defined as any DSM-IV diagnoses of use disorders of opiates, sedatives, tranquilizers, amphetamines, marijuana, hallucinogens, cocaine, inhalants, heroin, and/or other drugs. Depression was defined as any DSM-IV diagnosis of major depression.

## 2.3 Statistical analyses

Participants in each BMI category (normal weight, overweight, obese) were compared on demographic variables for descriptive purposes.

Analyses were performed to examine the main and interactive effects of depression and substance use disorders (alcohol use disorders, drug use disorders) on BMI status. Multinomial regressions were used to assess the associations of current diagnoses with BMI status, with normal weight individuals as the reference group. Two models (alcohol and depression, and drug and depression) were examined. In each model, participants who had neither diagnosis were the reference group against which participants with co-morbid diagnoses and single diagnoses were compared. Analyses were conducted with Stata version 11 (StataCorp, 2009) using survey (svy) commands to account for the complex sampling design of the NESARC.

## 3. Results

### 3.1 Demographics and rates of psychiatric and drug use disorders by BMI

See Table 1 for demographic characteristics of the sample overall and by the BMI index categories. Compared to overweight and obese individuals, normal-weight individuals tended to be younger, less likely to be married, and more likely to have some college education.

### 3.2 Normal weight, overweight, and obese status in individuals with and without a current psychiatric diagnosis, alcohol use disorder, and drug use disorder

See Table 2 for differences in BMI categories across each model. Individuals with depression, without alcohol or drug use disorders, were more likely to be obese than normal weight. Individuals with alcohol or drug use disorders, without depression, were more likely to be normal weight, than obese, compared to individuals with neither disorder. Individuals with co-morbid drug use disorders and depression had a greater likelihood of being normal weight than obese, compared to individuals with neither drug use disorders nor depression. Similarly, individuals with co-morbid alcohol use disorders and depression were less likely to be obese relative to individuals with neither alcohol use disorders nor depression.

## 4. Discussion

The current study is the first to examine the relationship between obesity and substance use disorders in the presence of a co-occurring psychiatric disorder. The inverse relation between substance use disorders and overweight/obesity status continued to occur in the presence of major depression. Thus, depression may be associated with either excess food consumption or substance use, but not the co-occurrence of both obesity and substance use disorders. This finding is consistent with the hypothesis that excess use of an addictive substance may reduce excess consumption of food, possibly due to shared reward circuitry (Kleiner et al., 2005). The current study also replicated previous findings that depression is associated with an increased likelihood of obesity, and that substance use disorders are significantly associated with a decreased likelihood of obesity (Simon et al., 2006; Pickering et al., in press; Pickering et al., 2007; Desai et al., 2009).

The current findings appear to support the similarities between excess food consumption and problematic substance use. If excess food consumption is capable of competing with addictive substances for similar neural systems, even in the presence of a shared risk factor (i.e., depression), it is possible that reward triggered by overconsumption of palatable foods may be akin to an addictive substance. Excess consumption of palatable food or addictive substances may result in similar reward dysfunction in the dopaminergic system (i.e., receptor downregulation; Johnson and Kenny, 2010; Avena et al., 2008; Wang et al., 2001). Moreover, problematic food consumption and substance use disorders are associated with many of the same behaviors (e.g., cravings, loss of control; Gearhardt et al., 2009), as well as risk factors (e.g., depression; Grant et al., 2004). The current findings appear to provide further support for the similarities between addictive disorders and excessive food consumption (Gearhardt et al., 2009; Volkow et al., 2008).

There are other interpretations that could plausibly explain the current results. First, it is possible that subtypes of depression could contribute to the inverse relationship between obesity and substance dependence in the context of mood disorders. Atypical depression is associated with hypersomnia and weight gain; whereas melancholic depression is linked with insomnia and weight loss (Matza et al., 2003). Thus, if atypical depression is associated with decreased use of substances, but melancholic depression is related to increased consumption of drugs/alcohol, an inverse relation between obesity and substance use disorders could occur due to the link between weight change and depressive subtypes. Yet, in contrast with this explanation, atypical depression relative to melancholic depression has been associated with an increased likelihood of co-occurring drug dependence (Matza et al., 2003). Second, some substance use disorders are related to the development of depression (Raimo and Schuckit, 1998) and malnutrition (Santolaria-Fernández et al., 1995), which could contribute to the current findings.

Although there were a number of strengths of the current research study, there are important limitations to consider. Obesity is used to indicate excess food consumption. Although obesity is strongly related to overconsumption of calorically dense foods, there are also other important factors that contribute to obesity, such as physical inactivity and medication side effects (Marcus and Wildes, 2009). Thus, obesity for some may not be driven by excess food consumption. Due to small base rates, disorders associated with all illicit substances were classified together. Drugs of abuse are heterogeneous in both their rewarding properties, as well as their impact on appetite (Foltin et al., 1998; Bray, 1993). Given an increased sample size, analysis by drug type may find that some drugs do not exhibit the same pattern of results. Eating disorder symptoms were not measured in the NESARC dataset, which precludes us from examining the relationship between disordered eating and substance use disorders (Bulik et al., 2002; Telch et al., 1988). The current data are cross-sectional in nature and future studies would benefit from the use of a longitudinal design to support causal interpretations.

Given these limitations, the current study has important implications. The replication of an elevated comorbidity between obesity and depression suggests that psychiatric treatment providers may need to manage obesity as part of an effective treatment. Furthermore, if the conceptualization of excess food consumption as a possible addictive behavior is correct, there may be a number of important implications in dealing with current obesity epidemic (Gearhardt et al., 2011). The use of therapeutic techniques that are effective in the treatment of substance dependence may also be beneficial in the treatment of obesity, such as craving management and motivational interviewing.

In summary, the current findings suggest that the inverse relation between substance use disorders and obesity is still present in the face of a shared risk factor of major depression. It will be important to replicate these findings, and to determine if findings extend to other psychiatric disorders. Furthermore, the current study replicated previous findings that depression and obesity exhibit an elevated co-occurrence and that obesity and substance use disorders are inversely related to one another. These findings, interpreted in the context of previous research, may provide further evidence for the similarities between excess food consumption and problematic substance use.

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**Table 1**

Distribution of Demographic Characteristics and Diagnoses by BMI categories

	All		Normal Weight <sup>a</sup>		Overweight		Obese	
	n	%	n	%	n	%	n	%
<b>Gender*</b>								
Male	17,937	49.1	5,957	40.3	7,856	59.4	4,124	48.5
Female	22,778	50.9	10,246	59.7	6,777	40.6	5,755	51.5
<b>Race/Ethnicity*</b>								
White, non-Hispanic	23,115	70.9	9,905	72.6	8,282	71.1	4,928	67.6
Black, non-Hispanic	7,775	11.1	2,367	8.5	2,715	10.8	2,693	16.0
Other, non-Hispanic	1,879	6.4	1,023	8.4	557	5.3	299	4.5
Hispanic	7,946	11.6	2,908	10.5	3,079	12.8	1,959	11.9
<b>Age at Wave 1 (mean, SD)*</b>	45.2, 37.3		43.3, 29.3		46.7, 29.0		46.4, 21.7	
<b>Marital Status at Wave 1*</b>								
Married	19,822	58.7	7,239	53.5	6,853	63.5	4,803	60.3
Not Currently Married	20,893	41.3	8,964	46.5	7,780	36.5	5,076	39.7
<b>Education at Wave 1*</b>								
< HS graduate	7,387	15.6	2,582	13.6	2,738	15.9	2,067	18.5
HS graduate	11,835	29.2	4,467	27.5	4,206	29.1	3,162	32.5
Some college	21,493	55.2	9,154	58.9	7,689	55.0	4,650	49.0
<b>Diagnoses<sup>#</sup></b>								
Alcohol Use Disorders <sup>b</sup>	3,230	8.7	1,383	44.2	1,183	36.7	664	19.1

	All		Normal Weight <sup>d</sup>		Overweight		Obese	
	n =	%	n	%	n	%	n	%
Drug Use Disorders <sup>c</sup>	750	2.1	364	49.2	237	32.8	149	18.0
Depression <sup>d</sup>	2,957	7.1	1,176	41.1	859	29.2	922	29.7
No Diagnosis <sup>e</sup>	31,724	77.4	12,685	40.9	11,645	37.0	7,394	22.1

n (unweighted) % (weighted);

\*  $p < .001$ ;

<sup>#</sup>For Diagnoses, frequencies by group indicate the percentage each group represents of the overall sample for each diagnosis.

<sup>a</sup>Groups are defined by BMI (body mass index) scores. Normal Weight = 18.5-24.9; Overweight = 25-29.9, and Obese = 30.

<sup>b</sup>Alcohol use disorders diagnosis is defined as any past 12 month DSM-IV Alcohol Abuse or Dependence diagnoses.

<sup>c</sup>Drug use disorders diagnoses is defined as any past 12 month DSM-IV diagnoses of use disorders of opiates, sedatives, tranquilizers, amphetamines, marijuana, hallucinogens, cocaine, inhalants, heroin, and/or other drugs.

<sup>d</sup>Depression diagnosis is defined as any past 12 month DSM-IV diagnosis of major depression.

<sup>e</sup>No diagnosis of alcohol use disorders, drug use disorders, or depression.

**Table 2**

Relative Risk Ratios for Diagnoses by Body Mass Index (BMI) Categories (n=40,715)

	Relative Risk Ratios (95% Confidence Intervals)	
	Overweight vs Normal (ref)	Obese vs Normal (ref)
Alcohol & Depression	0.62 (0.47-0.80) ***	0.63 (0.47-0.84) **
Alcohol without Depression	0.98 (0.86-1.10)	0.80 (0.69-0.92) **
Depression without Alcohol	0.83 (0.73-0.94) **	1.46 (1.29-1.66) ***
Neither Alcohol nor Depression	1.00	1.00
Drug & Depression	0.58 (0.37-0.90) *	0.54 (0.36-0.81) **
Drug without Depression	0.79 (0.63-1.00)	0.70 (0.54-0.91) **
Depression without Drug	0.80 (0.71-0.91) **	1.38 (1.22-1.55) ***
Neither Drug nor Depression	1.00	1.00

\*  
 $p < .05$ ;\*\*  
 $p < .01$ ;\*\*\*  
 $p < .001$  with neither diagnosis and normal weight BMI as referents Note: Sex, age, race, education, and marital status were evaluated as potential covariates but did not substantively change the pattern of results.