Obesity: Is it a Mental Disorder?

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ABSTRACT

Objective: Using Wakefield's conceptualization of mental disorder as "harmful mental dysfunction" (Wakefield, Am Psychol, 47, 373–388, 1992), we examined the evidence for including obesity as a mental disorder in DSM-V.

Method: We searched computer databases and examined reference lists from review articles published in the last 10 years to identify empirical papers relevant to the present review.

Results: Obesity is a condition of heterogeneous etiology that is harmful for most individuals. However, there is scant evidence that obesity, in general, is caused by mental dysfunction. Although recent work examining the neurocircuitry of energy balance has suggested that mental dysfunction may be involved in the etiology of specific obesity phenotypes, findings are too preliminary to support classification of obesity as a mental disorder. Nevertheless, there is evidence that obesity is related to mental disorder and many of the medications used to treat psychiatric illness.

Discussion: There is little evidence for including obesity as a mental disorder in DSM-V. However, results confirm the importance of monitoring adiposity routinely among patients with psychiatric illness. © 2009 American Psychiatric Association.

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Introduction

Publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (i.e., DSM-V) is on the horizon, and there is increasing interest in the role that obesity might play in the psychiatric nomenclature. Studies have documented high rates of obesity among individuals with binge eating disorder, bipolar disorder, major depressive disorder, schizophrenia, and other diagnoses.[1–5] Moreover, there is evidence that obesity negatively impacts illness course and response to treatment in some of these groups.[6,7] Epidemiologic studies have found a positive association between obesity and several forms of mental illness in general population samples,[8–11] indicating that comorbidity observed in clinic studies is not simply a detection artifact. Finally, similarities among obesity, drug addiction, and compulsive behaviors have led some observers to conclude that a form of obesity characterized by "compulsive food consumption" (p. 708) should be included as a mental disorder in DSM-V.[12–14]

In this article, we examine the evidence for including obesity as a mental disorder in DSM-V. To this end, we begin by defining what is meant by the term "mental disorder." Using our selected definition as a guide, we then review the extant literature with an eye to determining whether obesity might be considered a mental disorder. Finally, we consider an alternative approach to incorporating obesity in DSM-V that uses body mass index (BMI) as a dimensional index of adiposity.

What Is a Mental Disorder?

To address the question of whether or how obesity reflects mental disorder, one must first have a clear understanding of how the concept is defined. This is challenging, however, because there is no consensus about what constitutes disorder, as multiple observers have noted.[15–17] Arguably, the two most influential definitions of mental disorder are those employed by the World Health Organization (WHO) in the ICD-10 Classification of Mental and Behavioral Disorders[18] and the American

Psychiatric Association (APA) in the various editions of the DSM beginning with DSM-III.[19] In ICD-10,[18] the term disorder is used to "imply the existence of a clinically recognizable set of symptoms or behavior associated in most cases with distress and with interference with personal functions" (p. 11). The authors further specify that "social deviance or conflict alone, without personal dysfunction should not be included in mental disorder as defined here" (p. 11). Similarly, the most recent edition of the DSM (i.e., DSM-IV-TR)[20] conceptualizes mental disorder as a "clinically significant behavioral or psychological syndrome or pattern that occurs in an individual and that is associated with present distress (e.g., a painful symptom) or disability (i.e., impairment in one or more important areas of functioning) or with a significantly increased risk of suffering, death, pain, disability, or an important loss of freedom" (p. xxxi). Like ICD-10, DSM-IV-TR specifies that "deviant behavior" and conflicts between an individual and society cannot be classified as mental disorders unless "the deviance or conflict is a symptom of a dysfunction in the individual" (p. xxxi). Moreover, the clinically significant syndrome or pattern of behavior must not "merely be an expectable and culturally sanctioned response to a particular event," e.g., the death of a loved one (p. xxxi).

The ICD-10 and DSM definitions make several useful points that are relevant to the question of obesity as a mental disorder. For example, both conceptualizations emphasize that mental disorders involve personal (i.e., within the individual) dysfunction and are associated with distress, disability, or interference in other aspects of an individual's life. They also distinguish mental disorders from other nonpsychiatric problems in living including conflicts between an individual and society.

Nevertheless, there has been substantial criticism of the leading approaches to conceptualizing mental disorder, especially the approach employed by the various editions of the DSM.[17,21–23] In particular, the DSM-IV-TR definition of mental disorder is so broad that it may be used to either accept or reject the notion that obesity is a mental disorder. Thus, we turned to the work of Jerome Wakefield whose definition of mental disorder as "harmful mental dysfunction" (p. 384)[17] has been proposed for inclusion in DSM-V.[24] Specifically, Wakefield notes that although the current DSM definition of mental disorder has a number of strengths, its failure to explicate key constructs such as "dysfunction" leads to a lack of clarity about what does and does not qualify as a mental disorder. For example, DSM-IV-TR states that mental disorders must not be "expectable and

culturally sanctioned" responses to events (p. xxxi). However, as Wakefield[17,23] points out, some mental disorders may be quite expectable given the context [e.g., post-traumatic stress disorder (PTSD) following a severe trauma]. Moreover, there are many forms of unexpected, culturally unsanctioned behavior (e.g., bad manners, petty crime) that are not considered to be mental disorders.[24]

In an effort to improve the validity of the mental disorder construct, Wakefield[17,23] has proposed an alternative definition based on the notion of harmful dysfunction. He writes, "A condition is a mental disorder if and only if (a) the condition causes some harm or deprivation of benefit to the person as judged by the standard's of the person's culture, and (b) the condition results from the inability of some mental mechanism to perform its natural function, wherein a natural function is an effect that is part of the evolutionary explanation of the existence and structure of the mental mechanism" (p. 385).[17] Wakefield's concept of "harm" is similar to the distress and interference/disability components of both the ICD-10 and DSM conceptualizations of mental disorder. The requirement that dysfunction be present enables the user to distinguish between unexpected and harmful internal conditions that are not, in fact, disorders (e.g., illiteracy, greed, normal reactions to external stressors) and disordered presentations, which may (e.g., PTSD in response to severe trauma) or may not (e.g., auditory hallucinations related to schizophrenia) be expectable given the circumstances.[24] Although some have criticized Wakefield's conceptualization of mental disorder on various grounds,[16,25–28] we think that it provides a useful heuristic by which to evaluate the relation of obesity to psychiatric illness and thus have elected to adopt the "harmful mental dysfunction" concept in this article. Of particular relevance is the notion that "dysfunction exists when a person's internal mechanisms are not able to function in the range of environments for which they were designed" (p. 243).[23] As detailed below, one issue in evaluating obesity as a mental disorder involves determining the extent to which excessive weight gain is due to a dysfunction of internal mechanisms versus a mismatch between properly functioning internal mechanisms and an increasingly obesogenic environment.

Method

Guided by Wakefield's[17,23] conceptualization of mental disorder as harmful mental dysfunction, we identified

two major questions to be addressed by this review: (1) is obesity harmful? and (2) is there evidence that obesity is caused by mental dysfunction? To place these questions in the appropriate context, we determined that it was necessary first to provide a brief overview of what is meant by the term "obesity." Because the literature on the etiology and correlates of obesity is ever-expanding, we began by searching computer databases (e.g., MED-LINE, PsychINFO) for review articles published in the last 10 years in major journals. Reference lists of these articles were then used to identify empirical papers for review. In addition, we conducted targeted searches of computer databases to identify articles relevant to specific research methodologies (e.g., neuroimaging) or specific psychiatric correlates of obesity (e.g., depression, psychotropic medication). Search terms included, but were not limited to, obesity, overweight, adipose tissue, and body fat distribution combined with etiology, overeating, impulsivity, depression, reward, stress, and neuroimaging. The results of our selective review are presented below.

Results

What Is Obesity?

Obesity refers to an excess of body fat. In the broadest sense, obesity results from an imbalance between energy intake and energy expenditure; that is, when an individual ingests more than the body expends, excess energy intake is stored in body fat cells that enlarge or increase in number. At present, there is no clear division between normal and abnormal levels of fat.[29] However, body mass index (BMI), a ratio of weight to height calculated by weight in kilograms divided by the square of height in meters, is widely utilized to define obesity operationally given its robust associations with adiposity (i.e., BMI <18.5, underweight; BMI 18.5–24.9, normal weight; BMI 25–29.9, overweight; BMI ≥30, obese)[30] and medical comorbidity.

The prevalence of obesity has been increasing worldwide, and the WHO has estimated that globally there are 300 million obese individuals.[31] In the United States, the prevalence of obesity in adults aged 20 years and older doubled between 1980 and 2002, whereas rates in children aged 6–19 years tripled.[32] In 2003–2004, 32.2% of US adults and 17.1% of US children and adolescents were obese.[32] The prevalence of obesity in the United States varies by racial/ethnic group in women (rates for Non-Hispanic White, Mexican American, and Non-Hispanic Black women are 30%, 42.3%, and 53.9%,

respectively), but not men.[32] As documented below, the worldwide increase in rates of obesity will have profound health consequences.

Is Obesity Harmful?

There is little question that obesity is harmful for most individuals [but see Ref. 33]. The medical consequences of excess body fat are manifold and can be divided into those due to the added weight of the extra fat (e.g., osteoarthritis) and the metabolic changes associated with adiposity (e.g., diabetes).[34] Obesity is a risk factor for cardiovascular disease, diabetes, hypertension, kidney disease, obstructive sleep apnea, osteoarthritis, and several forms of cancer (i.e., colon, breast, esophageal, uterine, ovarian, kidney, and pancreatic).[35] The increased rate of mortality among obese persons, relative to lean individuals, is well-documented.[36]

Obesity also is associated with significant psychosocial impairment. Obese individuals are subject to weight-based stigmatization in a variety of settings,[37] and generally report poorer quality of life compared with lean individuals.[38] With respect to psychiatric correlates, epidemiologic studies have found positive associations between obesity and mood disorders, anxiety disorders, eating disorders, and personality disorders.[8–11,39] These relationships appear to be especially strong for women[40,41] and for individuals with more severe obesity (i.e., BMI ≥ 35),[8,10] although associations between excess body fat and psychiatric illness also have been documented in men[11] and in more moderately overweight individuals.[9] Finally, prospective longitudinal studies have shown that obesity predicts the onset of psychiatric symptoms[42–45] and vice versa.[46–48]

At a societal level, there are profound economic consequences associated with obesity in the form of direct medical costs and indirect costs (e.g., income lost from decreased productivity, worker absenteeism, restricted activity).[49] The health care costs related to obesity were estimated to account for 9.1% of US medical expenses in 1998,[50] and if current trends continue, obesity will account for 16% of US health care expenditures by 2030.[51] Studies conducted in European Union states also have documented that obesity-related health care accounts for a significant proportion of national health expenditures.[52] In consideration of the morbidity and mortality associated with obesity,[53] the Council of The Obesity Society recently concluded that obesity should be declared a disease.[54]

Is There Evidence That Obesity Is caused by Mental Dysfunction?

To consider whether obesity is caused by mental dysfunction, it is necessary first to provide a brief overview of current thinking about the etiology of obesity. Obesity research encompasses work in economics, sociology, epidemiology, nutrition, psychology, and biology, and a complete review is beyond the scope of this article. Nevertheless, there is consensus that the etiology of obesity is multifactorial such that a genetic diathesis interacts in an intricate fashion with individual and environmental factors that promote the expression of a heterogeneous condition. Moreover, there is agreement that given the primacy of nutrition for survival, humans have developed diverse and redundant mechanisms that favor energy intake. In the current US socioeconomic context, which is characterized by the availability of cheap, palatable (i.e., high in sugar and fat) food and a decrease in the amount of physical energy required to sustain survival, the multiple mechanisms that promote energy ingestion are no longer adaptive, but rather promote the development of obesity.[55]

There have been important advances in genetics and basic work serving to explicate the manifold central and peripheral signals that are involved in the regulation of energy balance in humans (for further information, the reader is referred to reviews of the biology of obesity[56] and to the extensive literature that details neural networks[57–59] and adipose tissue functions[60,61]). Research from family history and twin studies has documented that 40%–70% of the variance in obesity can be accounted for by genetic factors.[62] The identification of several monogenic mutations that cause obesity has helped elucidate etiologic pathways associated with genetic obesity syndromes[63]; however, these monogenic disorders account only for a small fraction of cases with early onset obesity. The preponderance of evidence indicates that a larger number of genes with small effects, but which occur commonly in the general population, explain most weight variation in humans.[64,65] The introduction of genome-wide association studies has promoted the identification of genes associated with ordinary obesity[66]; for example, common variants in the fat mass and obesity-associate (FTO) gene are related to BMI and hip circumference.[67,68] Nevertheless, the impact of these common genetic variants probably will be in influencing individual responses to environmental variables such as type of diet.[64] Thus, risk may ultimately be understood best by explicating gene environ-

ment interactions that impact appetite, satiety, activity levels, and the biology of fat storage.

Conceptualizations of the complex circuitry that comprises the internal system that regulates energy balance have advanced significantly. Central factors include homeostatic mechanisms in the hypothalamus and brainstem, reward circuitry in limbic and paralimbic structures, and cognitive mechanisms in the prefrontal and association cortices, which interact with peripheral signals from the gut, pancreas, liver, adipose tissue, and muscle.[69] Although specific examples of central factors that may relate to potential psychiatric aspects of obesity are considered below, it is important to acknowledge the diversity and redundancy of signals involved in energy balance. The caudal brainstem receives nutrition information from the taste buds and gut and controls the machinery involved in food ingestion. The hypothalamus is the major site for integration of nutrient balance information and coordination of adaptive responding. Cortico-limbic pathways are involved in the interaction with the environment in the procurement and consumption of food.

Finally, it may be useful to think of the etiology of obesity as involving more broadly conceived host and environmental factors.[70] Additional host factors may include intrauterine development,[71] gut microbiota,[72] and sleep.[71] Environmental factors include the availability of inexpensive, palatable foods and decreases in physical activity. Recent research also has considered an array of novel environmental factors that may contribute to increasing rates of obesity including viruses,[73] toxins,[74] drugs,[70] and stress.[55]

In summary, regulation of energy intake is crucial to human survival and consequently is protected by numerous redundant and overlapping central and peripheral processes. Clinical obesity reflects alterations in remarkably complex internal and environmental milieus that combine to form multiple pathways that result in obesity. Given the multiplicity of factors implicated in the etiology of obesity and the diversity of the resulting phenotypes, there is little evidence that supports a conclusion that obesity is a mental disorder. In fact, epidemiological observers have concluded that changes in prevalence rates of obesity may be largely due to modest changes in calorie intake and energy expenditure leading to a shift in population weights.[75] For example, if a person's daily energy intake exceeded expenditure by 100 kcal (e.g., a medium apple), the excess calories would lead to a weight gain of more than 10 pounds in a year.[76]

Are There Subtypes of Obesity Caused by Mental Dysfunction?

If there is little evidence that obesity, in general, is caused by mental dysfunction, it is possible that dysfunction can be implicated in individual cases of obesity. Moreover, it is possible that there is dysfunction "in the processing of psychological meanings that form the 'software' of the brain" (p. 24)[24]; in other words, neurological processes may be functioning as designed, but it is possible that the connection between these processes and the environment has become mismatched in some obese individuals. Several lines of research have increased interest in the potential dysfunction of central pathways that may be involved in obesity-related eating behavior. To explicate the notion that certain central functions may be involved in promoting or maintaining obesity, we first make a distinction between homeostatic and nonhomeostatic eating.[77] Then, we describe research related to two specific central pathways, one associated with homeostatic control of eating behavior and the other associated with nonhomeostatic eating, that serve as exemplars of the potential role of mental dysfunction in the pathophysiology of specific forms of obesity.

Homeostatic Versus Nonhomeostatic Eating

Central factors are involved in every aspect of eating behavior, and for conceptual purposes it is useful to make a distinction between homeostatic and nonhomeostatic eating. Homeostatic eating is governed by a complex neural regulatory feedback system designed to preserve energy balance and protect minimal levels of adiposity.[77] The hypothalamus serves to integrate nutrition and other information from orexigenic and anorexigenic peptides that are sensitive to circulating leptin and other hormones and metabolites. Second-order neurons in the paraventricular nucleus of the hypothalamus (PVH) are associated with autonomic and neuroendocrine functions, in particular, regulation of the hypothalamic-pituitary-adrenal (HPA) axis and stress response.

Nonhomeostatic eating refers to behavior that is initiated in the absence of any energy depletion signal. That is, information from the cortex and limbic system easily overrides hypothalamic regulatory information, and promotes energy ingestion.[77,78] As a result, individual differences in responsiveness to food-related cues can markedly affect energy intake. The prefrontal cortex receives information from external and internal sources and translates available homeostatic and external information into behavioral responses. In this regard, the right prefrontal cortex has been implicated in behavioral restraint and self-control[79]; damage to this area is associated with the "Gourmand" syndrome, which involves excessive intake of palatable food.[80] Reward from food, a crucial aspect of nonhomeostatic eating, involves a distributed neural network including the nucleus accumbens and ventral pallidum in the ventral striatum, the ventral tegmental area in the midbrain, and the prefrontal cortex, hippocampus, and amygdala.[69] Hedonic processes interact with homeostatic processes, but it is as yet unclear how to operationalize various aspects of the central control of food intake for human studies.

Homeostatic Eating, Stress, and Obesity

The notion that stress-related eating contributes to the development of obesity is not new,[81] and there is a diverse body of literature that provides indirect support for this idea. For purposes of this review, we consider evidence that the effects of chronic stress on central functioning may be a driver of human obesity. Observers have hypothesized that the combination of ongoing stress and the wide availability of inexpensive, highly palatable foods promote the development of overeating and obesity, in particular, abdominal obesity, in vulnerable individuals. Specifically, some people may overeat to modulate activity of the chronic stress network and reduce negative affect.[82] Thus, although the central mechanisms to cope with stress may be operating as designed, there may be a mismatch between these stress-response mechanisms and the current environment. Here we briefly examine evidence that stress effects on central functioning provide a plausible pathway that contributes to the development of obesity. Almost all available evidence is suggestive, rather than confirmatory, and the human literature is rife with methodological difficulties (in particular, the operationalization of chronic stress, which varies widely across studies). Nevertheless, selected findings from the animal literature and human studies linking stress and obesity are considered in turn.

There is an extensive animal literature that documents that the HPA axis is a crucial mediator of the vertebrate stress response system, which serves to maintain homeostasis and coordinate the organism's behavioral responses to internal and external threats.[83] Findings from this work indicate that although increased secretion of glucocorticoids (GCs) during acute stress inhibits HPA activity and decreases eating, the chronic effects of GCs are excitatory and associated with increased food

consumption.[82] High concentrations of GCs increase expression of corticotropin-releasing factor (CRF) in the HPA to enable the chronic stress network. Elevated GCs in the presence of insulin drive the intake of highly palatable foods, which mitigates unpleasant affect consequent to stress in the nucleus accumbens and prefrontal cortex.[84] Finally, elevated GCs promote the development of abdominal fat depots.[82] Animal studies that have manipulated GCs and insulin have documented that the joint presence of high cortisol and high insulin drives preference for fat intake.[85] Thus, animal data provide suggestive evidence that stress-induced eating occurs in animals and a similar phenomenon may occur in humans.

Numerous human studies have examined the impact of stress on eating. Greeno and Wing,[86] in a widely cited review, presented evidence for individual differences in stress-induced eating, and concluded that restrained eating predicts stress-induced eating in women. However, they documented the absence of direct tests of the hypothesis that stress leads to weight gain or the development of obesity. Epel et al. in a series of studies (see Ref. 87 for review), documented that individuals who responded to laboratory stressors with high levels of cortisol were likelier than low cortisol responders to ingest more calories after the stressor. In a subsequent field study, they demonstrated that daily stressors were related to greater intake of snack foods among high cortisol responders.[88] However, if stress-related eating drives human obesity one would expect differences between obese and lean individuals in stress-related eating. Torres and Nowson[89] reviewed several early studies comparing obese and lean individuals. Only one investigation[90] documented increased calorie intake in response to stress among obese compared with lean persons.

Several prospective studies have examined whether stress is associated with weight gain over time. For example, Van Strien et al.[91] examined the hypothesis that low emotional eaters would gain less weight in response to negative life events than high emotional eaters. Only male emotional eaters who experienced several negative life events exhibited greater increases in BMI over a 6-month period. In a study of more than 5,000 Finnish twin pairs, Korkeila et al.[92] examined the effects of baseline stress on the odds of substantial weight gain (more than 10 kg) at 6- and 15-year assessments. High levels of stress at baseline predicted major weight gain in men whereas neuroticism and low life satisfaction predicted weight gain in women. These effects were observed at 6 years, but were attenuated at 15 years. Finally, data from the Whitehall II study, which included almost 8,000 male and female British workers, were utilized to evaluate whether work stress had a differential effect on weight gain among lean and overweight individuals.[93] Results indicated that work stress was associated with subsequent weight gain among overweight and obese men, and weight loss among lean men. These bi-directional associations were not observed in women.

In another line of research, Bjorntorp and colleagues[94–96] have hypothesized that psychosocial stress may lead to chronic arousal of the HPA axis and increased cortisol secretion, which in turn promote increased insulin resistance, disturbed lipid and glucose metabolism, and accumulation of visceral fat. The approach taken in this work has been to identify psychosocial or socioeconomic handicaps and then to document increased cortisol secretion or HPA perturbations, and visceral and overall adiposity (see Ref. 97 and 98 for reviews). A review of this literature[97] concluded that although most of the available data are circumstantial, there is evidence that the HPA and other central regulatory systems are involved in the development of obesity.

Taken collectively, there is suggestive evidence that there may be a sub-group of stress-responsive obese individuals with a diathesis to overeat palatable food and gain weight over time. However, there is scant evidence that such obesity-related overeating should be considered a mental disorder. Rather, it probably is most useful to consider whether obese individuals with frankly aberrant eating patterns, such as those with binge eating disorder, differ in stress-responsivity and associated overeating from obese individuals without aberrant eating. Although early work comparing obese binge eaters to obese nonbinge eaters on dexamethasone suppression found little support for this hypothesis,[99,100] studies using neuroimaging or other more recently developed laboratory paradigms may shed additional light on the associations among stress-responsivity, obesity, and aberrant eating.

Nonhomeostatic Eating, Reward, and Obesity

Several recent models have emphasized the role of the neural reward system in the development and maintenance of obesity. Specifically, this research hypothesizes that dysfunction of brain reward circuitry in response to food cues may predispose some individuals to obesity via an increased likelihood of overeating, particularly excessive consumption of palatable foods. For

example, as noted in Devlin's[101] review of the potential role of obesity in DSM-V, the notion that some human obesity may result from food "addiction" has gained increased credence. Numerous observers have documented parallels between addictive behaviors and particular forms of overeating,[102,103] and more generally have conceptualized addiction as a process that occurs when any habitual behavior (e.g., eating, gambling) co-opts brain reward circuitry.[104] Work by Volkow and colleagues[12,14,105,106] has explicated the similarities between drug addiction and obesity, such as decreased levels of striatal dopamine D_2 receptors, and suggested that obesity, like drug addiction, is linked with exposure to and reward from powerful reinforcers (i.e., food).

Current conceptualizations of food hedonics or reward distinguish between wanting, i.e., the desire for or motivation to consume foods and liking, i.e., the degree of pleasure derived from food consumption (see Ref. 107 for review). In terms of wanting food, obese individuals may differentially seek food or respond in a heightened way to food cues. In terms of liking food, obese individuals may have a heightened hedonic response to food, and thus overeat. Conversely, obese individuals may have less pleasure from food, and consequently eat more highly palatable food to optimize pleasure. Neurobiological models also emphasize the role of learning in reward, noting that cognitive processes interact with motivational and affective mechanisms to influence reward.[108] A comprehensive examination of the research literature that examines food reward is beyond the scope of this article. Much of this work has focused on animals (see Refs. 109–112 for review), but there are several lines of research in human subjects that provide at least indirect support for the proposition that differences in reward neurocircuitry are involved in overeating associated with obesity.

For example, studies have examined human differences in sensitivity to reward (STR), a trait thought to be linked to the mesolimbic dopamine pathway. Davis et al.[113] measured STR by questionnaire and found that it was associated with emotional overeating in response to depressed mood and BMI in women. Similarly, research using functional magnetic resonance imaging (fMRI) has shown that healthy volunteers who self-report higher STR demonstrate greater activation in the frontal-striatal-amygdala-midbrain network in response to appetizing foods.[114] These findings are suggestive of an association between reward sensitivity and eating behavior. However, investigations that rely on self-report of reward sensitivity or that do not include comparisons of obese and lean individuals do not provide direct evidence that obese persons differ from their normal weight counterparts in hedonic responses to food.

There is a burgeoning literature comparing obese and lean individuals on measures of neural activation in response to food stimuli or neural correlates of food reward using neuroimaging techniques [i.e., positron emission tomography (PET), MRI, fMRI]. As reviewed in Supporting Information Table S1 (see Supporting Information on Wiley-Interscience), in general, this work suggests that relative to lean individuals, obese persons have increased activation to anticipated food reward (i.e., increased wanting) and decreased activation to food consumption (i.e., decreased liking), although specific findings have varied across studies.

Several reports have shown that exposure to palatable food stimuli, which may activate processes related to food wanting, is associated with greater neural activation among obese compared with lean individuals. For example, Karhunen et al.[115] found that obese women had increased activation in the right parietal and temporal cortices relative to normal-weight women in response to viewing, but not eating, a heated meal. Similarly, Rothemund et al.[116] reported that obese women had greater activation in the dorsal striatum, anterior insula, hippocampus, and parietal lobule than did lean women in response to viewing pictures of high-calorie foods. Stoeckel et al.[117] also found evidence of increased activation in the dorsal striatum, insula, and hippocampus, as well several other brain regions, in obese women relative to normal-weight controls while viewing high-calorie food images. Taken together, these findings provide support for the notion that obese individuals experience increased neural reactivity to palatable food cues, which may suggest the presence of heightened motivation for eating in this group. However, the results from one recent study suggest that these differences may be specific to obese individuals with comorbid binge eating,[118] which raises questions about the extent to which increased neural activation to food cues among obese persons is explained by higher rates of eating pathology in this group.

Research also has found differences between obese and lean individuals with respect to neural activation in response to tasting and consuming food. For example, in a series of studies using PET scans and MRI to examine neural responses to food reward in the context of extreme hunger (i.e., following a 36-h fast), Gautier, Del Parigi and colleagues[119–122] documented that obese individuals exhibit increased activation in the prefrontal cortex

(but see Ref. 122) and frontal operculum and decreased activation in the hippocampus, amygdala, cingulate cortex (but see Ref. 120), caudate nucleus, and putamen relative to lean controls in response to consuming a satiating liquid meal (i.e., 50% of estimated daily expenditure in the form of Ensure). Furthermore, in response to tasting a small quantity (i.e., 2 mL) of the liquid meal prior to full consumption, obese individuals showed increased activation in the insular cortex and midbrain compared with lean controls.[119,123] Of note, insular activity in response to anticipated food reward (i.e., a satiating meal in the context of extreme hunger) remained present in formerly obese individuals[119] and was correlated with disinhibition.[123]

Recent work has distinguished the neural correlates of anticipatory and consummatory food reward in obese and lean individuals. Stice et al.[124] found that obese relative to lean adolescent girls exhibited greater activation in the insular cortex, anterior cingulate cortex, and somatosensory cortex (i.e., Rolandic operculum, temporal operculum, parietal operculum) in response to cues signaling impending delivery of palatable food. In response to receipt of the palatable food, obese adolescents showed increased activation in the Rolandic operculum and left-frontal operculum compared to lean controls. Moreover, continuous analyses found a negative association between BMI and activity in the caudate nucleus in response to consummatory food reward, which is consistent with research indicating that obese individuals have reduced striatal dopamine receptor availability relative to lean persons and thus may experience diminished reward from eating.[13,105] Indeed, a follow-up study documented that presence of the *TaqIA* A1 allele, which is associated with reduced dopamine D_2 receptor gene binding in the striatum, moderated the relation between blunted striatal activation to consummatory food reward and BMI currently and at 1-year follow-up in adolescent and adult females[125] (Prospective analyses conducted only in adolescent females—see Supporting Information Table S1).

In summary, there is accumulating evidence that obese individuals differ from lean controls with respect to neural correlates of anticipated food reward and food consumption. These findings may suggest that mental mechanisms related to reward processing play a role in the onset and maintenance of obesity. However, as noted in Supporting Information Table S1, a number of questions remain unanswered regarding the presence of mental dysfunction related to reward circuitry in obese persons. First, although studies have documented differences between obese and lean individuals in neural responses to food stimuli, no research to date has provided conclusive evidence that these differences represent dysfunction, i.e., "the inability of some mental mechanism to perform its natural function" (p. 385).[17] Indeed, it is entirely possible that observed differences reflect normal variation in reward sensitivity that historically conferred an adaptive advantage, but no longer is adaptive in an obesogenic environment. Second, with the exception of one recent study[125] that documented that decreased striatal activation to consummatory food reward is associated with increases in BMI among adolescent females with the *TaqIA* A1 allele, no research has provided evidence that differences in neural activation in response to food reward are associated with the onset or maintenance of obesity. It seems equally plausible that observed differences may be a consequence or correlate of obesity. Third, although many investigators have hypothesized that activation of reward circuitry is related to overeating among obese individuals, no study has provided direct evidence that differences between obese and lean persons with respect to neural correlates of food reward are associated with in vivo eating behavior. Finally, studies focusing on reward processing in obese versus lean individuals typically have made little or no distinction for other behavioral or physiologic phenotypes that might refine our understanding of differences between these groups.[1] "Obese" and "lean" persons represent large and heterogeneous segments of the population. Moreover, as noted above, at least one report has suggested that differences in neural activation between obese and lean women in response to palatable food cues may be due to higher rates of eating-related psychopathology among obese persons.[118] If replicated, this work might suggest that mental dysfunction, if present among obese individuals, is limited to those with coexisting eating pathology.

Discussion

Using a definition of mental disorder based on the notion of harmful dysfunction,[17,23] we conclude that there is insufficient evidence for the inclusion of obesity in DSM-V. Although future work may well document central dysfunction in the pathogenesis of specific obesity phenotypes, current data do not support the idea that obesity is a mental disorder. Nevertheless, there are many reasons to consider adiposity in the assessment of psychiatric

illness. Below we briefly present three lines of evidence bearing on the clinical significance of obesity in psychiatric diagnosis: (1) the relation between disordered eating and obesity; (2) the relation between other psychiatric syndromes and obesity; and (3) the iatrogenic effects of psychotropic medications on weight gain and adiposity. We then close by summarizing the results of the present review and offering our recommendations for the inclusion of BMI (as an index of adiposity) in the assessment and management of psychiatric illness.

Disordered Eating and Obesity

Current evidence has implicated increases in energy intake (i.e., eating) as opposed to decreases in energy expenditure (i.e., physical activity) as the major contributor to the rise in obesity prevalence.[126,127] Although there are many factors that lead to increased energy intake, one potential contributor to weight gain among a subgroup of the obese population is disordered eating behavior. Epidemiologic studies have documented an association between disordered eating, particularly binge eating (i.e., episodes of uncontrolled overeating), and obesity.[8,128,129] For example, an investigation utilizing the cohort from the Coronary Artery Risk Development in Young Adults (CARDIA) study, found higher rates of self-reported binge eating disorder (BED) among overweight participants (defined as BMI $\geq$ 27.3 in women or $\geq$27.8 in men) than among the cohort as a whole (3.0% versus 1.5%).[129] Similarly, recent data from the National Comorbidity Survey Replication (NCS-R) showed a robust association between BED ascertained by structured diagnostic interview and severe obesity (BMI $\geq$ 40).[8] Finally, evidence from sequential general population surveys in Australia indicates that rates of comorbid obesity and eating disorder behaviors (primarily binge eating) increased from 1% to 3.5% in the period between 1995 and 2005.[128]

At present, psychiatric problems with eating are included in the DSM under Eating Disorders, which "are characterized by severe disturbances in eating behavior" (p. 583).[20] The Eating Disorders Work Group of the DSM-V Task Force is examining the current classification, which provides an opportunity to consider the role of obesity-related eating behaviors in DSM-V. Adiposity is included explicitly and implicitly in the current Eating Disorders. For example, anorexia nervosa (AN) is characterized by the inability to maintain a minimally adequate body weight and extreme dietary restriction, while bulimia nervosa (BN) is characterized by binge eating paired with compensatory behaviors to undo the

effects of overeating and presumably avoid undesirable weight gain. BED, a type of eating disorder not otherwise specified that is included as a provisional diagnosis for further study in DSM-IV-TR, also is characterized by recurrent binge eating, but without the regular compensatory behaviors seen in BN. Most, but not all, individuals with BED are overweight or obese.[20] Thus, there already is a place in the DSM for obesity phenotypes characterized by aberrant eating.[101] Nevertheless, given the relationship between binge eating, particularly BED, and adiposity, as well as the clinical salience of obesity, we recommend that BMI be included routinely in any assessment of disordered eating.

Other Psychiatric Syndromes and Obesity

It also is important to acknowledge the extensive literature linking obesity to non-eating-related mental disorders. This work is complex, and available data suggest that associations between obesity and psychiatric illness likely are moderated by numerous factors including degree of adiposity, type of psychiatric symptomatology, and population studied (e.g., males versus females, clinic versus community sample). Results from selected studies that have evaluated the cross-sectional association between obesity and mental disorders are presented in Supporting Information Table S2. Because an exhaustive review of this literature is beyond the scope of this article, we focus primarily on studies conducted in epidemiologic or community samples, as these data are not confounded by the effects of treatment-seeking status on rates of co-occurrence between medical conditions. Although differences in methodology make it somewhat difficult to draw definitive conclusions from this body of work, in general, current evidence suggests that there is a positive association between adiposity and mental disorder (Supporting Information Table S2) (but see Refs. 130–132).

For example, using data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), Petry et al.[9] found that obese (BMI = 30–39.9) and extremely obese (BMI $\geq$ 40) individuals were more likely than normal-weight (BMI = 18.5–24.9) persons to be diagnosed with a mood disorder, anxiety disorder, alcohol use disorder, or personality disorder. Similar findings were reported by a study using data from the NCS-R. Specifically, Simon et al.[11] documented positive, albeit modest (odds ratios = 1.1–1.6), associations between obesity (BMI $\geq$ 30) and current and lifetime mood and anxiety disorders. However, rates of substance use disorder were reduced in obese persons relative to

normal-weight controls. Finally, emerging evidence supports a positive link between obesity and attention-deficit-hyperactivity disorder (ADHD) in children and adults.[133,134]

The exact causes for the comorbidity of obesity and non-eating-related mental disorders remain unknown. However, there are several possible explanations that provide support for the clinical utility of considering BMI in the assessment of psychiatric illness. For example, obesity shares a number of symptomatic features in common with psychiatric disorders including increased appetite, decreased activity levels, and sleep disturbance. Indeed, changes in weight status or eating behavior are DSM-IV-TR criteria for major depressive episodes, dysthymia, and borderline personality disorder.[20] Furthermore, clinical observers have suggested that obese individuals display behaviors characteristic of addictive disorders[14] and impulse-control disorders.[135,136] Obesity also shares a number of correlates in common with mental disorders including biological abnormalities (e.g., HPA axis dysregulation, dopamine dysfunction)[14,137] and environmental precipitants (e.g., childhood trauma).[138–141] Thus, it is possible that increased adiposity in psychiatric patients may signal the presence of a clinically relevant third variable that could influence decisions about assessment and treatment planning. Finally, prospective longitudinal research indicates that there is a bidirectional association between obesity and mental disorder. In particular, current data suggest that the presence of psychiatric symptoms, particularly depression, increases the likelihood of developing obesity[46–48] and obesity-related medical comorbidities (e.g., cardiovascular disease, diabetes, metabolic syndrome)[142–144] and vice versa.[43–45,142,145]

The Iatrogenic Effects of Psychotropic Medication

A third reason to consider BMI and obesity routinely in psychiatric assessment is the potential impact of psychotropic drugs on body weight, which has been linked to medication noncompliance and the development of obesity-related comorbidities.[146] The majority of currently available psychiatric medications will lead to weight gains of 2–17 kg over the course of treatment.[147] Antipsychotic drugs (in particular, several second generation antipsychotic agents), antidepressants (especially tricyclics), and mood stabilizers (e.g., valproate and lithium) all are known to cause weight gain. In contrast, there are only a few medications that appear to be weight neutral (e.g., ziprasidone, lamotrigine) or associated with weight loss (e.g., topiramate, bupropion).[147] Because psychiatric medications affect multiple and diverse aspects of central functioning, there is no single cause of psychotropic-associated weight gain (see Refs. 148 and 149 for review). Furthermore, iatrogenic weight gain varies as a function of pharmacologic agent, psychiatric disorder, and individual patient factors.[147]

There has been a particular focus on the potential iatrogenic effects of second generation antipsychotic medications, especially clozapine and olanzapine.[150] For example, in one meta-analysis, clozapine and olanzapine were associated with weight gains of 4.5 kg and 4.0 kg, respectively, over a period of 10 weeks.[151] Moreover, use of these agents is associated with cardiovascular disease risk factors,[152,153] metabolic syndrome,[150] and diabetes.[154]

Data documenting the effects of psychiatric medications on the development of obesity and associated medical comorbidities underline the importance of choosing psychiatric medications carefully and monitoring their effects to facilitate early identification and treatment of associated medical problems.[148] Most importantly these data provide another reason why it is critical for clinicians to monitor BMI systematically in patients with psychiatric disorders.

Final Summary and Recommendations

In summary, this article sought to evaluate current evidence that obesity, defined as an excess of body fat, should be included as a mental disorder in DSM-V. Guided by Wakefield's conceptualization of mental disorder as "harmful mental dysfunction" (p. 384),[17] we identified two major criteria that need to be fulfilled in order for obesity to be considered a mental disorder: (1) there must be evidence that obesity is harmful; and (2) there must be evidence that obesity is caused by mental dysfunction. With respect to the first criterion, we conclude that there is evidence that obesity is harmful for many, if not most, individuals. Although a few scholars have questioned the public health significance of the findings,[33] a large body of research has documented that obesity is associated with increased rates of medical[34,35] and psychiatric[8–11] morbidity. Furthermore, there is evidence that obesity presents a significant economic burden for society.[49–52]

However, with respect to the second criterion, we find little evidence to support the notion that obesity is caused by mental dysfunction. The etiology of obesity is complex and reflects alterations in

numerous internal and environmental milieus. Moreover, epidemiological observers have concluded that recent changes in the prevalence of obesity are due, in large part, to modest changes in calorie intake and energy expenditure,[75] which does not support the idea that obesity is a mental disorder. Nevertheless, it is possible that mental dysfunction might be involved in the development of certain obesity phenotypes. We presented two such exemplars, one related to homeostatic eating (i.e., stress-induced obesity) and the other to non-homeostatic eating (i.e., reward-associated obesity), and examined available evidence in support of these pathways. Although some data are suggestive of obesity-related mental dysfunction, these findings are preliminary. Of note, future work is needed to address the extent to which mental dysfunction, when present in obese individuals, may be explained by coexisting psychopathology (e.g., binge eating, depression).

If there is little evidence to support the classification of obesity as a mental disorder in DSM-V, there are many reasons to consider adiposity in the assessment and management of psychiatric illness. We reviewed three lines of research bearing on the clinical significance of obesity in mental disorder: (1) the relation between disordered eating and obesity; (2) the relation between other psychiatric syndromes and obesity; and (3) the iatrogenic effects of psychotropic medication on weight gain and adiposity. On the basis of our findings, we make the following recommendations for the inclusion of adiposity in DSM-V: First, given the documented association between obesity and binge eating,[8,128,129] as well as the relation of adiposity to other disordered eating symptoms (e.g., extreme dietary restriction), we recommend that BMI be added as a dimensional assessment for all Eating Disorders. Second, because obesity is associated with a broad range of psychiatric disorders[9,134] and there is evidence that many of the drugs used to treat psychiatric illness lead to weight gain,[147] we recommend that clinicians monitor BMI routinely in all patients with mental disorders, particularly those taking psychotropic mediations, and refer individuals with marked increases in weight for additional medical assessment. These approaches will facilitate medical monitoring of psychiatric patients and stimulate future research.

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