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As the American Psychiatric Association committees begin formal work on DSM-V, we welcome brief editorials on issues that should be considered in its formulation.

Issues for DSM-V: Should Obesity Be Included as a Brain Disorder?

Obesity (body mass index >30), has increased significantly over the past 30 years (approximately 50% per decade) (1), afflicting 32.2% of adults in the United States (2). Obesity increases risk for cardiovascular disease, diabetes, cancer, and other diseases, resulting in annual health care costs conservatively estimated for the United States at $70 to $100 billion a year (3) as well as reductions in life expectancy by 5 to 20 years (4). These facts highlight the urgent need to develop strategies to prevent and treat those afflicted.

Although there have been major scientific advances in the treatment of the medical complications of obesity (i.e., diabetes, hypertension hypercholesterolemia), the morbidity from this disorder is hampered by the failure of interventions to sustain weight loss. Standard interventions based on promoting lifestyle changes to decrease excessive food consumption (dieting) and increased physical activity (exercise) are effective and can normalize weight if followed rigorously, but unfortunately they are incredibly difficult to sustain. The discrepancy between the successes of the metabolic treatments of consequences of obesity and the failures of behavioral treatments to prevent or reverse obesity highlight the fact that this condition is not only a metabolic disorder but also a brain disorder. Consideration of the mental component of obesity should be a key target in the treatment of obesity to facilitate compliance and minimize relapse. Here, we propose that some forms of obesity are driven by an excessive motivational drive for food and should be included as a mental disorder in DSM-V.

"Consideration of the mental component of obesity should be a key target in the treatment of obesity to facilitate compliance and minimize relapse."

DSM-IV recognizes eating disorders such as anorexia and bulimia as mental disorders with severe impairments and serious adverse outcomes but does not recognize obesity despite its devastating medical and psychological consequences. Obesity is characterized by compulsive consumption of food and the inability to restrain from eating despite the desire to do so. These symptoms are remarkably parallel to those described in DSM-IV for substance abuse and drug dependence (Table 1), which has led some to suggest that obesity may be considered a "food addiction" (5).

There are multiple mechanisms contributing to the vulnerability to obesity, including genetic, developmental, and environmental factors that are likely to interact in diverse ways among individuals to produce the behavioral phenotype of overeating (6). The "thrifty genotype" hypothesis suggests that evolution shaped the circuits involved in how our bodies store food as well as the circuits involved in the procurement of food in our ancestors when food was scarce. In current environments, where for the most part food is widely available and diverse, these circuits can lead to food overconsumption. The "developmental origin hypothesis" suggests that calorie content as well as exposure to certain nutrients during pregnancy modify how the body and brain develop in anticipation of future environments with similar nutrient characteristics.

What brain circuits are associated with obesity? The hypothalamus is recognized as the main brain region that controls the regulatory signals for food consumption. The genetic

TABLE 1. DSM-IV Substance Dependence Criteria With Suggested Corresponding Behaviors for Obesity

Substance Dependence Criteria	Corresponding Behaviors for Obesity
Tolerance: increasing amounts of drug to reach intoxication	Tolerance: increasing amounts of food to maintain satiety
Withdrawal symptoms upon drug discontinuation	Distress and dysphoria during dieting
Larger amounts of drug taken than were intended	Larger amounts of food eaten than were intended
Persistent desire and unsuccessful attempts to cut drug use	Persistent desire for food and unsuccessful attempts to curtail the amount of food eaten
Great deal of time spent on getting the drug, using the substance, or recovering from it	Great deal of time is spent eating
Important social, occupational, or recreational activities are given up or reduced because of substance abuse	Activities are given up from fear of rejection because of obesity
Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem caused or exacerbated by the drug	Overeating is maintained despite knowledge of adverse physical and psychological consequences caused by excessive food consumption

TABLE 2. Disrupted Brain Functions Implicated in the Behavioral Phenotypes of Addiction and Obesity and the Brain Regions Believed to Underlie the Disruption

Disrupted Function	Implicated Brain Region
Impaired inhibitory control (to drug intake in addiction; to food intake in obesity)	Prefrontal cortex; anterior cingulate gyrus
Enhanced reward (to drugs in addiction; to food in obesity)	Nucleus accumbens; ventral pallidum; hypothalamus
Conditioning/habits (to drugs and drug cues in addiction; to food and food cues in obesity)	Amygdala; hippocampus; dorsal striatum
Enhanced motivation/drive (to consume drugs in addiction; to consume food in obesity)	Orbitofrontal cortex; mesencephalic dopamine nuclei

products that modulate hypothalamic activity (i.e., leptin, ghrelin, insulin) are also expressed in limbic brain regions involved with reward, motivation, learning, emotion, and stress responses that are likely to modulate food consumption (7). In vulnerable individuals (because of genetic or developmental factors), how do these brain circuits become disrupted to produce compulsive food consumption? As shown in Table 2, we postulate that the underlying brain mechanisms are similar to those that ultimately result in the compulsive drug consumption in addiction (8). Both food consumption and drug use are driven by their rewarding properties, which have been linked to increases in dopaminergic activity in brain reward circuits, but they do this in different ways (9). Food activates brain reward circuitry via palatability (mediated in part by endogenous opioids and cannabinoids) and via increases in peptides that modulate dopamine activity (i.e., insulin, leptin) (10), whereas drugs activate this same circuitry directly through their pharmacological effects (mediated by their direct effects on dopamine cells or by their effects on neurotransmitters that modulate dopamine cells such as opioids, nicotine, GABA, and cannabinoids) (11). Repeated supraphysiological dopamine stimulation from chronic drug use is believed to induce plastic changes in brain (i.e., glutamatergic cortico-striatal pathways) that result in poor inhibitory control over drug consumption and compulsive drug intake (12). In parallel, dopaminergic stimulation facilitates conditioning to drugs and drug-associated stimuli as well as learned habits that then drive the behavior to take drugs when exposed to stimuli associated with drugs. Similarly, repeated exposure to certain foods (particularly those with a high fat and sugar content) in vulnerable individuals can also result in compulsive food consumption, poor food intake control, conditioning to food stimuli, and, over time, massive weight gain. It is not surprising that there is significant overlap in the medications that have been shown to interfere with drug and food consumption in animal models of drug abuse and obesity respectively (i.e., cannabinoid antagonists, baclofen, GABA agonists, and CRF antagonists) and in the behavioral interventions that are frequently used in the treatment of both conditions (incentive motivation, cognitive behavior therapy, and 12-step programs). Stimulants such as cocaine and methamphetamine can suppress appetite perhaps by satiating the reward system, but they often lead to abuse and to return of overeating

when tolerance develops or they are stopped. In contrast, partial blockade of the reward system by antipsychotics (dopamine D_2 receptor antagonists) can result in overeating and can increase the risk for obesity.

The increasing prevalence and impact of obesity in our society and the urgent need to develop better therapeutic interventions that help mitigate the pathologically intense drive for food consumption are clear. We have an opportunity in DSM-V to recognize a component of obesity as a mental disorder. Because of the complex ideologies of obesity it will be important to consider guidelines of which of these deserve to be classified as a mental disorder and which do not. This would facilitate the treatment of obesity not just as a metabolic disorder but also, when appropriate, as a mental disorder.

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NORA D. VOLKOW, M.D.
CHARLES P. O'BRIEN, M.D., PH.D.

Address correspondence and reprint requests to Dr. Volkow, Director, National Institute on Drug Abuse, 6001 Executive Blvd., Room 5274, Bethesda, MD 20892; nvolkow@nida.nih.gov (e-mail).

Dr. Volkow reports no competing interests. Dr. O'Brien is a member of the DSM-V Task Force and is a consultant to Alkermes and Forest Laboratories. Dr. Freedman has reviewed this editorial and found no evidence of influence from these relationships.

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