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BEHAVIORAL ADDICTIONS (A GEARHARDT, SECTION EDITOR)

Potential Role of Addiction Pharmacotherapy in Problematic Eating Behavior

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Abstract Obesity is pandemic worldwide, and hyperphagia remains extremely difficult for physicians to treat. Currently, appetite suppression continues to be the focus of antiobesity drugs, and these drugs are clearly unsuccessful in the long term. Although the food addiction concept remains controversial, this hypothesis provides a matrix in which to examine disordered eating behaviors and their similarities to addiction. This article looks at food addiction as the high end of an eating disorder continuum, with anorexia nervosa as the low end. Similarities with drug addiction provide an avenue leading to new and potentially more successful treatments.

Keywords Anorexia nervosa · Bulimia nervosa · Binge-eating disorder · Food addiction · Brain reward system · Withdrawal · Comorbidity · Behavioral addictions · Eating disorder treatment

Introduction

Obesity remains pandemic, and the public continues to spend billions of dollars each year on unsuccessful weight loss schemes. Physicians continue to find successful treatment of hyperphagia to be almost the "impossible dream." Then again, food addiction continues to be a controversial subject in spite of empirical evidence linking the brain and behavioral changes in food addiction to the same changes in drug addiction [1]. Although there are several successful pharmacological treatments for drug addiction, pharmacotherapy for the management of obesity continues to focus on overall appetite suppression.

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Problematic Eating Behavior

Eating behaviors that fall outside the parameters of the societal norms can be termed problematic or disordered. Disordered eating behaviors range on a continuum from eating extremely small amounts of food to severely overeating. Neurobiological changes, evidenced by brain scans, are expressed in neuropsychological dysfunction. Common eating disorders include anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED). A subset of people with obesity may also be classified as having an eating disorder, i.e., food addiction [2, 3].

A myriad of factors (genetic, social, biological, psychological, and behavioral) interact in a complex and ever-changing dance which can cause eating disorders. [4]. Avena et al. [5, 6] have shown a link between binge eating and obesity in animal studies. Human epidemiological studies also offer significant evidence of a linkage between binge eating and obesity [7–9]. Neuroimaging studies document human brain changes that are nearly identical in subjects viewing pictures of palatable food or drugs of abuse [10].

An overconcern and dissatisfaction with body weight and shape is the common characteristic of AN, BN, and BED. Eating disorders often have a long and relapsing course and have a high rate of comorbid psychiatric disorders. They are very difficult to treat, and especially in AN there is an increased risk of mortality [11].

Anorexia Nervosa

AN is characterized by very low body weight and an intense fear of getting "fat" or gaining weight. AN can be of restrictive

type (the person avoids food or eats very little) or purging type. Extreme exercising, laxatives, diuretics, and enemas or vomiting are all purging mechanisms. People with AN have a distorted perception of how their body looks and have persistent lack of recognition of the seriousness of their low body weight [12].

Bulimia Nervosa

Bulimia is characterized by periods of time (binges) when a significantly larger amount of food is consumed within a short period of time (2 h) than another individual would typically eat. Loss of control over eating and inability to stop eating are the defining characteristics along with compensatory behaviors following the binge to prevent the gaining of weight. These, as in AN, can be excessive exercising, or purging (vomiting, misuse of laxatives, diuretics, and enemas) [12].

Binge-Eating Disorder

BED is also characterized by the consumption of large amounts of food in a short time and a loss of control over eating. However, there are no compensatory behaviors present. Eating when not hungry, eating until feeling too full, eating alone to hide the quantity being eaten, an feeling ashamed and guilty over lack of control are all symptoms of BED. The binge-eater feels a significant amount of distress [12].

Food Addiction

Food addiction has been debated for many years, and its role in obesity is not yet fully defined. Not all obese people are food addicts. The Yale Food Addiction Scale (YFAS) was developed by Gearhardt et al. [2] as a screening instrument and is modeled on the same criteria as drug use disorder: tolerance, withdrawal, loss of control, failed attempts to stop, giving up other important activities owing to use, and emotional distress. Food addiction overlaps with BED symptoms [13]; the YFAS showed internal reliability, good convergent validity, and good discriminant validity. In their publication describing how the YFAS was validated, Gearhardt et al. [14] stated that the YFAS outperformed existing measures in predicting binge-eating behavior. Avena et al. [15•] found overlaps between substance abuse and overeating. They constructed a three-way juxtaposition of DSM-IV criteria for substance abuse to behaviors in animal studies and to clinical accounts of human behavior in BED. In one example, tolerance (needing larger and larger amounts to maintain the same effect) is a classic sign of substance addiction [16]. In animal studies, researchers found escalation of daily sugar intake over a 3-week access period [17]. Correspondingly, in humans, increased food consumption in each binge is often seen as the disorder becomes chronic [18]. The same three-way similarity was found for withdrawal symptoms and other criteria [15•].

Brain Reward Circuitry

The most decisive roles in the brain's reward system are played by the ventral tegmental area, located in the midbrain, the nucleus accumbens (NAc) which is innervated by the ventral tegmental area, and the prefrontal cortex, which plays a big role in the processes of attention and motivation. The operation of the NAc is dependent on two essential neurotransmitters, dopamine, which promotes desire, and serotonin, which controls satiety and inhibition. Dopamine and serotonin have an inverse relationship: when a stimulus increases the amount of dopamine in the NAc, the amount of serotonin is reduced, and the reverse is also true.

We know that drugs, including alcohol, hijack the reward system. After a period of time, continued use precipitates changes in the brain circuitry; it becomes dysregulated. Dopamine depletion in drug addiction has been known for some time [19]. Studies in both humans and other animals have supported the hypothesis that brain reward circuitry may be dysregulated in some cases of obesity, disordered eating, and more recently, food addiction [20–24]. Reward circuitry activation also regulates food and drug craving behavior [25].

The hypothalamus is recognized as the main center of the brain responsible for regulation of signals for food consumption. Hormones such as leptin, ghrelin, and insulin work on both the hypothalamus and the limbic system within areas such as the caudate nucleus, hippocampus, and insula—the same regions that participate in the control of reward, motivation, learning, emotion, and stress responses [26].

There are two rewards that are considered "natural rewards"; that is, food and sex. Both are essential to the continued existence of all life and were hard-wired into our being. However, food in the natural sense refers to "eating to live." Unfortunately, this has evolved in our modern time into "living to eat" for many people. Just as people may turn to alcohol or drugs as a way to deal with their problems, they may also turn to food. Might eating when stressed, eating when sad or unhappy, and eating when frustrated be how "comfort food" got its name?

Withdrawal

Alcohol

In a previous article [27], we wrote on hyperphagia resulting from withdrawal of drugs of abuse. The famous Alcoholics Anonymous acronym is HALT; whenever, I feel Hungry,

Angry, Lonely, or Tired, I need to HALT, identify, and address this need. Unfortunately, crunchy, salty, sweet, and fatty food can be the means of addressing that need. Many people with alcoholism in recovery show significant weight gain and tend to use food to distract themselves from alcohol craving.

If the craving for alcohol is blunted by ingesting highly palatable food, the alcohol craving is not gone, but is under control and the person with alcoholism is considered to be in recovery. However, take away the ability to access highly palatable food and alcohol craving returns, increasing the risk of relapse. Addiction transference is also a possibility, especially in food addiction [28]. Addiction transference has become commoner and commoner as a consequence of the rising number of bariatric surgical procedures performed [28]. Studies show that in the years following the procedure there is a higher risk of alcohol addiction [29–31].

As a result of the surgery, the absorption rate is changed and a serving of alcohol becomes much more potent. In addition, although the ability to eat a large amount of hyperpalatable food at one time is cut drastically by bariatric surgery, if the patient's food, relationship, and self-image issues are not addressed by therapy, then the risk of addiction transference is higher. Block the craving for addictive food by appetite suppression or bariatric surgery and you might as well spin the wheel of misfortune (see Fig. 1) to see which addiction will take the place of food.

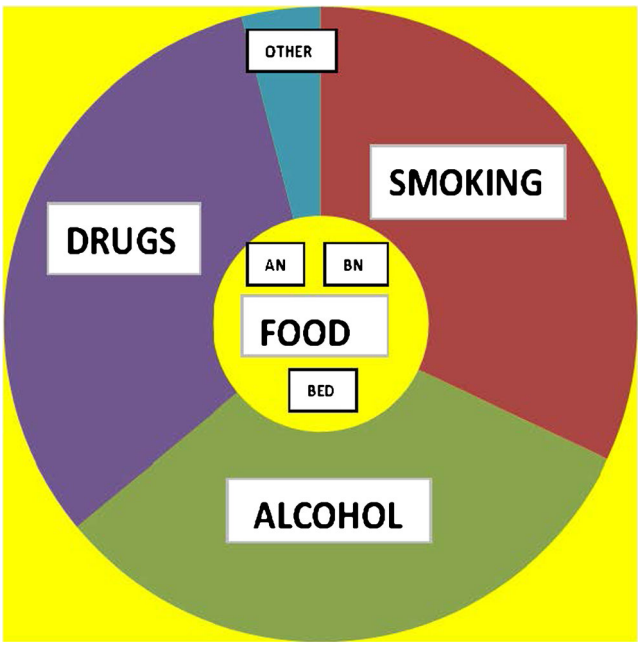

Fig. 1 Food is the solid center surrounded by a moveable wheel of the most popular addictions (drugs, tobacco, alcohol). If any of the addictive substances are blocked, food becomes the addiction. If, however, food is blocked, any of the addictions may occur. Similarly to the game show *Wheel of Fortune*, you spin the wheel and may not predict which addiction results; ergo "Wheel of Misfortune." *AN* anorexia nervosa, *BED* binge-eating disorder, *BN* bulimia nervosa

Remembering that the reward and withdrawal systems of the brain are separate entities, use of the addictive substance is mediated by reward rather than withdrawal avoidance. In other words, the substance stimulates its own self-administration [32], which is more powerful than the desire to avoid withdrawal.

Tobacco

Many lessons can be learned by looking at tobacco addiction. Tobacco is a good example of a self-perpetuating addiction, even though it is associated with a number of serious medical conditions, including cancers, and has a high rate of psychiatric comorbidities. In 2009, the relationship between BMI and the risk of substance use disorders was examined by Barry and Petry [33]. They found that overweight women were at increased risk of lifetime nicotine dependence, whereas overweight men were at decreased risk. Smoking is associated with decreased appetite and weight loss, and cessation of smoking is associated with increased appetite and weight gain [34].

Smoking has long been used as a weight control method by women with eating disorders. In a study that compared smoking behavior between female community controls and women with eating disorders, higher rates of smoking were found in women with eating disorders, especially those with binge/purge subtypes [35].

Cannabis

To date there is no effective pharmacological treatment for cannabis use disorder. Marijuana smoking creates strong cravings for and intensifying pleasure in hyperpalatable food, especially sweets and carbs, by stimulating cannabinoid receptors, which increase the drive to eat [36]. It was thought that blocking those receptors would decrease the drive to eat.; the promising drug rimonabant, although successful in animal studies, caused suicidal ideation in humans and was not approved by the FDA [27].

Amphetamines

These drugs were prescribed for decades for weight loss. Appetite was greatly decreased and energy was greatly increased as were alertness and weight loss. However, amphetamines are highly addictive, and long-term use causes a host of medical issues. Withdrawal from long-term stimulant drug exposure causes dysphoria, anhedonia, irritability, amotivation, and social dysfunction along with rebound hyperphagia and weight gain. Brain changes similar to those seen in trauma-induced brain injury are seen in methamphetamine addicts, and the changes may not ever reverse after withdrawal and abstinence [37].

Cocaine

Cocaine, like amphetamines, inhibits appetite, and withdrawal brings rebound hyperphagia and weight gain. All cocaine is addictive, but crack (a smokeable form of cocaine) is highly addictive compared with sniffed cocaine. As far back at the 1980s we were writing about cocaine abuse and eating disorders [38] and providing evidence that medications successfully used in addictions could also work in some eating disorders [39, 40].

Eating Disorders and Withdrawal

Both AN and BN have a high rate of psychiatric comorbidity: lifetime prevalence of substance use disorders is found in 55 % of people with BN and in 23 % of people with AN [41, 42]. Studies show that disordered eating also changes the neurocircuitry of the brain [43]. Additionally, the appetite-regulating hormones cortisol and peptide YY (PYY) are associated with psychological and behavioral dysfunction of disordered eating from AN to obesity [44, 45]. Lawson et al. [46] found that higher levels of cortisol and PYY are associated with disordered eating across the weight spectrum in women regardless of BMI. Cortisol and PYY levels are involved in regulating appetite and feeding behavior. In the study of Lawson et al., 65 women participated, divided into four groups (16 with AN, 17 overweight or obese, 12 with normal weight with hypothalamic amenorrhea, and 20 with normal weight in good health). Several hormones were measured, including PYY, leptin, ghrelin, and cortisol. The results showed that no matter which group the women were in, higher levels of cortisol and PYY were associated with disordered eating [46]. These results suggest that specific eating disorders may have abnormalities in appetite regulation. No one knows at this point how this will affect withdrawal of hyperpalatable food in BED or obesity. In a more recent study, Lawson et al. [47] found that increased hypothalamic–pituitary–adrenal drive is associated with decreased appetite and hypoactivation of food motivation neurocircuitry in AN.

Animal studies, reported by Avena et al. [48, 49] among others, have provided strong evidence that excessive sugar consumption operates in a similar manner as consumption of opiates, both in changes to the brain and behavior and in naloxone-precipitated withdrawal symptoms. Some of these symptoms were teeth chattering, tremor, anxiety, aggression, and distress vocalizations [15•]. Interestingly, fat bingeing and sugar bingeing have notable differences in behavior [50]. Sugar bingeing has opiate-like withdrawal symptoms, but fat bingeing does not; sugar bingeing does not affect body weight, but fat bingeing increases body weight. A sugar–fat combination produces addictive-like behaviors (including withdrawal symptoms) and also increases in body weight [51].

Highly palatable food is energy-rich, often consisting of carbs, sugars, fats, or various combinations of these foods. Although animal studies are important, they are not able to incorporate the emotional and cultural components of human binge eating [50]. It is our hypothesis that medications used successfully in treating addiction withdrawal may have a place in easing withdrawal for people with sugar and carb addictions.

A New Approach

Accepting the food addiction hypothesis as a matrix, our research group has been looking at new approaches to the problem of disordered eating [52]. Avena et al. [53] compared the effects of food restriction and overeating on brain reward systems, finding strong evidence linking overeating with changes in reward-related brain regions. The animal studies of Gold et al. [54, 55] have increased our understanding of food addiction and have provided evidence that drugs used successfully in addiction can be successful in treating overeating. Blum et al. have studied the regulation of food and drug craving behavior by reward circuitry dopaminergic activation [25], along with "liking" versus "wanting" and their links to reward deficiency syndrome [56].

During the same time period, Shriner and Gold [57, 58] have been working on procedures to treat the issues of patients with disordered eating. Many of the therapies successfully used in substance abuse treatment, such as cognitive behavioral therapy and motivational interviewing, may also be successful in treating disordered eating.

Conclusion

It is clear that appetite suppression as a treatment of disordered eating is not successful or able to be maintained over time. Yet both the drug companies and the public continue to search for the "magic pill" that will cure obesity without requiring any lifestyle changes or effort by the patient. Alternatively, some physicians continue to blame the patient as having a lack of willpower. The research is clear: food addiction and obesity are diseases of the brain; this statement is supported by brain imaging.

We recommend research trials combining use of the YFAS to identify food addicts and distinguish them from those with BED, followed by pharmaceutical treatment with medications used successfully in addiction along with therapy using procedures that have also proven to be successful in treating addiction. This three-pronged approach would offer new hope to the public and also to the medical profession.

Compliance with Ethics Guidelines

Conflict of Interest Paula J. Edge and Mark S. Gold declare that they have no conflict of interest.

Human and Animal Right and Informed Consent This article does not contain any studies with human or animal subjects performed by either of the authors.

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