Published in final edited form as:
J Addict Med. 2010 March 1; 4(1): 1–10. doi:10.1097/ADM.0b013e3181ce38e7.

The Treatment of Obesity and Its Co-occurrence with Substance Use Disorders

Katherine A. VanBuskirk, B.A.[1] and **Marc N. Potenza, MD, PhD**[2]

[1] Department of Psychiatry, Yale University School of Medicine, 2 Church Street South, Suite 215, New Haven, CT, 06519, USA

[2] Departments of Psychiatry and Child Study Center, Yale University School of Medicine, Connecticut Mental Health Center, 34 Park Street, New Haven, CT, 06519, USA

Abstract

Obesity and binge eating disorder are detrimental health conditions that are associated with lower qualities of life. Individuals with obesity often face societal discrimination and frequently experience related medical disorders such as diabetes, hypertension, and hyperlipidemia. Current research suggests neurobiological similarities between obesity, binge eating disorder, and substance dependence. In addition, behavioral similarities link the two conditions; obese and substance dependent individuals often report similar features such as loss of control towards food or substances, respectively, and cravings. Treatment options for obesity have begun to use this information to formulate pharmacological and therapeutic interventions that may provide greater results for weight loss and decreased binge frequency. Similarly, treatment approaches to substance addictions should consider aspects of weight management. Findings from research and treatment studies are presented with the aim of reviewing the current literature of obesity within the context of an addiction framework and providing information on empirically supported approaches to the treatment of co-occurring obesity and substance addiction.

Keywords

substance use disorders; obesity; comorbidity

Introduction - Obesity within a Mental Health Framework

Obesity, defined as a body mass index (BMI) greater than 30 kg/m^2, and has a prevalence rate of 32.2% among American adults (Ogden, Carroll, Curtin et al., 2006). Obesity is associated with multiple medical conditions including diabetes, hypertension, and hyperlipidemia (Banks, Marmot, & Oldfield, 2006), and the American Cancer society has estimated that nearly 90,000 of all cancer deaths a year are related to obesity (Calle, Rodriguez, Walker-Thurmond et al., 2003). In addition, obesity is associated with mood disorders (Stunkard, Faith, & Allison, 2003), possibly in part because the condition is stigmatized with a sense of moral failing, which may lead to depression, anxiety, and perception of discrimination (Puhl & Brownell, 2001). Obesity is classified as a medical disorder; however, factors in the development of the condition suggest that the disease may also be conceptualized as a behavioral disorder with a substantial psychiatric component. Conceptualizing obesity within a mental health framework from a motivational behavioral perspective could help improve existing prevention and treatment

Correspondence: Marc N. Potenza, CMHC, SAC, Room S-104, 34 Park Street, New Haven, CT 06519. Tel: 203-974-7356; fax: 203-974-7366; marc.potenza@yale.edu.

strategies. A focus on cognitive and motivational factors in eating behaviors also suggests important similarities with other psychiatric conditions including addictive disorders (Volkow & Wise, 2005).

Obesity can co-occur in the setting of other eating disorders, particularly binge-eating disorder (BED). BED was found to occur in 30.1% of subjects attending hospital-affiliated weight management programs and in 2% of the general population. The disorder is more common in females than in males and is associated with obesity (Spitzer, Devlin, Walsh et al., 1992). The disorder is marked by overconsumption of food without inappropriate compensatory weight-loss behaviors found in other eating disorders such as bulimia (Castonguay, Eldredge, & Agras, 1995). Although a "binge-eating syndrome" was originally described in 1959 (Stunkard, 1959; Stunkard, 1993), a set of diagnostic criteria for BED was not incorporated into the DSM-IV until 1994 (APA, 2000) when research criteria for the disorder were introduced. Therefore, diagnostic criteria have only recently been available to aid in the study of the symptoms and potential treatments of BED.

Given the relatively immature status of research into BED, the studies discussed here will focus on obesity. Nonetheless, BED may more closely share core features with substance use disorders (e.g., impaired impulse control) in domains that may represent putative endophenotypes and explain their co-occurrence. Several reviews have focused on the similarities in neurobiology between obesity and substance use disorders (Wang, Volkow, Thanos et al., 2004; Volkow & Wise, 2005; Rapaka, Schnur, Shurtleff, 2008; Volkow, Wang, Fowler, et al., 2008). In this review, we plan to extend current work by describing the implications for treatment, specifically focusing on the co-occurrence of obesity and substance use disorders. Findings from pre-clinical and clinical studies are presented to describe neurobiological and behavioral similarities between obesity and addictive disorders. In addition, findings from treatment studies of obesity are presented, and the manners in which weight concerns might be considered in the treatment of substance use disorders (SUDs) are discussed.

Methods

The Medline (1966 to present) database was searched using the MeSH (Medical Subject Heading) and textwords "obesity" and "substance-related disorders" to identify candidate articles for review. Potential articles were examined to determine if they met the following eligibility criteria: 1) were published in peer-reviewed journals between 1966 and 2007, 2) were written in English and involved pre-clinical and clinical experimentation, and 3) discussed the similarities and/or differences of obesity and substance-related disorders as related to neurobiology, treatment approaches, and treatment outcomes. Articles not meeting these criteria were not included in the review. Additional subsequent searches through Medline were utilized to find articles that addressed specific focused interests such as nutrition therapy, cognitive behavioral therapy, and aerobic exercise. These articles were again matched against the above eligibility criteria before inclusion.

Obesity and Addiction

There have been historical shifts in the use of the term "addiction" (Potenza, 2006). Although the original use of the word was not linked to excessive patterns of substance use, more recent use of the word has connoted an almost synonymous link with compulsive drug use. For example, during preparations for DSM-III-R in the 1980's, there was almost uniform agreement that "addiction" referred to compulsive drug-taking (O'Brien, Volkow, & Li, 2006). However, there has been a recent shift in the use of the term to consider non-substance behaviors (e.g., gambling) as potentially addictive (Holden, 2001). Investigations into

"behavioral" addictions such as pathological gambling have identified clinical, phenomenological, and neurobiological similarities with drug addictions (Potenza, 2008). Behavioral addictions share core elements with drug addictions (e.g., continued engagement despite adverse consequences, impaired control, an appetitive urge or craving state preceding behavioral engagement) that may take precedence over other life concerns (Avena, Rada, & Hoebel, 2008). In such cases, short-term gratification in a pleasurable or hedonic behavior is given precedence over longer term interests relating to occupation, family and health. If one considers food consumption within this framework, excessive patterns of eating may be conceptualized as addictive in nature and reflected in conditions like obesity and BED. In addition, SUDs may co-occur with obesity and BED, leading to the necessity for multi-faceted interventions that target each addictive behavior. As weight management may affect substance use, substance use may, in turn, modulate food consumption and weight control. Data are presented from the current literature of weight-related influences of substance dependence and interventions for substance dependence.

Co-Occurrence of Obesity and Addictions

The development of a pattern of excessive consumption of drugs or food is likely to involve multiple vulnerability factors including genetic predisposition, environmental exposure, and an interaction between these domains. Such vulnerabilities may involve an increased experience of reward from food or substances, a decreased ability to inhibit motivated drives towards food or substances and their related stimuli, and/or a more easily facilitated classical conditioning response to reinforcing food or substances (Volkow, Wang, Fowler et al., 2008). Predisposition to obesity and SUDs may be mediated by dopamine receptor genetic polymorphism, such as that expressed by the presence of the *Taq*IA A1 allele (Stice, Spoor, Bohon et al., 2008). This allele is associated with dysfunction in dopamine expression in the striatum and has been associated with greater reward sensitivity. Davis and colleagues (2007) theorize that the presence of the *Taq*IA A1 allele may interact with an additional genetic variant to lead to higher dopamine activity and greater reward sensitivity in those with obesity and BED as compared to normal-weight controls (Davis, Levitan, Kaplan et al., 2007). The A1 allele has been linked to impulsivity and "behavioral addictions" such as pathological gambling, but research results have been inconsistent (Lobo, Vallada, Knight et al., 2007; Esposito-Smythers, Spirito, Rizzo et al., 2009). Both feeding and substance use may represent reinforced behaviors involving rewarding experiences, and both behaviors may recruit brain areas implicated in motivation and reward processing (Volkow & Wise, 2005).

Imaging studies suggest that addictive drugs and addictive foods each activate key brain regions involved in reward processing and decision-making including the nucleus accumbens, ventral pallidum, orbitofrontal cortex, and anterior cingulate gyrus (Volkow, Fowler, & Wang, 2003). The desire and drive for drugs in addiction are proposed to result from neurobiological adaptations within the brain related to chronic, intermittent exposure to the reinforcing drugs; these exposures lead to downregulation of critical neurotransmitters and adaptations of neural circuits, and a similar process has been proposed for food (Volkow, Fowler, Wang et al., 2004; Avena, Rada, & Hoebel, 2008).

Research into simultaneous obesity and addiction investigates the question of whether there are particular vulnerabilities shared between the two conditions. The general scope of current research of eating disorders and SUDs suggests that one disorder may increase the likelihood of experiencing others. A common predisposition, such as increased psychological distress or failure to develop non-addictive coping mechanisms, has been proposed to explain why certain individuals may be more likely to use substances and binge-eat (White & Grilo, 2006).

Several lines of evidence link tobacco smoking and weight regulation. Smoking during pregnancy may increase the risk for obesity in individuals exposed *in utero* to nicotine (Toschke, Ehlin, von Kries et al., 2003). Overweight female smokers with childhood onset of weight problems were significantly more likely to have an earlier first usage of cigarettes and greater frequency of binge eating as compared to those with later onset of weight problems. In addition, those with earlier weight problems disclosed more severe symptoms of nicotine withdrawal during smoking abstinence as compared to the later onset group (Saules, Levine, Marcus et al., 2007). A study of individuals with BED found that those who had ever smoked (either currently or in the past) were more likely to have additional psychopathology than those who had never smoked. This suggests multiple forms of addictive behavior may reflect greater underlying psychological vulnerabilities or greater deficits in coping mechanisms (White & Grilo, 2006).

Co-occurrence between obesity and cocaine and stimulant use disorders is rare; cocaine, methylphenidate, and methamphetamines suppress the appetite presumably through dopamine-related influences. Stimulants are pro-dopaminergic, working to increase extracellular dopamine (DA), and are anorexigenic (Wang, Volkow, Logan et al., 2001; Volkow & O'Brien, 2007). Data suggesting that cocaine and glucose may operate on similar neural circuitry involve findings that the availability of saccharin or glucose solutions decreases cocaine self-administration (Carroll, Lac, & Nygaard, 1989).

The co-occurrence of obesity and SUDs has also been investigated in epidemiological studies. In one study, obesity was associated with alcohol use disorders but not for other SUDs (Petry, Barry, Pietrzak et al., 2008). Using the same data and focusing on past-year diagnoses, overweight body habitus was associated with drug abuse or dependence amongst women and was inversely associated with drug abuse or dependence among men, suggesting that gender considerations are important in understanding the relationship between eating and drug use behaviors and disorders (Desai, Manley, Desai et al., 2009). Amongst clinical samples, 36% of women in an alcohol treatment facility displayed symptoms of BED (Peveler & Fairburn, 1990). In a study of over 3500 female twin pairs, those who were classified as Weight Concerned, Dieters, or Eating Disordered were more likely to have SUDs than those who were classified as Unaffected [by weight concerns] or Low Weight Gain, meaning a natural failure to gain weight through aging (Duncan, Bucholz, Neuman et al., 2007). Among moderately and severely obese individuals, BED was associated with a family history of substance abuse and a higher likelihood of experiencing Axis I and II disorders (Yanovski, Nelson, Dubbert et al., 1993). Finally, individuals with gambling problems may have increased rates of obesity and binge eating as compared to the normal population (Lesieur & Blume, 1993; Desai, Desai, & Potenza, 2007). Together, data suggest that obesity and addictive disorders, both substance- and non-substance-related, may have shared underlying features explaining their co-occurrence. Below we will review treatment of obesity and SUDs, and discuss how understanding the shared mechanisms between the disorders may be used to improve existing interventions.

Treatment of Obesity and SUDs

Obesity and SUDs may be approached with a variety of treatment options, as summarized in Table 1. Treatment studies, meta-analyses, and alternative treatments are discussed below, as are potential gaps in understanding for which research in these areas may lead to the development of novel and potentially more efficacious treatments.

Obesity has long been treated with prescriptions for reduced-caloric diets and increased energy expenditure, though the efficacy of those measures has not been consistently established (Polivy & Herman, 1999; Urbszat, Herman, & Polivy, 2002). Dieting often involves restricted

ingestion of desired high-caloric foods, and unsuccessful dieting efforts may involve the resumption of excessive consumption or bingeing of the same foods. This pattern shares similarities with withdrawal and relapse behaviors in SUDs. Cycling between withdrawal and relapse may lead to compulsive eating through changes in neurocircuitry function underlying stress responsiveness. Animal studies have implicated specific brain neurochemicals (e.g., the neuropeptide corticotrophin-releasing factor) as linking stress responsiveness and the motivation to eat palatable foods, suggesting a pathway for the induction of compulsive eating and novel targets for the treatment of BED and obesity (Cottone, Sabino, Roberto et al., 2009).

Meta-analytic studies have found that the treatment option with greatest efficacy for BED is cognitive behavioral therapy (CBT). Remission rates for BED reach 50% using CBT, signifying a substantial decrease or complete remission of binge frequency, as well as improved psychosocial functioning (Wilson, Grilo, Vitousek, 2007; White, Grilo, O'Malley et al., in press). Pharmacotherapy has been found to be moderately efficacious as well, although CBT without simultaneous pharmacotherapy has been demonstrated to be most efficacious (Reas & Grilo, 2008). Despite moderate success in remission of binge frequency, these treatments have not led to substantial reduction in weight; the margins of weight lost through these treatments are usually not substantial enough to significantly reduce one's BMI or BMI category (Wilson, Grilo, & Vitousek, 2007). Thus, these treatments may not be efficacious to address the needs of obese individuals seeking to reduce a significant amount of body weight.

A meta-analysis found that nutrition and counseling activities alone may not yield long-term results in obese individuals; however, programs that targeted eating behaviors, physical activity, and counseling yielded greater efficacy. Incorporating a problem-solving component gave additional efficacy for long-term weight loss maintenance (Seo & Sa, 2008). Of the 24 studies examined in this review, four yielded significant long-term results; three of those studies incorporated a problem-solving component into the paradigm (Seo & Sa, 2008). An additional meta-analysis found that lifestyle interventions led to significantly reduced body weight, BMI, waist circumference and other health markers as compared to standard care (Galani & Schneider, 2007).

Further treatment development may be enhanced through a better understanding of the underlying biological mechanisms of obesity. Leptin, implicated in reward-processing, influences metabolic homeostasis and motivation for feeding behaviors. Endogenous and exogenous leptin administration leads to reduced food consumption (Enriori, Evans, Sinnayah, et al., 2006; Yip & Potenza, 2009). Ghrelin, a hormone produced within the lining of the stomach and in the pancreas, stimulates feelings of hunger. Ghrelin and leptin may act together to modulate feeding behaviors, and this relationship may be dysfunctional within obese individuals (Fulton, Woodside, Shizgal, 2000; Tschop, Weyer, Tataranni, et al., 2001; Yip & Potenza, 2009). These and other neurochemicals may represent important targets for the development of novel, complementary and potentially more efficacious treatments for weight loss. An understanding of the history and efficacy of treatment approaches for SUDs is also important in formulating innovative and effective treatment, particularly when considering co-occurring obesity and SUDs.

Some behavioral interventions for SUDs may have relevance for obesity and binge eating disorder (see Table 1 below). Alcoholics Anonymous was established in 1935 and contributed to the development of behavioral interventions that remain an important part of treatment for SUDs (Lemanski, 2001). One meta-analysis, utilizing 53 controlled trials of subjects with alcohol and/or substance use disorders, found that CBT produced a significant, although relatively small, treatment effect (Magill & Ray, 2009). These findings support the use of CBT across a broad range of SUDs, although alternative or combination therapies may enhance the robustness of treatment outcome. Dutra and colleagues (2008) found positive outcomes for

psychosocial interventions for SUDs in a meta-analysis. Contingency Management (CM) programs had the greatest efficacy, with 31% of subjects achieving post-treatment abstinence. Relapse prevention programs yielded high abstinence rates, as well, (39%), although the drop out rate for these programs was 57%. CBT treatment studies reported abstinence rates of 27% with drop out rates of 35% (Dutra, Stathopoulou, Basden et al., 2008). An important consideration is how well treatment responses are maintained, or gained, over time. For example, CBT in contrast to other behavioral interventions has been shown to have a "sleeper" effect in which treatment outcome improvement may be observed months or years after treatment delivery has ended (presumably related to individuals internalizing, developing and using skills related to CBT overt time). These findings suggest moderate success in treatment through psychosocial interventions, with the possibility of pharmacotherapy and combination therapy offering additional treatment utility.

For nicotine dependence, combination therapy (nicotine replacement patch with an additional component) was found to be significantly more efficacious in smoking cessation treatment than was monotherapy; these results were maintained at 3-, 6-, and 12-month follow-ups (Shah, Wilken, Winkler et al., 2008). For the treatment of opioid dependence, maintenance programs are often utilized to aid opioid detoxification. Amato and colleagues (2008) meta-analyzed randomized controlled trials to investigate potential added benefits of pairing psychosocial therapy with pharmacological treatments. The combination therapy was found to have greater efficacy than pharmacological interventions alone. The added psychosocial component may aid in the maintenance of drug-free behaviors to maintain detoxification (Amato, Minozzi, Davoli et al., 2008).

Alternative Treatments

Research that investigates non-substance related ways to influence DA systems may help to expand treatment options for individuals with obesity and SUDs, as DA is implicated in reward-processing and reinforcement. Exercise interventions have been found to be effective in increasing DA D2-like dopamine receptors in animal studies. In rodents, exercise training increased striatal DA D2 receptors (MacRae, Spirduso, Walters et al., 1987; Wang, Volkow, Logan et al., 2001). In epileptic and spontaneously hypertensive rats, each with pre-intervention low levels of DA, DA levels were normalized in the neostriatum and nucleus accumbens (Sutoo & Akiyama, 2003). These brain regions are strongly associated with reward processing and addictive disorders (Volkow, Fowler, & Wang, 2003). Exercise may increase DA function through exercise-related increases in calcium-serum levels (Sutoo & Akiyama, 1996; Sutoo & Akiyama, 2003).

In humans, after high-impact running, subjects were found to have higher catecholamine (DA, epinephrine, and norepinephrine) levels as compared to groups in no exercise and low-impact exercise conditions (Winter, Breitenstein, Mooren et al., 2007). However, Wang, Volkow, Fowler and colleagues (2000) found that subjects who underwent 30 minutes of treadmill running exercise did not have significantly higher levels of striatal DA. The methodology may be limited due to the research design in which subjects underwent PET imagery after exercise completion, thus potentially limiting the ability to identify transient DA increases that may have occurred during the exercise. This hypothesis is supported through rodent studies in which rats had DA levels 50%–80% above baseline during exercise as compared to 10%–50% after exercise completion (Meeusen, Smolders, Sarre et al., 1997; Wang, Volkow, Fowler et al., 2000). In addition, the subjects who were recruited for this study were physically fit and without medical problems; therefore, it is possible that their baseline DA levels were higher as compared to individuals seeking treatment for obesity or an addictive disorder (Wang, Volkow, Fowler et al., 2000).

Aerobic exercise has been associated with better executive functioning. In rodents, exercise training is associated with better performance on memory tasks (Harburger, Kzerem, Frick, 2007). In one study of overweight children, cognitive processes were better in those subjects who had undergone a high-dose aerobic exercise condition (40 min/5 days a week/15 weeks) (Davis, Tomporowski, Boyle et al., 2007). Studies seeking to mitigate cognitive decline in aging populations have found that aerobic exercise aids in the maintenance of executive functioning and enhances brain plasticity (Cotman & Berchtold, 2002). These findings suggest that exercise may be an appropriate component of treatment for obese individuals, as well as those with SUDs, as it may help to increase DA levels in brain regions associated with addictive disorders and to improve executive functioning and inhibition.

An additional alternative treatment involves meditation or mindfulness-based therapy in the treatment of addiction. Meditation, the conscious, effortful practice of calming thoughts and emotions, has been recently investigated in the treatment of addiction (Brewer, Smith, Bowen et al., in press). Meditating subjects have been found to exhibit increased endogenous DA release in the ventral striatum and increased DA levels were correlated with a reduced readiness for action, a quality that may be helpful in increasing inhibitory responses towards substance and food cravings (Kjaer, Bertelsen, Piccini et al., 2002). Mindfulness-based interventions that incorporate elements of meditation have shown preliminary promise in the treatment of substance addictions (Brewer, Sinha, Chen et al., in press) and warrant further study in the treatment of obesity.

Treatment of Obesity: Insights from SUDs

Cognitive Therapies

In the treatment of dependence, programs of a methodical, gradual pace have been proposed as being more successful (Thornley, McRobbie, Eyles et al., 2008). CBT, experiential-cognitive therapy, and twelve-step programs, such as Overeaters Anonymous, may allow for gradual, methodical treatment approaches and are discussed below.

For BED, CBT can be an effective treatment, producing significant reductions in days binged, BMI, depression, and remission rates (Gorin, LeGrange, & Stone, 2003; Hilbert & Tuschen-Caffier, 2004). In addition, CBT and interpersonal therapy may reduce binge frequency with gains maintained at a four-month follow-up (Wilfley, Welch, Stein et al., 2002). Experiential-cognitive therapy as compared to those who received standard CBT or nutritional therapy (NT) may produce a greater weight reduction. Experiential-cognitive therapy seeks to address body dissatisfaction in obese patients with the aims of increasing self-confidence as well as aiding in contingency planning and problem-solving in the face of weight reduction and maintenance obstacles such as social situations and food shopping (Riva, Bacchetta, Cesa et al., 2006). Experiential-cognitive therapy utilizes virtual reality simulation in an effort to present subjects with simulated scenarios in which they may problem-solve and rehearse different approaches to weight maintenance obstacles. The virtual reality simulation is meant to influence subjects' perceived sense of control, perceived competence, and goal internalization by allowing the subject to formulate and practice weight reduction strategies in real-time virtual reality. The practice scenarios consist of various virtual reality placements such as "Home", "Supermarket", "Pub", and "Gymnasium" (Riva, Bacchetta, Cesa et al., 2006).

Mann, Tomiyama, Westling and colleagues (2007) conducted a review of obesity treatments and found that most treatments employed food restriction and dieting techniques in order to achieve a goal of weight loss. Their results corroborated with those of Jeffery, Drewnoski, Epstein and colleagues (2000); diets were found to be primarily ineffective in the treatment of weight disorders. These reviews found that while restrictive diets may achieve short-term weight loss, long-term maintenance was rare. Overeaters Anonymous, founded on the twelve-

step process of Alcoholics Anonymous, stresses social support and personal responsibility and honesty (Overeaters Anonymous, 2001). This approach may help to improve the effectiveness of a restricted dietary regime.

Pharmacotherapy

Gradually released pharmacotherapies also warrant consideration for obesity and SUDs. For example, in smoking cessation, nicotine patch, associated with slow nicotine release, increases the likelihood of effective cessation (West & Schiffman, 2004). Similarly, it has been proposed that slow release of sugar and foods with high glycemic indices may help to gradually mitigate food addiction or obesity (Thornley, McRobbie, Eyles et al., 2008).

Selective serotonin reuptake inhibitors (SSRIs) have been found to be helpful in the treatment of bulimia nervosa, an eating disorder that has addiction-like symptoms such as bingeing and diminished behavioral control (Fluoxetine, 1992). Another SSRI, sertraline appears moderately effective in the treatment of BED (McElroy, Casuto, Nelson et al., 2000). Similar studies using SSRIs have found moderate and temporary relief from symptoms of BED (Stunkard, Berkowitz, Tanrikut et al., 1996; Hudson, McElroy, Raymond et al., 1998; Arnold, McElroy, Hudson et al., 2002).

In one study, obese subjects with BED were treated with group psychotherapy and fluoxetine (Tammela, Rissanen, Kuikka et al., 2003). To assess post-treatment effects, fluoxetine was discontinued for three months before a post-treatment single-photon emission computed tomography (SPECT) paired with a tracer designed to identify 5-HT activity. In the post-treatment SPECT, the researchers found improved 5-HT transporter binding, supporting previous findings that 5-HT transporter is associated with eating behaviors, as well as suggesting that this treatment may help to improve 5-HT activity in patients with BED.

Sibutramine, a serotonin-norepinephrine reuptake inhibitor, may alter internal signals that inform the perception of hunger and satiation. Sibutramine treatment has been associated with weight loss in obese patients (Arterburn, Crane, & Veenstra, 2004) and to decrease binge frequency (Appolinario, Bacaltchuk, Sichieri et al., 2003; Wilfley, Crow, Hudson et al., 2008).

When treated with topiramate, patients with comorbid mood disorders and BED exhibited diminished symptoms of BED (Shapira, Goldsmith, & McElroy, 2000). Similar findings have been observed in patients with epilepsy treated with the drug (Smith, Axelsen, Hellebo-Johanson et al., 2000). Topiramate may aid in weight loss through reduction in the activity of salivary enzymes or reduced leptin, corticosteroid, serum glucose, or insulin concentrations; however, the precise process by which the medication mitigates weight loss is incompletely understood (Goldfarb, 2005).

Considerations of Weight Management in the Treatment of SUDs—The treatment of SUDs often involves pharmacological therapy, psychotherapy, or a combination of the two. The treatments for substance dependence currently available may have varying side effects. Weight gain may be associated with drug abstinence and represent an obstacle in successful abstinence in weight-concerned individuals. In an inpatient treatment facility, over the course of 60 days, subjects in recovery from addictive disorders related to alcohol and illicit substances gained an average of 1.58 BMI points, with those who also smoked cigarettes gaining more weight than did nonsmoking subjects (Hodkins, Cahill, & Seraphine, 2004). Given these findings, an awareness of weight management in the treatment of SUDs may aid in successful abstinence.

Nicotine

Tobacco smoking is associated with poor health behaviors such as low physical activity, unbalanced diet, overweight and obesity. In addition, women smokers are twice as likely to be inactive as compared to nonsmokers (Kaleta, Makowiec-Dabrowska, Polanska et al., 2009). Achieving smoking abstinence may be prevented by fears related to potential effects of smoking cessation, particularly weight gain (Perkins, 1993; Jeffery, Hennrikus, Lando et al., 2000). The belief in the efficacy of smoking as a mechanism for weight control is more pronounced in women, especially those with disordered eating patterns (McKee, Nhean, Hinson et al., 2006). Data have suggested that smoking cessation leads to a variable weight gain of about six kilograms (approximately 13 pounds) in approximately 80% of those who attempt to quit (Samet, 1990; Klesges, Winders, Meyers et al., 1997; Munafo, Murphy, & Johnstone, 2006; Aubin, Berlin, Smadja et al., 2009). However, the magnitude of the weight gain may match that of never-smokers. Smokers as compared with non-smokers have been found to have lower BMIs by an average of three kilograms (Klesges, Klesges, & Meyers, 1991). Over time, ex-smokers tend to achieve a mean BMI equivalent to those of never-smokers, whereas non-abstinent smokers have a lower mean BMI by an average of 1.6 kg/m^2 (Munafo, Tilling, & Ben-Shlomo, 2009). In smokers, factors related to weight concerns related to smoking cessation include frequent food restriction for weight loss, high nicotine dependence, and high cigarette use (Pomerleau, Zucker, & Stewart, 2001; Aubin, Berlin, Smadja et al., 2009).

In the treatment of cigarette smoking, nicotine replacement and bupropion are frequently used pharmacotherapies (Jorenby, Leischow, Nides et al., 1999). In efforts to mitigate post-cessation weight gain found in smokers attempting to quit, Toll and colleagues (2008) used a combination of naltrexone, an opioid antagonist, and bupropion, a norepinephrine and DA reuptake inhibitor and nicotinic acetylcholine receptor antagonist. In the combination treatment group, post-cessation weight gain was lower than in the bupropion-only group, suggesting that a combination pharmacotherapy may be helpful in minimizing weight gain in smoking cessation (Toll, Leary, Wu et al., 2008). Alone, bupropion has been found to be effective in reducing post-cessation weight gain (Jorenby, Hays, Rigotti et al., 2006). In a review of smoking cessation interventions, three studies found that subjects taking bupropion gained significantly less weight at the end of treatment as compared to those taking varenicline, a nicotinic receptor partial agonist (Parsons, Shraim, Inglis et al., 2009). Post smoking cessation treatment, varenicline was not found to significantly reduce amount of weight gained (Jorenby, Hays, Rigotti et al., 2006). Fluoxetine, a SSRI, dose-dependently suppressed post-cessation weight gain; however, this administration resulted in dose-dependent weight rebound upon termination of pharmacotherapy. The post-termination weight gain observed was comparable to that observed during cessation with placebo. Despite the weight rebound, this delay in post-cessation weight gain may aid in successful cigarette abstinence so that quitters may focus on their treatment rather than weight concerns (Borrelli, Spring, Niaura et al., 1999). An exercise component to smoking cessation treatment may aid in effective abstinence and help ward off weight gain. In comparison of CBT paired with moderate-intensity exercise and CBT alone, female smokers were equally likely to achieve smoking cessation at the end of treatment across the two groups and the CBT-exercise group was more likely to report smoking cessation at 3-month follow-up. Among those within the CBT-exercise group, there was a positive correlation between smoking cessation and exercise adherence (Marcus, Lewis, Hogan et al., 2005).

Cannabis and Opiates

Cannabinoids, the active compounds found within cannabis, bind to cannabinoid receptors, including the CB1 receptor, located in the brain and throughout the body (Akbas, Gasteyger, Sjodin et al., 2009). Use of a CB1-selective antagonist SR141716 may block the psychological and physiological effects of marijuana use in humans (Huestis, Gorelick, Heishman et al.,

2001). Cannabis may be used in the treatment of such conditions as nausea, vomiting, muscle spasms associated with multiple sclerosis, diminished appetite, and migraines (Gurley, Aranow, & Katz, 1998; Rosenthal & Kleber, 1999). Cannabis has a pro-appetitive effect in users; however, evidence suggests that this effect may be temporary since no substantial weight difference has been observed between users and non-users. In addition, there is not a higher prevalence of cannabis use among overweight populations (Horcajadas, 2007).

The endocannabinoid system is an area of research in the treatment of obesity, as blocking the endocannabinoid system may aid in weight management and evidence suggests that endocannabinoids directly influence regulatory systems that mitigate hunger, food craving, and the enjoyment of the sensory properties of food (Kirkham, 2005; Van Gall, Rissanen, Scheen et al., 2005). In mice, blocking the CB1 receptor led to diminished responsiveness to cannabinoid drugs; the reinforcing properties and withdrawal symptoms relating to morphine were significantly reduced (Ledent, Valverde, Cossu et al., 1999). Evidence suggests an overlap between the appetite-enhancing roles of opiates and cannabis and, inversely, the anorexigenic effects of their antagonists. Cannabinoid-induced overconsumption of food appears to be mitigated by the administration of opioid receptor antagonists and, in converse, in mice, opiate self-administration is reduced by the CB1 receptor antagonist rimonabant (Navarro, Carrera, Fratta et al., 2001; Cota, Marsicano, Tschop et al., 2003; Tallett, Blundell, & Rodgers, 2009).

Animal studies suggest that rimonabant may have additional metabolic effects. Tolerance to the anorexigenic effect of rimonabant was observed 4–5 days after rimonabant administration; however, weight loss persisted until discontinuation of the intervention, suggesting that a metabolic effect continues despite tolerance to the anorexigenic effect (Vickers, Webster, Wyatt et al., 2003). Methadone treatment is associated with higher consumption of and desires for sweet foods, and higher BMIs are observed in methadone-maintained individuals (Zador, Wall, & Webster, 1996; Nolan & Scagnelli, 2007). Administration of naloxone to rats currently undergoing morphine withdrawal is associated with decreased food consumption (Gellert & Sparber, 1977). Further, a combination therapy of naloxone and rimonabant may prove efficacious in simultaneously treating opiate addiction and aiding weight management. In mice, the combination therapy reduced food consumption and time spent feeding and each antagonist has been to be found efficacious in the treatment of SUDs (Tallett, Blundell & Rodgers, 2008).

Cocaine

Cocaine use is not associated with weight gain, perhaps due to its anorexigenic effects, and weight gain during recovery may reflect a beneficial restoration of weight. Indatraline and sustained-release methamphetamine are each associated with significantly reduced cocaine use and craving, as well as increased weight loss (Negus, Brandt, & Mello, 1999; Mooney, Herin, Schmitz et al., 2009). In contrast, quetiapine has been associated with efficacy in reducing cocaine use and cravings, but a higher likelihood of weight gain throughout treatment (Kennedy, Wood, Saxon et al., 2008). As an alternative or compliment to pharmacological interventions, aerobic exercise has been found to reduce the reinforcing effects of cocaine in rats and would likely aid in weight management (Smith, Schmidt, Iordanou et al., 2008). As discussed above, aerobic exercise has been found to influence DA systems in rodents (Sutoo & Akiyama, 2003) and existing human research corroborates these findings (Wang, Volkow, Fowler et al., 2000). Treatment of cocaine dependence may benefit from screening for food restriction and eating-disordered thinking. Cocaine dependent females, and males to a lesser extent, may present with eating disordered symptoms and report using cocaine as a method of weight management. For successful treatment of this subset of cocaine dependent individuals,

identifying and targeting eating disordered symptoms appears particularly important (Cochrane, Malcolm, & Brewerton, 1998).

Alcohol

Binge drinking is associated with poor diet, body dissatisfaction, sedentary behavior, and poor weight control. Alcohol-related food consumption is associated with increased likelihood of overweight and obesity (Nelson, Lust, Story et al., 2009). Alcohol dependence is associated with greater preference and desire for sweet foods, though after 6 months of abstinence, alcohol dependent subjects were significantly less likely to prefer sweet foods than those who did not maintain abstinence (Krahn, Grossman, Henk et al., 2006). In recovery from alcohol dependence, patients may be told to use sweet substances as a way to manage alcohol craving (Alcoholics Anonymous, 1975; Gorski & Miller, 1986), although empirical studies have failed to establish a significant effect of sweet substances on alcohol cravings (Krahn, Grossman, Henk et al., 2006). Over six months, alcohol dependent individuals attempting to remain abstinent gained more weight than did healthy controls and non-abstinent alcohol dependent individuals; however statistical significance was only reached between the abstinent alcohol dependent subjects and healthy controls (Krahn, Grossman, Henk et al., 2006). Given these considerations, weight gain during recovery from alcohol dependence represents a clinically significant consideration.

Nalmefene, an opioid receptor antagonist used primarily in the treatment of alcohol dependence, was found to suppress appetite in diet-induced mice, but subsequently led to a significant gain in cumulative food intake and body weight at 21 days of treatment (Chen, Huang, Shen et al., 2004). Varenicline, a nicotinic receptor partial agonist used primarily for smoking cessation, was associated with successful treatment of alcohol dependence (Streensland, Simms, Holgate et al., 2007) and weight loss in a case study (Cocores & Gold, 2008). However, in smoking cessation studies, varenicline was not found to significantly reduce amount of weight gained post-cessation (Jorenby, Hays, Rigotti et al., 2006).

Conclusion

Obesity and SUDs share commonalities in neural circuitry, suggesting that treatment advances in the field of SUDs may inform advancements in the treatment of obesity and vice versa. Pharmacological and psychotherapeutic interventions may simultaneously target obesity and SUDs, and non-standard approaches involving exercise and mindfulness training may have important roles in the treatments of obesity and SUDs. Weight management may represent an important part of achieving successful recovery from SUDs, particularly amongst weight-concerned individuals. Future research should investigate the degree to which treatment interventions for SUDs aid or hinder weight management. Further research is needed to determine more precisely the extent to which obesity and SUDs share similarities as well as contain unique elements, such that prevention and treatment strategies may be optimized for the disorders.

Acknowledgments

Acknowledgments and Disclosures: We thank Iris Balodis, PhD, for helpful comments on an earlier draft of the manuscript. This work was supported by the NIH grants R01 DA020908, RL1 AA017539, P50 DA09241, P50 DA16556, UL1 DE19586, NIH Roadmap for Medical Research/Common Fund, Office of Research on Women's Health, and the VA VISN1 MIRECC. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of any of the funding agencies. Ms. VanBuskirk has no disclosures to declare. Dr. Potenza has received financial support or compensation for the following: Dr. Potenza consults for and is an advisor to Boehringer Ingelheim; has consulted for and has financial interests in Somaxon; has received research support from the National Institutes of Health, Veteran's Administration, Mohegan Sun Casino, the National Center for Responsible Gaming and its affiliated Institute for Research on Gambling Disorders, and Forest Laboratories, Ortho-McNeil, Oy-Control/Biotie and Glaxo-SmithKline pharmaceuticals; has participated in surveys, mailings or telephone

consultations related to drug addiction, impulse control disorders or other health topics; has consulted for law offices and the federal public defender's office in issues related to impulse control disorders; provides clinical care in the Connecticut Department of Mental Health and Addiction Services Problem Gambling Services Program; has performed grant reviews for the National Institutes of Health and other agencies; has given academic lectures in grand rounds, CME events and other clinical or scientific venues; and has generated books or book chapters for publishers of mental health texts.

LIST OF REFERENCES

Akbas F, Gasteyger C, Sjodin A, Astrup A, Larsen TM. A critical review of the cannabinoid receptor as a drug target for obesity management. Obes Rev 2009;10:58–67. [PubMed: 18721231]

Alcoholics Anonymous. Living Sober. New York: Alcoholics Anonymous World Services; 1975.

Amato L, Minozzi S, Davoli M, Vecchi S, Ferri MM, Mayet S. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. Cochrane Database Syst Rev 2008;4:CD005031. [PubMed: 18843675]

APA. Diagnostic and Statistical Manual of Mental Disorders. 4. Washington DC: American Psychiatric Association; 2000. Text Revision

Appolinario JC, Bacaltchuk J, Sichieri R, et al. A randomized, double-blind, placebo-controlled study of sibutramine in the treatment of binge-eating disorder. Arch Gen Psychiatry 2003;60:1109–1116. [PubMed: 14609886]

Arnold LM, McElroy SL, Hudson JI, Welge JA, Bennett AJ, Keck PE. A placebo-controlled, randomized trial of fluoxetine in the treatment of binge-eating disorder. J Clin Psychiatry 2002;63:1028–1033. [PubMed: 12444817]

Arterburn DE, Crane PK, Veenstra DL. The efficacy and safety of sibutramine for weight loss: a systematic review. Arch of Intern Med 2004;164:994–1003. [PubMed: 15136309]

Aubin HJ, Berlin I, Smadja E, West R. Factors associated with higher body mass index, weight concern, and weight gain in a multinational cohort study of smokers intending to quit. Int J Environ Res Public Health 2009;6:943–957. [PubMed: 19440425]

Avena N, Rada P, Hoebel B. Evidence for sugar addiction: Behavioral and neurochemical effects of intermittent, excessive sugar intake. Neurosci Biobehav Rev 2008;32:20–39. [PubMed: 17617461]

Banks J, Marmot M, Oldfield Z, et al. Disease and disadvantage in the United States and in England. JAMA 2006;295:2037–2045. [PubMed: 16670412]

Borrelli B, Spring B, Niaura R, Kristeller J, Ockene JK, Keuthen NJ. Weight suppression and weight rebound in ex-smokers treated with fluoxetine. J Consult Clin Psych 1999;67:124–131.

Brewer JA, Sinha R, Chen JA, et al. Mindfulness training reduces stress reactivity and relapse in substance abuse: results from a randomized, controlled pilot study. Subst Abus. in press.

Brewer JA, Smith JT, Bowen S, Marlatt GA, Potenza MN. Mindfulness-based treatments for co-occurring depression and substance use disorders: what can we learn from the brain? Addiction. in press.

Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003;348:1625–1638. [PubMed: 12711737]

Carroll ME, Lac ST, Nygaard SL. A concurrently available nondrug reinforcer prevents acquisition or decreases the maintenance of cocaine-reinforced behavior. Psychopharmacol 1989;97:23–29.

Castonguay LG, Eldredge KL, Agras WS. Binge eating disorder: current state and future directions. Clin Psych Rev 1995;15:865–890.

Chen RZ, Huang RR, Shen CP, MacNeil DJ, Fong TM. Chronic administration of nalmefene leads to increased food intake and body weight gain in mice. Euro J Pharmacol 2004;495:63–66.

Cochrane C, Malcolm R, Brewerton T. The role of weight control as a motivation for cocaine abuse. Addict Behav 1998;23:201–207. [PubMed: 9573424]

Cocores JA, Gold MS. Varenicline, appetite, and weight reduction. J Neuropsychiatry Clin Neurosci 2008;20:497–498. [PubMed: 19196942]

Cota D, Marsicano M, Tschop M, et al. The endogenous cannabinoid system affects energy balance via central orexigenic drive and peripheral lipogenesis. J Clin Invest 2003;112:423–431. [PubMed: 12897210]

Cotman CW, Berchtold NC. Exercise: a behavioral intervention to enhance brain health and plasticity. Trends Neurosci 2002;25:295–301. [PubMed: 12086747]

Cottone P, Sabino V, Roberto M, et al. CRF system recruitment mediates dark side of compulsive eating. Proc Natl Acad Sci USA.

Davis C, Levitan RD, Kaplan AS, et al. Reward sensitivity and the D2 dopamine receptor gene: a case control study of binge eating disorder. Progress Neuro-Psychopharmacology & Bio Psychiatry 2008;32:620–628.

Davis CL, Tomporowski PD, Boyle CA, Waller JL, Miller PH, Naglieri JA, Gregoski M. Effects of aerobic exercise on overweight children's cognitive functioning: a randomized controlled trial. Res Quart Exercise Sport 2007;78:510–519.

Desai RA, Desai MM, Potenza MN. Gambling, health, and age: data from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychology Addict Behav 2007;21:431–440.

Desai RA, Manley MJ, Desai MM, Potenza MN. Gender differences in the association between body mass index and psychopathology. CNS Spectr 2009;14:372–383. [PubMed: 19773713]

Duncan AE, Bucholz KK, Neuman RJ, Agrawal A, Madden PA, Heath AC. Clustering of eating disorder symptoms in a general population female twin sample: A latent class analysis. Psychol Med 2007;37:1097–1107. [PubMed: 17472759]

Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance use disorders. Am J Psychiatry 2008;165:179–187. [PubMed: 18198270]

Enriori PJ, Evans AE, Sinnayah P, Cowley MA. Leptin resistance and obesity. Obesity 2006;14:254S–258S. [PubMed: 17021377]

Esposito-Smythers C, Spirito A, Rizzo C, McGeary JE, Knopik VS. Associations of the DRD2 TaqIA polymorphism with impulsivity and substance use: preliminary results from a clinical sample of adolescents. Pharmacol Biochem Behav 2009;93:306–312. [PubMed: 19344737]

Fluoxetine Bulimia Nervosa Collaborative Study Group. Fluoxetine in the treatment of bulimia nervosa: a multicenter, placebo-controlled double-blind trial. Arch of Gen Psychiatry 1992;49:139–147. [PubMed: 1550466]

Fulton S, Woodside B, Shizgal P. Modulation of brain reward circuitry by leptin. Science 2000;287:125–128. [PubMed: 10615045]

Galani C, Schneider H. Prevention and treatment of obesity with lifestyle interventions: review and meta-analysis. Int J Public Health 2007;52:348–59. [PubMed: 18368998]

Gellert VF, Sparber SB. A comparison of the effects of naloxone upon body weight loss and suppression of fixed-ratio operant behavior in morphine-dependent rats. Pharmacol Exp Ther 1977;201:44–54.

Goldfarb B. Topiramate and weight loss… does it work? American Diabetes Assoc: DOC News 2005;2:5.

Gorin AA, Le Grange D, Stone AA. Effectiveness of spouse involvement in cognitive behavioral therapy for binge eating disorder. Int J Eating Disord 2003;33:421–433.

Gorski, TT.; Miller, M. Staying Sober. Independence, MO: Herald House/Independence Press; 1986.

Gurley JR, Aranow R, Katz M. Medical marijuana: a comprehensive review. J Psychoactive Drugs 1998;30:137–147. [PubMed: 9692375]

Grant LP, Haughton B, Sachan DS. Nutrition education is positively associated with substance abuse treatment program outcomes. J Am Dietetic Assoc 2004;104:604–610.

Harburger LL, Nzerem CK, Frick KM. Single enrichment variables differentially reduce age-related memory decline in female mice. Behav Neurosci 2007;121:679–688. [PubMed: 17663593]

Hilbert A, Tuschen-Caffier B. Body image interventions in cognitive-behavioural therapy of binge-eating disorder: a component analysis. Behav Res Ther 2004;42:1325–1339. [PubMed: 15381441]

Hodgkins CC, Cahill KS, Seraphine AE, Frost-Pineda K, Gold MS. Adolescent drug addiction treatment and weight gain. J Addict Disord 2004;23:55–66.

Holden C. 'Behavioral' addictions: Do they exist? Science 2001;294:980–982. [PubMed: 11691967]

Horcajadas FA. Cannabinoids in eating disorders and obesity. Mol Neurobiol 2007;36:113–128. [PubMed: 17952656]

Hudson JL, McElroy SL, Raymond NC, et al. Fluvoxamine in the treatment of binge-eating disorder: a multicenter placebo-controlled, double-blind trial. Am J Psychiatry 1998;155:1756–1762. [PubMed: 9842788]

Huestis MO, Gorelick DA, Heishman SJ, et al. Blockade of effects of smoked marijuana by the CB1-selective cannabinoid receptor antagonist SR141716. Arch of Gen Psychiatry 2001;58:322–328. [PubMed: 11296091]

Jeffery RW, Drenowski A, Epstein LH, et al. Long-term maintenance of weight loss: current status. Health Psychol 2000;19:5–16. [PubMed: 10709944]

Jeffery RW, Hennrikus DJ, Lando HA, Murray DM, Liu JW. Reconciling conflicting findings regarding postcessation weight concerns and success in smoking cessation. Health Psychol 2000;19:242–246. [PubMed: 10868768]

Jorenby DE, Hays JT, Rigotti NA, et al. Efficacy of varenicline, an α4β2 nicotinic receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation. JAMA 2006;296:56–63. [PubMed: 16820547]

Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 1999;340:685–691. [PubMed: 10053177]

Kaleta D, Makowiec-Dabrowska T, Polanska K, Dziankowska-Zaborszczyk E, Drygas W. Tobacco smoking and other negative lifestyle behaviors among economically active individuals. Med Pr 2009;60:7–14. [PubMed: 19603691]

Kennedy A, Wood AE, Saxon AJ, et al. Quetiapine for the treatment of cocaine dependence: an open-label trial. J Clin Psychopharmacol 2008;28:221–224. [PubMed: 18344735]

Kirkham TC. Endocannabinoids in the regulation of appetite and body weight. Behav Pharmacol 2005;16:297–313. [PubMed: 16148436]

Klesges RC, Klesges LM, Meyers AW. Relationship of smoking status, energy balance, and body weight: analysis of the Second National Health and Nutrition Examination Survey. J Consult Clin Psychology 1991;59:899–905.

Klesges RC, Winders SE, Meyers AW, Eck LH, Ward KD, Hultquist CM, Ray JW, Shadish WR. How much weight gain occurs following smoking cessation? A comparison of weight gain using both continuous and point prevalence abstinence. J Consult Clin Psychol 1997;65:286–291. [PubMed: 9086692]

Kjaer TW, Bertelsen C, Piccini P, Brooks D, Alving J, Lou HC. Increased dopamine tone during meditation-induced change of consciousness. Cogn Brain Res 2002;13:255–259.

Krahn D, Grossman J, Henk H, Mussey M, Crosby R, Gosnell. Sweet intake, sweet-liking, urges to eat, and weight change: relationship to alcohol dependence and abstinence. Addict Behav 2006;31:622–631. [PubMed: 15990241]

Ledent C, Valverde O, Cossu G, et al. Unresponsiveness to cannabinoids and reduced addictive effects of opiates in CB1 receptor knockout mice. Science 1999;283:401–404. [PubMed: 9888857]

Lemanski, M. A History of Addiction and Recovery in the United States. Tuscon, AZ: See Sharp Press; 2001.

Lesieur HR, Blume SH. Pathological gambling, eating disorders, and the psychoactive substance use disorders. J Addict Dis 1993;12:89–102. [PubMed: 8251548]

Lobo DS, Vallada HP, Knight J, Martins SS, Tavares H, Gentil V, Kennedy JL. Dopamine genes and pathological gambling in discordant sib-pairs. J Gambling Studies 2007;23:421–433.

MacRae PG, Spirduso WW, Walters TJ, Farrar TP, Wilcox RE. Endurance training effects on striatal D2 dopamine receptor binding and striatal dopamine metabolites in presenescent older rats. Psychopharmacology 1987;92:236–240. [PubMed: 3110847]

Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: a meta-analysis of randomly controlled trials. J Studies Alc Drugs 2009;70:516–527.

Mann T, Tomiyama AJ, Westling E, Lew A-M, Samuels B, Chatman J. Medicare's search for effective obesity treatments: diets are not the answer. Am Psychol 2007;62:220–233. [PubMed: 17469900]

Marcus BH, Lewis BA, Hogan J, et al. The efficacy of moderate-intensity exercise as an aid for smoking cessation in women: a randomized controlled trial. Nicotine Tob Res 2005;7:871–880. [PubMed: 16298722]

McElroy SL, Casuto LS, Nelson EB, et al. Placebo-controlled trial of sertraline in the treatment of binge eating disorder. Am J Psychiatry 2000;157:1004–1006. [PubMed: 10831483]

McKee SA, Nhean S, Hinson RE, Mase T. Smoking for weight control: effect of priming for body image in female restrained eaters. Addict Behav 2006;31:2319–2323. [PubMed: 16567057]

Meeusen R, Smolders I, Sarre S, et al. Endurance training effects on neurotransmitter release in rat striatum: an in vivo microdialysis study. Acta Physiologica Scandinavica 1997;159:335–341. [PubMed: 9146755]

Mooney ME, Herin DV, Schmitz JM, Moukaddam N, Green CE, Grabowski J. Effects of oral methamphetamine on cocaine use: a randomized, double-blind, placebo-controlled trial. Drug Alcohol Depend 2009;101:34–41. [PubMed: 19058926]

Munafo MR, Murphy MF, Johnson EC. Smoking cessation, weight gain, and DRD4 -521 genotype. Am J Med Genet B Neuropsychiatr Genet 2006;141B:398–402. [PubMed: 16526060]

Munafo MR, Tilling K, Ben-Shlomo Y. Smoking status and body mass index: a longitudinal study. Nicotine Tob Res 2009;11:765–771. [PubMed: 19443785]

Navarro M, Carrera MR, Fratta W, et al. Functional interaction between opioid and cannabinoid receptors in drug self-administration. J Neurosci 2001;21:5344–5350. [PubMed: 11438610]

Negus SS, Brandt MR, Mello NK. Effects of the long-lasting monoamine reuptake inhibitor indatraline on cocaine self-administration in rhesus monkeys. J Pharmacol Exp Ther 1999;291:60–69. [PubMed: 10490887]

Nelson MC, Lust K, Story M, Ehlinger E. Alcohol use, eating patterns, and weight behaviors in a university population. Am J Health Behav 2009;33:227–237. [PubMed: 19063644]

Nolan LJ, Scagnelli LM. Preference for sweet foods and higher body mass index in patients being treated in long-term methadone maintenance. Subst Use Misuse 2007;42:1555–1566. [PubMed: 17918026]

Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 2006;295:1549–1555. [PubMed: 16595758]

O'Brien CP, Volkow N, Li TK. What's in a word? Addiction versus dependence in DSM-V. Am J Psychiatry 2006;163:764–765. [PubMed: 16648309]

Overeaters Anonymous. Overeaters Anonymous. 2. California: Overeaters Anonymous, Incorporated; 2001.

Parsons AC, Shraim M, Inglis J, Aveyard P, Hajek P. Interventions for preventing weight gain after smoking cessation. Cochrane Database Sys Rev 2009;1:CD006219.

Perkins KA. Weight gain following smoking cessation. J Consult Clin Psychol 1993;61:768–777. [PubMed: 8245274]

Petry NM, Barry D, Pietrzak RH, Wagner JA. Overweight and obesity are associated with psychiatric disorders: results from the National Epidemiologic Survey on alcohol and related conditions. Psychosom Med 2008;70:288–297. [PubMed: 18378873]

Peveler R, Fairburn C. Eating disorders in women who abuse alcohol. Br J Addict 1990;85:1633–1638. [PubMed: 2289064]

Polivy J, Herman CP. Distress and eating: why do dieters overeat? Int J Eating Disord 1999;26:153–164.

Pomerleau CS, Zucker AN, Stewart AJ. Characterizing concerns about post-cessation weight gain: results from a national survey of women smokers. Nicotine Tob Res 2001;3:51–60. [PubMed: 11260811]

Potenza MN. The neurobiology of pathological gambling and drug addiction: an overview and new findings. Phil Trans R Soc B 2008;363:3181–3189. [PubMed: 18640909]

Potenza MN. Should addictive disorders include non-substance-related conditions? Addiction 2006;101:142–151. [PubMed: 16930171]

Puhl RM, Brownell KD. Obesity, bias, and discrimination. Obes Res 2001;8:788–805. [PubMed: 11743063]

Rapaka R, Schnur P, Shurtleff D. Obesity and addiction: common neurological mechanisms and drug development. Physiol Behav 2008;95:2–9. [PubMed: 18571681]

Reas DL, Grilo CM. Review and meta-analysis of pharmacotherapy for binge eating disorder. Obesity 2008;16:2024–2038. [PubMed: 19186327]

Riva G, Bacchetta M, Cesa G, et al. Is severe obesity a form of addiction?: rationale, clinical approach, and controlled clinical trial. CyberPsychol Behav 2006;9:457–479. [PubMed: 16901250]

Rosenthal MS, Kleber HD. Making sense of medical marijuana. Proc Assoc Am Physicians 1999;111:159–165. [PubMed: 10220811]

Samet JM. The 1990 report of the Surgeon General: the health benefits of smoking cessation. Am Rev Respir Dis 1990;142:993–994. [PubMed: 2240852]

Saules KK, Levine MD, Marcus MD, Pomerleau CS. Differences in smoking patterns among women smokers with childhood versus later onset of weight problems. Eat Behav 2007;8:418–422. [PubMed: 17606240]

Seo D-C, Sa J. A meta-analysis of psycho-behavioral obesity interventions among US multiethnic and minority adults. Preventative Med 2008;47:573–582.

Shah SD, Wilken LA, Winkler SR, Lin SJ. Systematic review and meta-analysis of combination therapy for smoking cessation. J Am Pharmacists Assoc 2008;48:659–665.

Shapira NA, Goldsmith TD, McElroy SL. Treatment of binge-eating disorder with topiramate: a clinical case series. J Clin Psychiatry 2000;61:368–372. [PubMed: 10847312]

Smith U, Axelsen M, Hellebo-Johanson E, Lundgren B, Ben-Menachem E. Topiramate, a novel antiepileptic substance, reduces body weight and food intake in obesity. Obes Res 2000;8:10S.

Smith MA, Schmidt KT, Iordanou JC, Mustroph ML. Aerobic exercise decreases the positive-reinforcing effects of cocaine. Drug Alcohol Depend 2008;98:129–135. [PubMed: 18585870]

Spitzer RL, Devlin M, Walsh BT, et al. Binge eating disorder: a multisite field trial of the diagnostic criteria. Int J Eating Disord 1992;11:191–203.

Steensland P, Simms JA, Holgate J, Richards JK, Bartlett SE. Varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, selectively decreases ethanol consumption and seeking. Proc Natl Acad Sci 2007;104:12518–12523. [PubMed: 17626178]

Stice E, Spoor S, Bohon C, Small DM. Relation between obesity and blunted striatal response to food is moderated by *Taq*lA A1 allele. Science 2008;322:449–452. [PubMed: 18927395]

Stunkard, AJ. A history of binge eating. In: Fairburn, C.; Wilson, G., editors. Binge eating: Nature, assessment, and treatment. New York: Guilford Press; 1993.

Stunkard AJ. Eating patterns and obesity. Psychiatr Q 1959;33:284–295. [PubMed: 13835451]

Stunkard AJ, Berkowitz R, Tanrikut C, Reiss E, Young L. *D*-Fenfluramine treatment of binge eating disorder. Am J Psychiatry 1996;153:1455–1459. [PubMed: 8890680]

Stunkard AJ, Faith MS, Allison KC. Depression and obesity. Biol Psychiatry 2003;54:330–337. [PubMed: 12893108]

Sutoo D, Akiyama K. The mechanism by which exercise modifies brain function. Physiol Behav 1996;60:177–181. [PubMed: 8804660]

Sutoo D, Akiyama K. Regulation of brain function by exercise. Neurobiol Dis 2003;13:1–14. [PubMed: 12758062]

Tallett AJ, Blundell JE, Rodgers RJ. Effects of acute low-dose combined treatment with naloxone and AM 251 on food intake, feeding behavior and weight gain in rats. Pharmacol Biochem Behav 2009;91:358–366. [PubMed: 18755211]

Tallett AJ, Blundell JE, Rodgers RJ. Endogenous opioids and cannabinoids: system interactions in the regulation of appetite, grooming and scratching. Physiol Behav 2008;94:422–431. [PubMed: 18394662]

Tammela LI, Rissanen A, Kuikka JT, et al. Treatment improves serotonin transporter binding and reduces binge eating. Psychopharmacology 2003;170:89–93. [PubMed: 12768277]

Thornley S, McRobbie H, Eyles H, Walker N, Simmons G. The obesity epidemic: is glycemic index the key to unlocking a hidden addiction? Med Hypotheses 2008;71:709–714. [PubMed: 18703288]

Toll BA, Leary V, Wu R, Salovey P, Meandzija B, O'Malley SS. A preliminary investigation of naltrexone augmentation of bupropion to stop smoking with less weight gain. Addict Behav 2008;33:173–179. [PubMed: 17587504]

Toschke AM, Ehlin AG, von Kries R, Ekbom A, Montgomery SM. Maternal smoking during pregnancy and appetite control in offspring. J Perinat Med 2003;31:251–256. [PubMed: 12825482]

Tschop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. Diabetes 2001;50:707–709. [PubMed: 11289032]

Urbszat D, Herman CP, Polivy J. Eat, drink, and be merry, for tomorrow we diet: effects of anticipated deprivation on food intake in restrained and unrestrained eaters. J Abnormal Psych 2002;111:396–401.

Van Gaal LF, Rissanen AM, Scheen AJ, Ziegler O, Rossner S. Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet 2005;365:1389–1397. [PubMed: 15836887]

Vickers SP, Webster LJ, Wyatt A, Dourish CT, Kennett GA. Preferential effects of the cannabinoids CB1 receptor antagonist, SR 141716, on food intake and body weight gain of obese (fa/fa) compared to lean Zucker rats. Psychopharmacology 2003;167:103–111. [PubMed: 12632249]

Volkow ND, Fowler JS, Wang GJ. The addicted human brain: insights from imaging studies. J Clin Invest 2003;111:1444–1451. [PubMed: 12750391]

Volkow ND, Fowler JS, Wang G-J, Swanson JM. Dopamine in substance abuse and addiction: results from imaging studies and treatment implications. Mol Psychiatry 2004;9:557–569. [PubMed: 15098002]

Volkow ND, O'Brien CP. Issues for DSM-V: should obesity be included as a brain disorder? Am J Psychiatry 2007;164:708–710. [PubMed: 17475727]

Volkow ND, Wise RA. How can substance addiction help us understand obesity? Nat Neuroscience 2005;8:555–560.

Volkow ND, Wang GJ, Fowler JS, Telang F. Overlapping neuronal circuits in addiction and obesity: evidence of systems pathology. Philos Trans R Soc Lond B Biol Sci 2008;363:3191–3200. [PubMed: 18640912]

Wang GJ, Volkow ND, Fowler JS, et al. PET studies of the effects of aerobic exercise on human striatal dopamine release. J Nuclear Medicine 2000;41:1352–1356.

Wang GJ, Volkow ND, Logan J, et al. Brain dopamine and obesity. Lancet 2001;357:354–357. [PubMed: 11210998]

Wang GJ, Volkow ND, Thanos PK, Fowler JS. Similarity between obesity and drug addiction as assessed by neurofunctional imaging: a concept review. J Addict Disord 2004;23:39–53.

West, R.; Schiffman, S. Smoking cessation fast facts: indispensible guides to clinical practice. Oxford: Oxford Health Press Limited; 2004.

Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). JAMA 1998;279:839–846. [PubMed: 9515998]

White MA, Grilo CM. Psychiatric comorbidity in binge-eating disorder as a function of smoking history. J Clin Psychiatry 2006;67:594–599. [PubMed: 16669724]

White MA, Grilo CM, O'Malley SS, Potenza MN. Clinical case discussion: binge eating disorder, obesity, and tobacco smoking. J Addict Med. in press.

Wilfey DE, Crow SJ, Hudson JI, et al. Efficacy of sibutramine for the treatment of binge eating disorder: a randomized multicenter placebo-controlled double-blind study. Am J Psychiatry 2008;165:51–58. [PubMed: 18056225]

Wilfley DE, Welch RR, Stein RI, et al. A randomized comparison of group cognitive-behavioral therapy and group interpersonal psychotherapy for the treatment of overweight individuals with binge-eating disorder. Arch Gen Psychiatry 2002;59:713–721. [PubMed: 12150647]

Wilson GT, Grilo CM, Vitousek K. Psychological treatments for eating disorders. Am Psychol 2007;62:199–216. [PubMed: 17469898]

Winter B, Breitenstein C, Mooren FC, et al. High impact running improves learning. Neurobiol Learn Mem 2007;87:597–609. [PubMed: 17185007]

Yanovski SZ, Nelson JE, Dubbert BK, Spitzer RL. Association of binge eating disorder and psychiatric comorbidity in obese subjects. Am J Psychiatry 1993;150:1472–1479. [PubMed: 8379549]

Yip, SW.; Potenza, MN. Understanding 'behavioral' addictions: insights from research. In: Ries, R.; Fiellin, D.; Miller, S.; Saitz, R., editors. Principles of Addiction Medicine. 4. New York: Wolters Kluwer; 2009. p. 45-63.

Zador D, Wall PML, Webster I. High sugar intake in a group of women on methadone maintenance in South Western Sydney, Australia. Addiction 1996;91:1053–1061. [PubMed: 8688819]

Table 1

Proposed Similarities and Differences Between Obesity, SUDs, and BED

	Obesity	SUDs	BED
Use despite adverse Consequences	+	+	+
Compulsive Use	+	+	+
Appetitive Urge	+	+	+
Diminished Control	+	+	+
Behavioral Therapies	Vary	Vary	Vary
Self-help treatment (AA, NA, OA groups)	+	+	+
Pharmacotherapies	Vary	Vary	Vary
Physiological Role of Substance	Necessary for survival	Unnecessary for survival	Necessary for survival
Learning, Habits, CRs	+	+	+
Role of Stress	+	+	+

SUDs = Substance Use Disorders

BED = Binge eating disorder

“Vary” indicates a role for treatments that show varying efficacies for each category of disorders.

AA = Alcoholics Anonymous

NA = Narcotics Anonymous

OA = Overeaters Anonymous

CRs= Conditioned Responses