14 Clinical Applications of the Food Addiction Concept

14.1 Treatment Overview

As discussed in Chap. 4, there is a pressing need for more efficacious, tolerable, and safe treatments for people with obesity and binge eating. In Chap. 5 we introduced several areas of current ongoing controversy about FA, but argued there are many reasons to hope that applying this concept will improve clinical outcomes. In Chap. 13, nutritional interventions to help people with FA were discussed. Here we will discuss non-nutritional interventions for FA treatment, many of which are derived from SUD treatment principles. Table 14.1 summarizes what we will be discussing in detail in the rest of this chapter.

SUD are associated with a lifelong (albeit diminishing with time in recovery) risk of relapse. This is because the brain, which has been damaged by chronic use and conditioning, takes time to heal. Treatment goals involve minimizing negative affect states, reducing substance and environmental cue reactivity, preventing habitual responding, and improving impulse control. Like in SUD, treatment of FA will involve long-term maintenance of brain health.

SUD are often treated with medications to reduce withdrawal symptoms, but much more importantly, medications are utilized to reduce relapse risk in the long term by re-balancing the brain reward and impulse control system. Examples of medications that work via some or all of these mechanisms for SUD include naltrex-

Table 14.1 Overview of treatment recommendations

Psychoeducation	Decreases self-blame, stigma, and reluctance to accept evidence-based medications
Psychosocial interventions	Cognitive behavioral therapy Behavioral weight management Motivational interviewing Mindfulness-based therapies DBT/ACT targeting emotion regulation Body image work
Sleep, Exercise	Improves impulse control Enhances mood Promotes recovery from FA
Medications	Naltrexone/bupropion SR Topiramate/phentermine Bupropion Lisdexamfetamine Naltrexone Topiramate Zonisamide Selective serotonin reuptake inhibitors Liraglutide
Treatment of underlying psychiatric disorders	Medications Evidence-based therapies
Self-help groups/12-step/Other support	Overeaters anonymous, food addicts anonymous, intensive outpatient or residential treatment program (SHiFT recovery by acorn for e.g.), sponsor or dietitian/nutritionist for food plan development and accountability
TMS	On the horizon, stay tuned
Surgery	Bariatric surgery

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one, acamprosate, topiramate, and disulfiram for alcohol use disorder; varenicline, bupropion, and nicotine replacement therapy for nicotine use disorder; and methadone, buprenorphine, and naltrexone for opioid use disorder [1]. Evidence-based psychosocial interventions for SUD (provided in either group or individual formats) include cognitive behavior therapy (CBT), mindfulness-based (MB) relapse prevention, interventions which improve emotion regulation such as dialectical behavior therapy (DBT), and acceptance and commitment therapy (ACT), 12-step facilitation approaches, and motivational interviewing [2] (see Appendix for extensive list of useful therapy manuals).

Notably, many of the evidence-based interventions for SUD are already adapted for and being utilized to treat obesity and EDs (Chaps. 2 and 3), which provides further reason to believe that many might also prove beneficial for the treatment of FA. However, there has been little treatment research on FA, so most of these recommendations are speculative and need further formal study in randomized clinical trials before widespread deployment.

The transdiagnostic model for ED treatment assumes that all EDs will respond to a similar therapeutic approach [3–7], and this assumption has led providers to assume that the approaches utilized for anorexia and bulimia will also work for binge eating disorder (BED), which was only recently included in the *Diagnostic and Statistical Manual* (DSM). However, it is not known whether ED approaches are best for all cases of BED and bulimia nervosa, especially where FA symptoms predominate or in people who also have obesity [3–7]. An alternate approach, outlined in one recent paper [4], argues that people with FA should utilize an abstinence-based nutritional approach (Chap. 13) (which would not be encouraged in a typical ED treatment program) and should also have the following three focuses during treatment: (1) reduction of habitual responding (e.g., conditioning based food cues) and impulsivity through psychotherapy, cognitive training techniques, and medications; (2) diminishment of negative reinforcement based behaviors (e.g., emotional eating) by reducing negative affect and increasing coping skills and alternate behaviors and social connection; and (3) reduction of compensatory behaviors such as vomiting or excessive exercise with psychoeducation and coping mechanisms skills training. This model directly speaks to what we extensively discussed in Chap. 8 regarding the underlying neurobiological causes of FA-like behavior.

In addition to abstinence, interventional strategies that successfully reduce craving for and consumption of alcohol, tobacco, and illicit drugs will also likely reduce craving for and compulsive consumption of food [8–10].

14.2 Supplemental Programmatic Elements Which Might Be Useful for Treatment of FA

14.2.1 Psychoeducation: FA Is a Brain-Based Disorder

Patients with FA and their providers should understand that the overeating is not due to character weakness or a problem of "willpower" but is rooted in brain chemistry. They should also understand how some of the suggested treatments would be expected to work, mechanistically, as this may enhance adherence to a particular dietary recommendation or medication. For example, knowing that sugar causes craving and loss of control via a biological cascade of events outside of one's control may help someone to stay on track with a commitment not to eat sugar. Understanding that it's not just about the calories, but that particular palatable foods may lead to loss of control of eating in some people, could motivate people to stay away from those particular foods and enhance their chances of success.

A brain-based explanation of SUD is often referred to as the disease-based model of addiction and is known to decrease stigma and self-blame [6, 11–13]. Patients can be educated utilizing materials such as Figs. 7.1 and 7.2 (Chap. 7) to explain the neurobiological underpinnings of addictive behavior. Such models of understanding may also benefit people with obesity and binge eating, in addition to FA [6, 14–16]. This is impor-

tant in light of the fact that shame worsens mood, and therefore recovery outcomes, since increasing negative affect can trigger increased emotional eating for self-soothing. Indeed, studies show that fear of being stigmatized predicts worsening FA status, maladaptive eating behaviors, stress, and weight gain [3, 17, 18]. However, it is also posited that biological explanations might reduce self-efficacy and might undermine someone's motivation to reduce calorie intake or change their eating patterns [6, 15, 19]. At this point it is not yet known what effects emphasizing the neurobiology might have on individual perceptions, attitudes, and behavior in FA, but based on the effects of such psychoeducation in SUD, it will likely be recommended [6].

Recall, from Chap. 4 the low acceptability among providers and the public of medications for obesity treatment [20]. Widespread psychoeducation regarding the neurobiology of overeating may also increase providers' inclination to suggest evidence-based medication treatments and patients to accept such suggestions. Indeed, physicians are, in general, less likely to believe in brain-based aspects of SUD than attorneys, showing physicians may have more stigmatizing beliefs than others, which is an obvious problem that should be addressed through increased provider education [13].

14.2.2 Psychosocial Interventions

There are numerous manuals available to guide providers in the application of evidence-based psychosocial interventions for SUDs, EDs, and psychiatric comorbidities (Appendix).

14.2.2.1 CBT

CBT is a therapeutic approach extensively informed by research for the treatment of EDs, obesity, and SUD, alike [7]. Generally, CBT interventions ask patients to critically evaluate the thoughts, feelings, and behaviors that result in maladaptive eating and then to modify them, helping patients to recognize potential triggers and develop appropriate coping strategies [7]. CBT for SUD, obesity, and ED targets irrational beliefs and cognitive distortions, focuses on identification of and use of effective coping skills, and emphasizes identifying and avoiding triggers (environmental, food/substance cue-related, and emotional triggers) [6, 21, 22]. CBT for ED differs from that utilized for SUD and obesity, however, in that CBT for EDs also includes a non-abstinence-based, all-foods-included nutritional component as previously discussed.

In FA or FA-like patients, CBT-approaches will likely prove useful. One study examined 47 internet sources to extract the CBT-like strategies endorsed by self-perceived sugar addicts. Actional strategies that reportedly worked for the participants included avoidance, meal consumption-planning, environmental restructuring, professional and social support, addressing underlying issues, and urge management, among others [3, 23]. Another group has developed a mobile health CBT-based strategy which includes CBT therapeutic components and also involves a staged food withdrawal from problem foods and between-meal or excessive eating, and it is described in detail in Chap. 13 [24]. Others have proposed a body-focused repetitive behavior (BFRB) approach for FA adapted from treatment utilized for other compulsive disorders such as nail-biting, skin picking, and hair pulling [25]. BFRB therapies incorporate distractions, competing behaviors, triggers avoidance, relaxation methods, aversion techniques, and distress tolerance. Adding action-based CBT components improved the weight loss more than just the sensory-based CBT components in the BFRB approach for FA, and weight loss was maintained for 5 months afterwards [25].

Another CBT-like approach, which hasn't been formally studied but which could be integrated in to CBT for FA, emphasizes the roles of attentional bias (excessive focus on food or emotional cues), temporal discounting (undervaluing future rewards), and the cold-hot empathy gap (when individuals are in a "hot," motivated state they overestimate the degree to which they will value a reward, in comparison to a non-motivated, neutral, "cold" state). This approach suggests distinguishing between temptation resistance strategies aimed at overcoming temptation while

it is experienced and temptation prevention strategies that seek to avoid or minimize exposure to tempting stimuli since inhibiting habitual cue-driven behaviors during a "hot" state is much more difficult and requires prospective thinking to identify and avoid exposure to foods that may challenge future self-control [10, 26]. The latter kind of strategy places emphasis on minimizing temptation through stimulus control (removing tempting food from the home), scheduling and planning, time locking safes, or even financial contracting (punishment strategy) or social contracting (publicly committing to the goal) [10], and it dovetails well with abstinence-based nutritional approaches. The treatment plan (what foods to abstain from, how to reduce exposure to triggering simuli) can be decided upon when someone is ideally in a "cold state" and cognitive functions are intact.

14.2.2.2 Behavioral Weight Management

In addition to CBT, behavioral weight management (Chap. 2) shows promise in several uncontrolled studies for FA. For example, a 14-week group lifestyle modification program including caloric reduction significantly reduced addictive eating behaviors in one study [3, 27]. A 6-week integrative group for weight management in another study reduced FA from pre to post and utilized strategies such as mindful eating, keeping a food diary, carrying out an exercise plan, regular weigh-ins, and planning for social eating [3, 28].

14.2.2.3 Motivational Interviewing (MI)

MI is extensively utilized in SUD to motivate change in behavior [8, 29]. Indeed, it may help for FA as well, although it has not been hugely successful in obesity, in general [30]. In one study, a person-centered MI-based intervention was delivered in three sessions via telehealth to individuals with FA and obesity or overweight called "FoodFix." This intervention was associated with a reduction in energy intake from "non-core foods" (i.e., foods with added or high amounts of salt, sugar, and/or fat) compared with the waitlist control intervention, but both the active and control groups showed reductions in Yale Food Addiction Scale (YFAS) scores [31].

14.2.2.4 Psychotherapy to Reduce Negative Affect States, Improve Emotion Regulation, and Address Alexithymia

Several bodies of work indicate that emotional eating (or eating to self-sooth, the basis of negative reinforcement-driven eating) may be more resistant to change and extinction compared to external (food-cue driven) eating [32, 33]. For example, 4 years after a diet intervention, scores on emotional eating had hardly changed in both the male and the female patients with diabetes type 2, whereas scores on external eating had declined significantly in the female patients [33]. This might indicate a need for people with FA and emotional eating to do more extensive work on emotion regulation and deeper psychological issues. Such work may involve efforts to teach people how to recognize their own emotions, since "difficulty identifying feelings" (alexithymia) was associated with emotional eating and may mediate the relationship between depression and emotional eating [33]. Other emotion regulation-focused psychotherapeutic strategies such as DBT and ACT might be particularly useful for people who struggle with emotional eating, but more work needs to be done in this area to confirm.

14.2.2.5 Mindfulness-Based (MB) Approaches

MB interventions and emotion regulation-based strategies, like DBT and ACT, which incorporate mindfulness are helpful in SUD, ED, and obesity populations (reviewed in Chaps. 2 and 3) but have not been formally studied in FA. Lower interoceptive awareness was found to be associated with FA in an ED population, indicating that more work on mindful eating and becoming aware of internal hunger and satiety cues might prove useful in this population [34]. Furthermore,

impulsivity is a major contributor to FA, and mindfulness work has been shown to improve impulse control in numerous populations [35]. These interventions can be utilized now and should be studied in people with FA.

14.2.2.6 Body Image Work

Body image work may also prove important in FA treatment, when relevant. Shape/weight overvaluation is associated with BED and bulimia [3, 36–38]. Relatedly, those with heightened body image disturbance are more likely to engage in dietary restraint [3, 37], which may contribute to bingeing as well as FA symptoms [3]. However, weight loss might be the most effective way to improve body image in individuals with FA [39].

14.2.3 Importance of Sleep

As described in Chap. 9, adequate sleep is important for improvement in mood, executive function, impulse control, and recovery from both SUD and disorders of overeating. Patients with sleep disturbance should be counseled to adopt sleep hygiene techniques and, if prescribed, take sleeping supplements. Melatonin may especially be helpful, and some early work indicates that it may have secondary utility in reducing adiposity [40]. In fact, setmelanotide is a melanocortin-4 receptor agonist under study for obesity treatment [41]. Getting adequate exercise, which improves sleep in people with a variety of psychiatric illness [42], should be recommended. Patients with difficulty sleeping and FA might also benefit from CBT for insomnia [43].

14.2.4 Importance of Exercise

Clearly, exercise is important for treatment of obesity, and it can reduce appetite, increase calories burned, and slightly increase resting metabolic rate as discussed in Chap. 2. However, there is growing evidence that exercise will likely be key for FA treatment for other reasons including its beneficial effects on dysphoria and negative affect [44] and impulse control [45] the latter of which may be mediated by restoring type 2 and type 3 dopamine receptors (D2) in the dorsal striatum (Chaps. 7 and 8) [46]. More studies are needed in this area as well.

14.2.5 Importance of Getting Psychiatric and Psychological Care

As we discussed in Chap. 6, FA is associated with and likely made worse by a variety of psychiatric comorbidities, including major depressive disorder (MDD), bipolar disorder, anxiety disorders, attention deficit hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD), and personality disorders. Since many studies show that stress and negative affect can drive habitual behaviors via negative reinforcement [47], and that impulsivity can contribute to loss of control of eating, treatment of FA should involve aggressive assessment for and management of these comorbid disorders. Evidence-based psychotherapies such as CBT, ACT, DBT, other emotion regulation trainings, MB interventions, interpersonal psychotherapy (IPT), and psychodynamic therapy can be utilized. Furthermore, psychiatric evaluation for possible pharmacotherapeutic management of an underlying disorder should always be considered. Medications targeting these comorbidities and evidence-based treatments are key.

Failure to recognize and treat PTSD and other trauma-based sequelae is a major contributor to poor outcomes in the treatment of EDs and obesity and is also believed to play a big role in some people FA as well which we have discussed in more detail in Chap. 6 [48]. Multiple studies indicate childhood maltreatment predicts FA which then predicts obesity [48]. This link is also likely maintained through negative reinforcement learning and connected to emotional eating [47]. Evidence-based trauma therapies such as exposure therapy or trauma-focused CBT may be useful for these individuals for reducing FA symptoms, although this has not been directly studied.

14.2.6 Neuromodulation Techniques

There has been recent explosion in research on and use of non-convulsive (e.g., not electroconvulsive therapy) brain stimulation techniques for the treatment of a variety of psychiatric disorders. This includes a growing body of work exploring their potential for reducing craving and addictive behavior [49, 50]. The most commonly applied stimulation method clinically is repetitive transcranial magnetic stimulation (rTMS), although transcranial direct current stimulation, vagal nerve stimulation, and even deep brain stimulation are being studied for obesity and BED, too [7, 51]. rTMS is Food and Drug Association (FDA)-approved for the treatment of several disorders [MDD, obsessive compulsive disorder (OCD)] using more than one approach [49, 50], and it is a safe way to focally affect brain activation [51]. rTMS is used in awake participants and is therefore minimally disruptive, associated with minimal side effects, and is quite safe when used appropriately within guidelines [7, 49, 50, 52–54]. rTMS works via a number of potential mechanisms to alter neural activity, including by increasing connectivity and increasing dopamine function for example [7, 8, 55, 56]. rTMS studies have primarily focused on stimulating the (usually left) dorsolateral prefrontal cortex (DLPFC), to enhance cognitive control. Some rTMS studies are now starting to explore other targets such as the anterior cingulate cortex (ACC) and cerebellum [57]. Moreover, deep rTMS, which allows for access to deeper brain structures in a noninvasive way, is being studied for other psychiatric disorders and may one day prove useful for reduction of drug and food cravings, since the circuitry involved in regulating feeding tend to be deeper (the insula striatum and hypothalamus are inaccessible with standard rTMS coils) [49, 50].

When applied to the DLPFC, rTMS has been shown to effectively reduce cravings for cigarettes, alcohol, and other drugs of abuse, especially when applied for multiple sessions, and may be useful for drug use reduction in cocaine and nicotine use disorders [49, 50]. The DLPFC is an area involved extensively in inhibitory control, and stimulation of this region may act to boost self-control, potentially by increasing dopamine release in the caudate nucleus, which rTMS has been shown to do [7].

rTMS is also currently being investigated for its potential to reduce food craving and consumption [7] and shows promise for this purpose too. Application of rTMS to DLPFC reduces self-reported food craving and appetite in single and multi-session format [6, 51, 56, 58, 59]. For example, rTMS to the left DLPFC did not affect cue-induced craving for palatable foods, whereas there was an increase in craving in the sham group [7, 60]. Most definitively, a randomized controlled trial of rTMS delivered to the left DLPFC was effective in decreasing food intake and facilitating weight loss in obese patients, suggesting that rTMS could be an effective treatment option for obesity and FA [61].

14.2.7 12-Step Programs and Other Support

Studies show that Alcoholics Anonymous (AA) and Narcotic Anonymous (NA) attendance predicts abstinence for individuals with alcohol and other SUD [62, 63]. 12-step programs are believed to work as a consequence of the fellowship and community-building, an increased sense of goal directedness and structure, use of more effective coping skills (often learned through sponsorship and step work), engagement in sober activities, and increased self-efficacy and hope [64]. Increased spirituality and reduction in depression are also important mechanisms by which these programs promote recovery [65–67]. Providers are encouraged to recommend AA and NA to people in recovery to promote better functioning and reduced substance use in individuals with SUD. 12-step facilitation is an established evidence-based treatment for SUD that focuses on getting people engaged in AA or NA [68].

The Overeaters Anonymous (OA) organization is a 12-step-based program that promotes the central belief that obesity is a symptom of "compulsive overeating," an addictive-like illness with

physical, emotional, and spiritual components [3, 7, 8, 69, 70]. Individuals are required to acknowledge that compulsive overeating is beyond their willpower to overcome alone, and, to control their food intake, overeaters are encouraged to adopt a food plan and surrender to a "higher power." "Food Addicts Anonymous" (another 12-step program affiliated with OA) is similar, but has a more rigid, one-sized-fits-all food plan [3, 7, 8, 69, 70]. The primary goal of 12-step program treatment for "compulsive overeating" is abstinence, like in NA and AA. Abstinence is definable by the overeater in OA in collaboration with their sponsor (and might involve three meals a day and up to two snacks "with nothing in between" or avoiding particular trigger foods) or by adherence to a uniform food plan for Food Addicts Anonymous [3, 7, 8, 69, 70]. Just like AA and NA, OA and FA involve group meetings for individuals to share their feelings and experiences [3, 7, 8, 69, 70].

Unlike AA, very little research into the efficacy of OA has been done [7]. Some individuals struggling with overeating report that applying an abstinence model helped them to control their eating [8, 69, 70]. But little is known about the long-term success (and possible adverse effects) of such an approach. In a study of 60 women, 12-step self-help groups for compulsive eating have been shown to reduce anxiety and depression, but not FA [3]. Larger, long-term studies are needed.

That said, OA and related programs may serve many of the needs of the person with FA and support many of the recommendations made in this chapter and Chap. 13. Going to a meeting can provide distraction and replace a counterproductive behavior (e.g., bingeing or eating a palatable food) with a more productive one. Animal studies show that environmental enrichment reduces food seeking and taking in rats [71]: "keeping busy" is an oft-cited coping mechanism by many people in recovery from SUD. Reducing loneliness, isolation, and shame, all of which can fuel obesity, BE, FA, and other addictions [72–75], may be another benefit of 12-step participation. As discussed earlier, overweight and obesity are associated with higher shame and guilt and a preference for isolative activities [7, 76]. This social isolation can subsequently exacerbate overeating, creating a vicious cycle [77, 78]. With engagement in a fellowship of people with similar struggles, and with increased support and socialization, one would expect to see a reduction in the shame and isolation, breaking this vicious cycle.

There are numerous additional resources which patients can access to obtain increased structure and support. For example, a virtual intensive outpatient and a residential treatment program are available through SHiFT Recovery by Acorn (www.foodaddicion.com) and food addiction recovery retreats are available through COR (https://cormn.org). Many people with FA find it almost impossible to develop a food plan and stick with it without outside support from a sponsor or dietitian/nutritionist: the "addict brain" fights hard to keep less helpful foods (foods that are both craved and that trigger the disease) in the food plan, ultimately sabotaging attempts to stay abstinent, whereas the "eating disorder" brain over-restricts caloric intake. Sponsor- and dietitian/nutritionist-involvement can help the person with FA find that middle ground between succumbing to justifications/rationalizations to overeat versus over restricting which can then trigger binge eating.

14.2.8 Medications

There are a number of evidence-based pharmacotherapeutic treatments for obesity, BED, and bulimia nervosa (Chaps. 2 and 3), albeit with some downfalls (Chap. 4), working via several important addiction-based mechanisms (Chap. 10) (see Table 2.1). Early work is starting to show these medicines also reduce FA symptoms. For example, an open-label trial on the efficacy and tolerability of naltrexone/bupropion SR for treating altered eating behaviors and weight loss in BED showed a significant and similar weight loss (approximately 8%) and reductions in YFAS scores for both a group of people with obesity plus BED and BED alone [79].

For people with FA, it is wise to chose pharmacotherapies approved both for the treatment of

BED and obesity that target reward, conditioning, negative reinforcement and impulse control mechanisms. For example, topiramate and possibly zonisamide likely act by reducing cue reactivity and global impulse control; naltrexone (in naltrexone/bupropion) may reduce cue reactivity, food elicited pleasure/liking, and improve impulse control, especially during exposure to impulsivity during opioid release; stimulants like bupropion, lisdexamfetamine, and phentermine (in topiramate/phentermine) likely also improve impulse control; selective serotonin reuptake inhibitors likely reduce and anxiety and depression symptoms; and glucagon-like peptide 1 agonists (e.g., liraglutide) act on primary homeostatic appetitive mechanisms but may also have direct effects on addiction/reward circuitry like pleasure from food and cue reactivity [1, 3, 6, 41, 79–84]. Any of these medicines would be reasonable first-line choices in FA, although one may be more suited to one patient over another based on individual vulnerabilities, such as emotion regulation, food cue-induced reactivity, impulse control difficulties, depression or anxiety, or sensitivity to just a taste of pleasurable food. One can also make medication choices based on the patient's medical history, keeping in mind side effect profiles and medical or psychiatric contraindications [84] (Table 2.1).

Whether stimulants are safe to prescribe to people with FA is not yet known, and these medications should be used with caution. Bupropion/naltrexone and phentermine/topiramate contain stimulants (bupropion and phentermine both have stimulant activity) and are approved for long-term weight management [6, 41, 81, 85]. Lisdexamfetamine is also approved for BED and promotes weight loss. On the one hand, one would surmise that since stimulants (especially lisdexamfetamine and bupropion) reduce impulsivity and enhance prefrontal activity in some people [86, 87], they would be useful in addictive disorders. However, stimulants also have high addictive potential, and, as we have seen in Chap. 6, and addiction transfer is not uncommon. Prescribed long acting stimulants are used in stimulant use disorder treatment [88] but have not been found to be highly effective in other drug use disorders like alcohol or nicotine use disorders [89], perhaps because they prime the reward system. Research is needed to test long-term outcomes of these medicines in people with especially severe FA symptomatology. One study found that a stimulant appetite suppressant that enhanced dopamine functioning was not effective in adults who screened positive for FA on the YFAS compared with controls [90]. Further work to investigate for whom stimulants are most helpful and for whom they are most harmful is needed. Of the stimulants, bupropion is probably the least addictive and most safe for use in FA populations, with the caveat that it is contraindicated in patients with concurrent purging behaviors. Also, recall that any expected potential health benefits from the modest weight loss during treatment with stimulants, like lisdexamfetamine and phentermine, are likely nullified by their adverse cardiovascular effects (heart rate and blood pressure elevations), and, therefore, from a cardiovascular perspective, many professionals are of the opinion that stimulants have a net negative effect on health outcomes.

Future work could also consider exploring the utility of already approved medicines like prazosin [91, 92] in people with comorbid PTSD (for which prazosin is often prescribed) and FA, or anti-obesity medicines like glucagon like-1 (GLP-1) agonists that also enhance hippocampal functioning may show promise in treatment of SUD's via improved hippocampal functioning and other reward-based mechanisms [41, 93–95].

14.2.9 Bariatric Surgery

Bariatric surgery appears to be an effective treatment for FA [96]. Recall that bariatric surgery is indicated and highly effective for people with severe obesity, inducing significant weight loss in the majority of patients, and that the weight loss is more often than not maintained over years [97] (Chap. 2). Surgery-induced weight loss is also associated with remission of FA symptoms [98–100]. In one study, the proportion of individuals meeting criteria for a FA diagnosis reduced to 2% post-surgery from 32% pre-surgery [97, 100]. Another long-term follow-up study found that the rates of FA reduced from 58% to 7% at 6 months

although there was some rebound in FA rates later on, with rates of FA up to 14% at 12 months after surgery [97, 101]. A third study also showed some evidence of FA resurgence after long-term follow-up: FA was identified in 41% and BE in 48% of individuals before sleeve gastrectomy (all FA patients also had BE), and at month 3, FA was seen in 10% of patients and at month 6, 7%. However, at month 12, 29% of patients met FA criteria again. BE, however, was still lower than baseline at all time points (17% at month 12) [96]. The group of women with FA had lower weight loss outcomes and a higher average body mass index (BMI) at month 12 as well [96, 102].

Several scientific studies have uncovered possible mechanisms for the beneficial effect of surgery on FA symptoms which we review in Chap. 10 in detail. In brief, surgery causes reversal of dopamine receptor downregulation in the striatum and hyperreactivity to food cues, restores the brain-gut-microbiome axis imbalance, and dampens excessive dopamine release to sweet consumption and food reward.

14.3 Subtyping and FA Treatment Matching

Obesity is increasingly recognized as a heterogeneous condition [103, 104], and experts believe that there are likely many different reasons why people gain excess weight. The same is likely true of BED and bulimia nervosa [39]. One important theme in obesity and ED research is to better identify and understand possible subtypes [103–106] which could then segue into studies to identify which treatments work best in which subtypes, in order to match treatments to the individual's particular needs [103, 104, 106, 107]. Indeed there is great variability in the degree of weight change in obesity and ED clinical trials [39, 103, 104], with some individuals gaining and others losing large amounts of weight, and by doing mean effects, rather than identifying subgroups more likely to respond, current analyses are potentially masking hidden benefits of our treatments. This push to identify subtypes is in line with efforts to utilize more "precision-medicine" across all fields [108, 109].

14.3.1 Within-FA Treatment Matching

One possible way to look for treatment matching effects is to explore whether or not different subgroups exist within the population of those with an FA diagnosis. Subgroups could be defined by co-occuring disorders, or by traits and vulnerabilites (e.g. by those more driven by food cues versus negative affect versus those with impulsivity issues). Indeed, we can probably already start making some of our management decisions in this way. For example, we can choose medicines based on comorbidities as discussed above. If someone has comorbid depression or anxiety, we could prescribe a selective serotonin reuptake inhibitor; if they have comorbid alcohol use disorder, we might prescribe topiramate or zonisamide; if they have comorbid ADHD, we might prescribe lisdexamfetamine or bupropion; if they have comorbid PTSD, we might prescribe prazosin; or if the person with FA is obese or has type II diabetes, we might prescribe a GLP-1 agonist. Although rTMS is not approved for the treatment of obesity or EDs, in the case of someone with treatment-resistant MDD or OCD (two diagnoses for which there are commonly utilized FDA-approved rTMS stimulation protocols [49, 50]) who also has comorbid FA, we could be more inclined to refer for rTMS treatment. For those that are especially sensitive to the effects of food cues, abstinence (which will promote faster extinguising of conditioning), and naltrexone or topiramate (which reduce the power of cues to trigger food-seeking) might be especially useful. For those that struggle with negative reinforcement based eating or comfort eating, SSRIs, interpersonal therapy, social support and sleep might be especially useful. For those that go through severe food withdrawal, time "clean" might be strongly encouraged. For those with high levels of impulsivity, exercise, sleep, medications like lisdexamfetamine, bupropion and topiramate (which are known to improve impulse control), and psychotherapies like DBT and ACT may be good to emphasize.

An intriguing recent study identified three subtypes of FA [98]: a dysfunctional group, Cluster 1, characterized by the highest ED severity and psy-

chopathology, for which authors propose treatment focused on ED symptomatology and FA only secondarily; Cluster 2 with better levels of functioning, but the highest levels of FA for which authors proposed treatment could target FA aggressively, focusing on reward related processes and conditioning, perhaps encouraging a more restrictive food plan; and Cluster 3 with a high prevalence of obesity but more grazing behavior than bingeing for whom authors suggested that focusing on reduction in BMI first might then lead to reductions in FA and craving and/or that this group could be a surgery target [98].

Another recent article examined external eating (cue-driven and dependent on positive reinforcement mechanisms) and emotional eating (related to negative reinforcement), modeling these as different constructs [33]. This may, incidentally, map onto a growing body of work in the alcohol literature by researchers examining motivations for drinking and which shows that those that drink for reward may be in a separate category from those who drink for relief of negative affect and out of habit (the latter two motivations overlap) [110]. This categorization is likely to apply in FA. For example, in other work in FA, authors found that impulsivity contributes directly to external eating, whereas depression and alexithymia as well as impulsivity contributed to emotional eating [33]. Furthermore, weight loss resulted in reductions in external eating over time, but emotional eating did not remit [33, 111, 112]. It is also theorized that the alexithymia may contribute to impulsive overeating via an additional inability to read visceral sensations [33]. These findings would imply that people who suffer from emotional eating should engage in some deeper therapy work and work to help them identify their emotions and/or consider psychiatric evaluation for medication treatment to reduce risk of relapse, whereas those with external eating might best focus on weight loss, avoiding foods and triggers. Both might benefit from medications or interventions (e.g., exercise) that reduce impulsivity.

Another subgroup within FA populations might be those with a history of trauma or high levels of stress. Studies show that food addiction is a mediator of psychological distress [113] or perceived stress [114] and BMI. FA is also a mediator of early life adversity (ELA) on obesity, [3, 115–117]. These findings would indicate that targeting FA as soon as it develops holds promise for people with stress and trauma as it could prevent obesity later on. Early intervention for ELA may prevent obesity since usually the FA and obesity develop later in life or the trauma might be a target of treatment that could help reduce BMI. The same kinds of relationships are seen for ED symptoms in that childhood maltreatment, especially physical neglect and physical abuse, was associated with higher global ED severity scores, and this effect was mediated by FA scores [118]. This would imply that targeting FA in people with a history of trauma early could prevent ED development and/or might also reduce ED symptoms in those who have already developed it [119, 120] and further emphasizes the importance of providing trauma treatment to prevent and promote recovery from obesity and EDs and FA alike.

Finally, female gender was a predictor of severe food addiction, and high reward sensitivity was significantly associated with more severe FA symptoms in females [98, 121]. This is consistent with what's seen in females with SUD deemed "telescoping" which is believed in part to be due to estrogen enhancing dopaminergic activity (and therefore conditioning process etc.). Theoretically women could require more attention to dopamine-mediated processes such as reward and conditioning, and treatments targeting these processes over others might be useful.

14.3.2 Using FA as a Treatment Matching Variable for Patients with Obesity and BE

FA started off as a concept to explain a potential subtype of obesity [98, 120, 122, 123] that might provide more information than the presence or absence of a comorbid BED or bulimia nervosa diagnosis. And using the presence of FA to identify a subtype of obesity which might be more responsive to treatment with addiction-like

models including abstinence-based approaches and brain-based interventions holds promise. Those with a diagnosis of FA might be more susceptible to highly processed foods, too [124]. Although not yet studied, people with FA would also be expected to respond to MI more than those without, given the robust effects of MI in SUD populations. Although BED did not moderate outcome to MI (which was less effective than nutritional psychoeducation) [30], one wonders if FA diagnosis might. Unfortunately, very little has been done in this area, and more research is needed. There are no studies (clinical trials) looking at food addiction as a predictor of outcome to particular diets, psychosocial interventions, or medications. FA also seems like an excellent potential matching variable for studies looking at the effects of more restrictive diets on treatment outcomes in individuals with BED and obesity to answer questions about in whom a more restrictive diet is safe and in whom it is not.

A few studies do deserve mention, however, showing poorer response to treatment with those with FA in response to standard treatment. One study showed that women with FA had less favorable weight loss outcomes and BMI post sleeve gastrectomy at year one [96, 102]. In another study, FA was found to be a mediator in the relationship between ED severity and treatment outcome [125] indicating that those with higher FA symptoms were less likely to respond to the standard ED treatment provided in that study. Finally in an intervention study among women with bulimia, those with higher FA severity at baseline were less likely to obtain abstinence from binge-purge episodes following treatment [3, 126]. If nothing else, it is clear that patients with FA should potentially be watched more closely and given more intensive initial intervention than those without.

14.4 Conclusion

There is currently a paucity of research into non-nutritional treatment of patients with FA. However, there is a growing body of preliminary evidence to support a number of possible treatment options, many of which have been borrowed or adapted from current treatments for SUDs, EDs, and obesity. Additionally, combining several treatment modalities may provide additive or synergistic benefit to selective patients. Considering an individual patient's unique symptoms and comorbidities will provide practitioners guidance in determining the best course of treatment for their patients.

References

1. Wilcox CE, Bogenschutz MB. Psychopharmacologies for alcohol and drug use disorders. In: McCrady BS, Epstein EE, editors. Addictions: a comprehensive guidebook. 2nd ed. New York: Oxford University Press; 2013. p. 526–50.
2. Center for Substance Abuse Treatment. Groups and substance abuse treatment. In: Substance abuse treatment: group therapy, Treatment improvement protocol (TIP) series, No. 41. Rockville: Substance Abuse and Mental Health Services Administration (US); 2005. Available from: https://www.ncbi.nlm.nih.gov/books/NBK64223/.
3. Wiss D, Brewerton T. Separating the signal from the noise: how psychiatric diagnoses can help discern food addiction from dietary restraint. Nutrients. 2020;12(10):2937.
4. Treasure J, Leslie M, Chami R, Fernandez-Aranda F. Are trans diagnostic models of eating disorders fit for purpose? A consideration of the evidence for food addiction. Eur Eat Disord Rev. 2018;26(2):83–91.
5. Carter A, Hardman CA, Burrows T. Food addiction and eating addiction: scientific advances and their clinical, social and policy implications. Nutrients. 2020;12(5):1485.
6. Carter A, Hendrikse J, Lee N, Yucel M, Verdejo-Garcia A, Andrews ZB, et al. The neurobiology of "food addiction" and its implications for obesity treatment and policy. Annu Rev Nutr. 2016;36:105–28.
7. Adams RC, Sedgmond J, Maizey L, Chambers CD, Lawrence NS. Food addiction: implications for the diagnosis and treatment of overeating. Nutrients. 2019;11(9):2086.
8. Meule A. A critical examination of the practical implications derived from the food addiction concept. Curr Obes Rep. 2019;8(1):11–7.
9. May J, Andrade J, Kavanagh DJ, Feeney GF, Gullo MJ, Statham DJ, et al. The craving experience questionnaire: a brief, theory-based measure of consummatory desire and craving. Addiction. 2014;109(5):728–35.
10. Appelhans BM, French SA, Pagoto SL, Sherwood NE. Managing temptation in obesity treatment: a neurobehavioral model of intervention strategies. Appetite. 2016;96:268–79.

11. Meurk C, Fraser D, Weier M, Lucke J, Carter A, Hall W. Assessing the place of neurobiological explanations in accounts of a family member's addiction. Drug Alcohol Rev. 2016;35(4):461–9.
12. Dackis C, O'Brien C. Neurobiology of addiction: treatment and public policy ramifications. Nat Neurosci. 2005;8(11):1431–6.
13. Avery JJ, Avery JD, Mouallem J, Demner AR, Cooper J. Physicians' and attorneys' beliefs and attitudes related to the brain disease model of addiction. Am J Addict. 2020;29(4):305–12.
14. Latner JD, Puhl RM, Murakami JM, O'Brien KS. Food addiction as a causal model of obesity. Effects on stigma, blame, and perceived psychopathology. Appetite. 2014;77:77–82.
15. Pearl RL, Lebowitz MS. Beyond personal responsibility: effects of causal attributions for overweight and obesity on weight-related beliefs, stigma, and policy support. Psychol Health. 2014;29(10):1176–91.
16. Sikorski C, Luppa M, Kaiser M, Glaesmer H, Schomerus G, Konig HH, et al. The stigma of obesity in the general public and its implications for public health – a systematic review. BMC Public Health. 2011;11:661.
17. Meadows A, Higgs S. Internalized weight stigma and the progression of food addiction over time. Body Image. 2020;34:67–71.
18. Puhl RM, Himmelstein MS, Pearl RL. Weight stigma as a psychosocial contributor to obesity. Am Psychol. 2020;75(2):274–89.
19. Lee NM, Carter A, Owen N, Hall WD. The neurobiology of overeating. Treating overweight individuals should make use of neuroscience research, but not at the expense of population approaches to diet and lifestyle. EMBO Rep. 2012;13(9):785–90.
20. Gadde KM, Atkins KD. The limits and challenges of antiobesity pharmacotherapy. Expert Opin Pharmacother. 2020;21(11):1319–28.
21. Fairburn CG. Overcoming binge eating, second edition: the proven program to learn why you binge and how you can stop. New York: The Guilford Press; 2013.
22. Lanza PV, Garcia PF, Lamelas FR, Gonzalez-Menendez A. Acceptance and commitment therapy versus cognitive behavioral therapy in the treatment of substance use disorder with incarcerated women. J Clin Psychol. 2014;70:644–57.
23. Rodda SN, Booth N, Brittain M, McKean J, Thornley S. I was truly addicted to sugar: a consumer-focused classification system of behaviour change strategies for sugar reduction. Appetite. 2020;144:104456.
24. Vidmar AP, Pretlow R, Borzutzky C, Wee CP, Fox DS, Fink C, et al. An addiction model-based mobile health weight loss intervention in adolescents with obesity. Pediatr Obes. 2019;14(2):e12464.
25. Pretlow RA, Stock CM, Roeger L, Allison S. Treatment of the sensory and motor components of urges to eat (eating addiction?): a mobile-health pilot study for obesity in young people. Eat Weight Disord. 2020;25(6):1779–87.
26. Seligman ME, Railton P, Baumeister RF, Sripada C. Navigating into the future or driven by the past. Perspect Psychol Sci. 2013;8(2):119–41.
27. Chao AM, Wadden TA, Tronieri JS, Pearl RL, Alamuddin N, Bakizada ZM, et al. Effects of addictive-like eating behaviors on weight loss with behavioral obesity treatment. J Behav Med. 2019;42(2):246–55.
28. Miller-Matero LR, Brescacin C, Clark SM, Troncone CL, Tobin ET. Why WAIT? Preliminary evaluation of the weight assistance and intervention techniques (WAIT) group. Psychol Health Med. 2019;24(9):1029–37.
29. Hettema JE, Hendricks PS. Motivational interviewing for smoking cessation: a meta-analytic review. J Consult Clin Psychol. 2010;78(6):868–84.
30. Barnes RD, Ivezaj V, Martino S, Pittman BP, Grilo CM. Back to basics? No weight loss from motivational interviewing compared to nutrition psychoeducation at one-year follow-up. Obesity. 2017;25(12):2074–8.
31. Burrows T, Collins R, Rollo M, Leary M, Hides L, Davis C. The feasibility of a personality targeted intervention for addictive overeating: FoodFix. Appetite. 2021;156:104974.
32. van Strien T, Ouwens MA. Effects of distress, alexithymia and impulsivity on eating. Eat Behav. 2007;8(2):251–7.
33. Ouwens MA, van Strien T, van Leeuwe JF. Possible pathways between depression, emotional and external eating. A structural equation model. Appetite. 2009;53(2):245–8.
34. Fauconnier M, Rousselet M, Brunault P, Thiabaud E, Lambert S, Rocher B, et al. Food addiction among female patients seeking treatment for an eating disorder: prevalence and associated factors. Nutrients. 2020;12(6):1897.
35. Janssen L, Kan CC, Carpentier PJ, Sizoo B, Hepark S, Schellekens MPJ, et al. Mindfulness-based cognitive therapy v. treatment as usual in adults with ADHD: a multicentre, single-blind, randomised controlled trial. Psychol Med. 2019;49(1):55–65.
36. Forrest LN, Jacobucci RC, Grilo CM. Empirically determined severity levels for binge-eating disorder outperform existing severity classification schemes. Psychol Med. 2020:1–11.
37. Andres A, Saldana C. Body dissatisfaction and dietary restraint influence binge eating behavior. Nutr Res. 2014;34(11):944–50.
38. Thompson KJ. Body image, eating disorders and obesity: an integrative guide for assessment and treatment. Washington, DC: American Psychological Association; 2000.
39. Pacanowski CR, Mason TB, Crosby RD, Mitchell JE, Crow SJ, Wonderlich SA, et al. Weight change over the course of binge eating disorder treatment: relationship to binge episodes and psychological factors. Obesity. 2018;26(5):838–44.
40. Genario R, Cipolla-Neto J, Bueno AA, Santos HO. Melatonin supplementation in the management

of obesity and obesity-associated disorders: a review of physiological mechanisms and clinical applications. Pharmacol Res. 2021;163:105254.
41. Coulter AA, Rebello CJ, Greenway FL. Centrally acting agents for obesity: past, present, and future. Drugs. 2018;78(11):1113–32.
42. Lederman O, Ward PB, Firth J, Maloney C, Carney R, Vancampfort D, et al. Does exercise improve sleep quality in individuals with mental illness? A systematic review and meta-analysis. J Psychiatr Res. 2019;109:96–106.
43. van der Zweerde T, Bisdounis L, Kyle SD, Lancee J, van Straten A. Cognitive behavioral therapy for insomnia: a meta-analysis of long-term effects in controlled studies. Sleep Med Rev. 2019;48:101208.
44. Schuch FB, Stubbs B. The role of exercise in preventing and treating depression. Curr Sports Med Rep. 2019;18(8):299–304.
45. Lambez B, Harwood-Gross A, Golumbic EZ, Rassovsky Y. Non-pharmacological interventions for cognitive difficulties in ADHD: a systematic review and meta-analysis. J Psychiatr Res. 2020;120:40–55.
46. Robertson CL, Ishibashi K, Chudzynski J, Mooney LJ, Rawson RA, Dolezal BA, et al. Effect of exercise training on striatal dopamine D2/D3 receptors in methamphetamine users during behavioral treatment. Neuropsychopharmacology. 2016;41(6):1629–36.
47. Koob GF, Powell P, White A. Addiction as a coping response: hyperkatifeia, deaths of despair, and COVID-19. Am J Psychiatry. 2020;177(11):1031–7.
48. Wiss DA, Brewerton TD. Adverse childhood experiences and adult obesity: a systematic review of plausible mechanisms and meta-analysis of cross-sectional studies. Physiol Behav. 2020;223:112964.
49. Wilcox CE. Non-convulsive neurostimulation for the treatment of psychiatric disorders part I: FDA-approved treatments. American Physician Institute; 2020. Available from: CMEToGo.com.
50. Wilcox CE. Non-convulsive neurostimulation for the treatment of psychiatric disorders part II: emerging treatments. American Physician Institute; 2020. Available from: CMEToGo.com.
51. Val-Laillet D, Aarts E, Weber B, Ferrari M, Quaresima V, Stoeckel LE, et al. Neuroimaging and neuromodulation approaches to study eating behavior and prevent and treat eating disorders and obesity. Neuroimage Clin. 2015;8:1–31.
52. Maizey L, Allen CP, Dervinis M, Verbruggen F, Varnava A, Kozlov M, et al. Comparative incidence rates of mild adverse effects to transcranial magnetic stimulation. Clin Neurophysiol. 2013;124(3):536–44.
53. Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009;120(12):2008–39.
54. Taylor R, Galvez V, Loo C. Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists. Australas Psychiatry. 2018;26(2):189–92.
55. Feil J, Zangen A. Brain stimulation in the study and treatment of addiction. Neurosci Biobehav Rev. 2010;34(4):559–74.
56. Hall PA, Vincent CM, Burhan AM. Non-invasive brain stimulation for food cravings, consumption, and disorders of eating: a review of methods, findings and controversies. Appetite. 2018;124:78–88.
57. Wilcox CE, Clifford J, Ling J, Mayer AR, Bigelow R, Bogenschutz MP, et al. Stroop-related cerebellar and temporal activation is correlated with negative affect and alcohol use disorder severity. Brain Imaging Behav. 2020;14:586–98.
58. Wilcox CE. Binge eating disorder. American Physician Institute; 2019. Available from: CMEtoGo.com.
59. Kinasz KR, Ross DA, Cooper JJ. Eat to live or live to eat? The neurobiology of appetite regulation. Biol Psychiatry. 2017;81(9):e73–e5.
60. Uher R, Yoganathan D, Mogg A, Eranti SV, Treasure J, Campbell IC, et al. Effect of left prefrontal repetitive transcranial magnetic stimulation on food craving. Biol Psychiatry. 2005;58(10):840–2.
61. Kim SH, Chung JH, Kim TH, Lim SH, Kim Y, Lee YA, et al. The effects of repetitive transcranial magnetic stimulation on eating behaviors and body weight in obesity: a randomized controlled study. Brain Stimul. 2018;11(3):528–35.
62. Kelly JF, Stout RL, Magill M, Tonigan JS, Pagano ME. Mechanisms of behavior change in alcoholics anonymous: does Alcoholics Anonymous lead to better alcohol use outcomes by reducing depression symptoms? Addiction. 2010;105(4):626–36.
63. Tonigan JS, Toscova R, Miller WR. Meta-analysis of the literature on Alcoholics Anonymous: sample and study characteristics moderate findings. J Stud Alcohol. 1996;57(1):65–72.
64. Donovan DM, Ingalsbe MH, Benbow J, Daley DC. 12-step interventions and mutual support programs for substance use disorders: an overview. Soc Work Public Health. 2013;28(3–4):313–32.
65. Tonigan JS. Spirituality and alcoholics anonymous. South Med J. 2007;100(4):437–40.
66. Tonigan JS. Alcoholics anonymous outcomes and benefits. Recent Dev Alcohol. 2008;18:357–72.
67. Wilcox CE, Pearson MR, Tonigan JS. Effects of long-term AA attendance and spirituality on the course of depressive symptoms in individuals with alcohol use disorder. Psychol Addict Behav. 2015;29(2):382–91.
68. MATCH. Matching alcoholism treatments to client heterogeneity: project MATCH posttreatment drinking outcomes. J Stud Alcohol. 1997;58(1):7–29.
69. Rodriguez-Martin BC, Gallego-Arjiz B. Overeaters anonymous: a mutual-help fellowship for food addiction recovery. Front Psychol. 2018;9:1491.
70. Russell-Mayhew S, von Ranson KM, Masson PC. How does overeaters anonymous help its members? A qualitative analysis. Eur Eat Disord Rev. 2010;18(1):33–42.
71. Grimm JW, Sauter F. Environmental enrichment reduces food seeking and taking in rats: a review. Pharmacol Biochem Behav. 2020;190:172874.

72. Sun Y, Li Y, Bao Y, Meng S, Sun Y, Schumann G, et al. Brief report: increased addictive internet and substance use behavior during the COVID-19 pandemic in China. Am J Addict. 2020;29(4):268–70.
73. Rolland B, Haesebaert F, Zante E, Benyamina A, Haesebaert J, Franck N. Global changes and factors of increase in caloric/salty food intake, screen use, and substance use during the early COVID-19 containment phase in the general population in France: survey study. JMIR Public Health Surveill. 2020;6(3):e19630.
74. Cherikh F, Frey S, Bel C, Attanasi G, Alifano M, Iannelli A. Behavioral food addiction during lockdown: time for awareness, time to prepare the aftermath. Obes Surg. 2020;30(9):3585–7.
75. Van de Graaf RC, Hofstra L. Obesity and covid-19: the role of the food industry. BMJ. 2020;370:m2813.
76. Hayden-Wade HA, Stein RI, Ghaderi A, Saelens BE, Zabinski MF, Wilfley DE. Prevalence, characteristics, and correlates of teasing experiences among overweight children vs. non-overweight peers. Obes Res. 2005;13(8):1381–92.
77. Neumark-Sztainer D, Falkner N, Story M, Perry C, Hannan PJ, Mulert S. Weight-teasing among adolescents: correlations with weight status and disordered eating behaviors. Int J Obes Relat Metab Disord. 2002;26(1):123–31.
78. Pretlow RA. Addiction to highly pleasurable food as a cause of the childhood obesity epidemic: a qualitative Internet study. Eat Disord. 2011;19(4):295–307.
79. Carbone EA, Caroleo M, Rania M, Calabro G, Staltari FA, de Filippis R, et al. An open-label trial on the efficacy and tolerability of naltrexone/bupropion SR for treating altered eating behaviours and weight loss in binge eating disorder. Eat Weight Disord. 2021;26:779–88.
80. Hutson PH, Balodis IM, Potenza MN. Binge-eating disorder: clinical and therapeutic advances. Pharmacol Ther. 2018;182:15–27.
81. Vetter ML, Faulconbridge LF, Webb VL, Wadden TA. Behavioral and pharmacologic therapies for obesity. Nat Rev Endocrinol. 2010;6(10):578–88.
82. Rubio G, Martinez-Gras I, Manzanares J. Modulation of impulsivity by topiramate: implications for the treatment of alcohol dependence. J Clin Psychopharmacol. 2009;29(6):584–9.
83. Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Addiction. 2013;108(2):275–93.
84. Khalil H, Ellwood L, Lord H, Fernandez R. Pharmacological treatment for obesity in adults: an umbrella review. Ann Pharmacother. 2020;54(7):691–705.
85. Jung J, Fugh-Berman A. Marketing messages in continuing medical education (CME) modules on binge-eating disorder (BED). J Am Board Fam Med. 2020;33(2):240–51.
86. Brady KT, Gray KM, Tolliver BK. Cognitive enhancers in the treatment of substance use disorders: clinical evidence. Pharmacol Biochem Behav. 2011;99(2):285–94.
87. Spencer RC, Devilbiss DM, Berridge CW. The cognition-enhancing effects of psychostimulants involve direct action in the prefrontal cortex. Biol Psychiatry. 2015;77(11):940–50.
88. Moeller FG, Schmitz JM, Herin D, Kjome KL. Use of stimulants to treat cocaine and methamphetamine abuse. Curr Psychiatry Rep. 2008;10(5):385–91.
89. Joos L, Goudriaan AE, Schmaal L, Fransen E, van den Brink W, Sabbe BG, et al. Effect of modafinil on impulsivity and relapse in alcohol dependent patients: a randomized, placebo-controlled trial. Eur Neuropsychopharmacol. 2013;23(8):948–55.
90. Davis C, Levitan RD, Kaplan AS, Kennedy JL, Carter JC. Food cravings, appetite, and snack-food consumption in response to a psychomotor stimulant drug: the moderating effect of "food-addiction". Front Psychol. 2014;5:403.
91. Hicks C, Sabino V, Cottone P. The alpha-1 adrenergic receptor antagonist prazosin reduces binge-like eating in rats. Nutrients. 2020;12(6):1569.
92. Wilcox CE, Tonigan JS, Bogenschutz MP, Clifford J, Bigelow R, Simpson T. A randomized, placebo-controlled, clinical trial of prazosin for the treatment of alcohol use disorder. J Addict Med. 2018;12(5):339–45.
93. Clasen MM, Riley AL, Davidson TL. Hippocampal-dependent inhibitory learning and memory processes in the control of eating and drug taking. Curr Pharm Des. 2020;26(20):2334–52.
94. Farr OM, Sofopoulos M, Tsoukas MA, Dincer F, Thakkar B, Sahin-Efe A, et al. GLP-1 receptors exist in the parietal cortex, hypothalamus and medulla of human brains and the GLP-1 analogue liraglutide alters brain activity related to highly desirable food cues in individuals with diabetes: a crossover, randomised, placebo-controlled trial. Diabetologia. 2016;59(5):954–65.
95. Hernandez NS, Schmidt HD. Central GLP-1 receptors: novel molecular targets for cocaine use disorder. Physiol Behav. 2019;206:93–105.
96. Ben-Porat T, Weiss R, Sherf-Dagan S, Rottenstreich A, Kaluti D, Khalaileh A, et al. Food addiction and binge eating during one year following sleeve gastrectomy: prevalence and implications for postoperative outcomes. Obes Surg. 2021;31(2):603–11.
97. Sarkar S, Kochhar KP, Khan NA. Fat addiction: psychological and physiological trajectory. Nutrients. 2019;11(11):2785.
98. Jimenez-Murcia S, Aguera Z, Paslakis G, Munguia L, Granero R, Sanchez-Gonzalez J, et al. Food addiction in eating disorders and obesity: analysis of clusters and implications for treatment. Nutrients. 2019;11(11):2633.
99. Murray SM, Tweardy S, Geliebter A, Avena NM. A longitudinal preliminary study of addiction-like

responses to food and alcohol consumption among individuals undergoing weight loss surgery. Obes Surg. 2019;29(8):2700–3.
100. Pepino MY, Stein RI, Eagon JC, Klein S. Bariatric surgery-induced weight loss causes remission of food addiction in extreme obesity. Obesity. 2014;22(8):1792–8.
101. Sevincer GM, Konuk N, Bozkurt S, Coskun H. Food addiction and the outcome of bariatric surgery at 1-year: prospective observational study. Psychiatry Res. 2016;244:159–64.
102. Ivezaj V, Wiedemann AA, Grilo CM. Food addiction and bariatric surgery: a systematic review of the literature. Obes Rev. 2017;18(12):1386–97.
103. Higgins GA, Sellers EM, Fletcher PJ. From obesity to substance abuse: therapeutic opportunities for 5-HT2C receptor agonists. Trends Pharmacol Sci. 2013;34(10):560–70.
104. Higgins GA, Zeeb FD, Fletcher PJ. Role of impulsivity and reward in the anti-obesity actions of 5-HT2C receptor agonists. J Psychopharmacol. 2017;31(11):1403–18.
105. Blundell JE, Dulloo AG, Salvador J, Fruhbeck G, EASO SAB Working Group on BMI. Beyond BMI--phenotyping the obesities. Obes Facts. 2014;7(5):322–8.
106. Field AE, Camargo CA Jr, Ogino S. The merits of subtyping obesity: one size does not fit all. JAMA. 2013;310(20):2147–8.
107. Ziauddeen H, Fletcher PC. Is food addiction a valid and useful concept? Obes Rev. 2013;14(1):19–28.
108. Dishman E. Precision medicine. 2018. https://www.nih.gov/precision-medicine-initiative-cohort-program. Accessed 2018.
109. Bearden CE, Thompson PM. Emerging global initiatives in neurogenetics: the enhancing neuroimaging genetics through meta-analysis (ENIGMA) consortium. Neuron. 2017;94(2):232–6.
110. Grodin EN, Bujarski S, Venegas A, Baskerville WA, Nieto SJ, Jentsch JD, et al. Reward, relief and habit drinking: initial validation of a brief assessment tool. Alcohol Alcohol. 2019;54(6):574–83.
111. Forman EM, Shaw JA, Goldstein SP, Butryn ML, Martin LM, Meiran N, et al. Mindful decision making and inhibitory control training as complementary means to decrease snack consumption. Appetite. 2016;103:176–83.
112. Van Strien T, Van de Laar FA. Intake of energy is best predicted by overeating tendency and consumption of fat is best predicted by dietary restraint: a 4-year follow-up of patients with newly diagnosed type 2 diabetes. Appetite. 2008;50(2–3):544–7.
113. Lin YS, Tung YT, Yen YC, Chien YW. Food addiction mediates the relationship between perceived stress and body mass index in Taiwan young adults. Nutrients. 2020;12(7):1951.
114. Lin CY, Cheung P, Imani V, Griffiths MD, Pakpour AH. The mediating effects of eating disorder, food addiction, and insomnia in the association between psychological distress and being overweight among Iranian adolescents. Nutrients. 2020;12(5):1371.
115. Romano KA, Heron KE, Amerson R, Howard LM, MacIntyre RI, Mason TB. Changes in disordered eating behaviors over 10 or more years: a meta-analysis. Int J Eat Disord. 2020;53(7):1034–55.
116. Elsenburg LK, Smidt N, Liefbroer AC. The longitudinal relation between accumulation of adverse life events and body mass index from early adolescence to young adulthood. Psychosom Med. 2017;79(3):365–73.
117. Elsenburg LK, van Wijk KJE, Liefbroer AC, Smidt N. Accumulation of adverse childhood events and overweight in children: a systematic review and meta-analysis. Obesity. 2017;25(5):820–32.
118. Bou Khalil R, Sleilaty G, Richa S, Seneque M, Iceta S, Rodgers R, et al. The impact of retrospective childhood maltreatment on eating disorders as mediated by food addiction: a cross-sectional study. Nutrients. 2020;12(10):2969.
119. Cope EC, Gould E. New evidence linking obesity and food addiction. Biol Psychiatry. 2017;81(9):734–6.
120. Sinha R. Role of addiction and stress neurobiology on food intake and obesity. Biol Psychol. 2018;131:5–13.
121. Loxton NJ, Tipman RJ. Reward sensitivity and food addiction in women. Appetite. 2017;115:28–35.
122. Gearhardt AN, Boswell RG, White MA. The association of "food addiction" with disordered eating and body mass index. Eat Behav. 2014;15(3):427–33.
123. Ferrario CR. Food addiction and obesity. Neuropsychopharmacology. 2017;42(1):361.
124. Seid H, Rosenbaum M. Low carbohydrate and low-fat diets: what we don't know and why we should know it. Nutrients. 2019;11(11):2749.
125. Romero X, Aguera Z, Granero R, Sanchez I, Riesco N, Jimenez-Murcia S, et al. Is food addiction a predictor of treatment outcome among patients with eating disorder? Eur Eat Disord Rev. 2019;27(6):700–11.
126. Hilker I, Sanchez I, Steward T, Jimenez-Murcia S, Granero R, Gearhardt AN, et al. Food addiction in bulimia nervosa: clinical correlates and association with response to a brief psychoeducational intervention. Eur Eat Disord Rev. 2016;24(6):482–8.