Low carbohydrate ketogenic therapy as a metabolic treatment for binge eating and ultraprocessed food addiction

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Purpose of review
The aim of this study was to highlight the recent advancements and future directions for potential use of a low carbohydrate ketogenic dietary approach to treat binge eating and ultraprocessed food addiction. Herein, we explore proposed mechanisms of why a diet low in refined carbohydrates, processed sugar and higher fat content may be helpful in alleviating symptoms.

Recent findings
Emerging evidence suggests there may be a metabolic role in development of maladaptive eating. These findings broaden our understanding of eating psychopathology causes. Ultraprocessed, refined or high glycemic index carbohydrates are a possible trigger mediating neurochemical responses similar to addiction. The carbohydrate-insulin model of obesity supports observations of these foods triggering abnormal blood sugar and insulin spikes subsequently leading to changes in metabolic and neurobiological signaling. This results in overeating symptoms and hunger exacerbation, which differs from observed effects of healthy fat consumption and lack of similar insulin spikes. As supported in recent case series, significantly reducing or abstaining from these addictive-like ultraprocessed foods and highly refined carbohydrates could be considered a treatment approach.

Summary
The current review highlights recent and pertinent evidence with respect to theoretical and practical application of low carbohydrate ketogenic therapeutic approaches for ultraprocessed food addiction and binge eating symptoms (see supplemental video).

Keywords
binge eating, ketogenic diet, low carbohydrate, obesity, ultraprocessed food addiction

INTRODUCTION

Binge eating disorder (BED) was introduced as a clinical entity for the first time in 2013 in the DSM-5. It is characterized by recurrent and persistent episodes of binge eating (i.e. loss of control over consumption of an objectively large amount of food consumed in a discrete period of time), marked distress regarding binge eating and absence of regular compensatory behaviours [1]. BED increases the risk of obesity/severe obesity and other metabolic abnormalities [2]. Although the lifetime prevalence of BED is estimated to be 3.5% among women and 2% among men in the USA, approximately 40–80% of those with BED suffer from obesity [3]. Physical comorbidities associated with both binge eating and obesity include but not limited to diabetes, hypertension, dyslipidaemia, coronary heart disease, congestive heart failure and various types of cancer. One factor that may contribute to binge eating is an addictive response to ultraprocessed foods that are often much higher in refined carbohydrates, combined with unhealthy fats and salt (e.g. breads, cookies, cakes, chips) [4]. Much like addictive drugs, highly processed foods trigger dopamine reward pathways and induce behaviors indicative of addiction. These behavioural symptoms include intense

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KEY POINTS

- Highly refined carbohydrates and ultraprocessed foods can alter brain signalling, appetite-satiety mechanisms and reward signaling, which can promote binge eating and addictive-like behaviour.
- Consistent with the carbohydrate-insulin model of obesity, both animal and human studies show consumption of ultraprocessed food and highly refined carbohydrates promote insulin resistance and overeating behaviours.
- Preliminary data show that a low carbohydrate ketogenic diet may be beneficial for binge eating and ultraprocessed food addiction symptoms through improvements in metabolic and neurobiological pathways. However, further research involving randomized controlled trials are needed.

cravings, feelings of withdrawal when cutting down on ultraprocessed food, continued consumption despite knowledge of adverse consequences, repeated unsuccessful attempts to quit and consumption in larger quantities or over longer periods than intended [5]. The prevalence of obesity, binge eating and addictive-like eating have risen in concordance with the increasing dominance of ultraprocessed foods in the modern food environment [6▪]. The prevalence of ultraprocessed food addiction symptoms among individuals with obesity ranges from 20 to 42% across a number of studies and 50% among those with BED [7–11].

If ultraprocessed foods are a key component of binge and addictive-like eating, then reducing consumption of these foods may be an important component of treatment. Although dietary restriction is thought to exacerbate binge eating, some studies specifically examining the effects of promoting healthier lower calorie dieting in BED have reported significant reductions and even remission of binge eating [12–15]. Subsequent reintroduction of normal western dietary patterns is accompanied by an increase in binge eating. However, the severity does not reach pretreatment levels and many patients no longer meet criteria for BED [12,14,15]. One treatment approach that has not yet been rigorously tested in those with BED and ultraprocessed food addiction is the use of a low carbohydrate ketogenic diet.

A ketogenic diet is a high-fat, low-carbohydrate, moderate protein diet that shifts body metabolism to utilization of fatty acids, for example burning fat and ketones as the primary source of energy rather that glucose or carbohydrates. Amongst many other potential neurometabolic effects, this state results in a reduction of circulating glucose and insulin, inducing physiological changes such as appetite suppression, decreased hunger, greater satiety, greater rates of lipolysis, reduction of lipogenesis and increased metabolic costs of gluconeogenesis and thermic effect of proteins [16]. Ketogenic diets are well known for successful use in paediatric epilepsy, diabetes and obesity. A comprehensive review by Kraeuter *et al.* [17▪] showed that increased ketone levels are needed to achieve effective ketogenic diet induced symptom control in neurodegenerative and neurodevelopmental disorders, with potential mechanisms broadly including oxidative stress reduction, decrease in inflammation and changes in energy metabolism. Less is known regarding ketogenic diet treatment effects for other mental health conditions such as binge eating and ultraprocessed food addiction. In this review, we will explore the potential mechanisms and rationale for a low carbohydrate ketogenic diet to treat processed food addiction and binge eating symptoms. Subsequently, we highlight limitations and important future directions.

POTENTIAL MECHANISMS AND RATIONALE FOR USE

The mechanisms by which a low carbohydrate ketogenic diet influence binge eating and ultraprocessed food addiction symptoms are likely complex, multifactorial, and may involve the effects of nutritional ketosis and its ensuing metabolic effects. Major mechanisms proposed in the literature include both neurobiological and metabolic diseases. Proposed neurobiological changes involve alteration in neurochemical signals and changes in activation of the mesolimbic dopamine reward pathway implicated in addiction [18,19,20▪]. See Fig. 1. Proposed metabolic changes include both physiological and hormonal changes affecting both reward and appetite-satiety signaling [21▪,22,23].

Neurobiological and metabolic mechanisms

Animal and human experiments with functional magnetic resonance imaging (fMRI) studies have recently shown that ultraprocessed foods affect the neurobiological reward pathway and the degree of alteration is dependent on metabolic signals, such as glucose oxidation [19]. For example, in humans, processed foods high in refined carbohydrates and fats are particularly effective in activating reward-associated related neural regions, such as the caudate and putamen, which predicts an increased willingness to pay more money on these foods [4]. Animal models further find that a diet dominated by

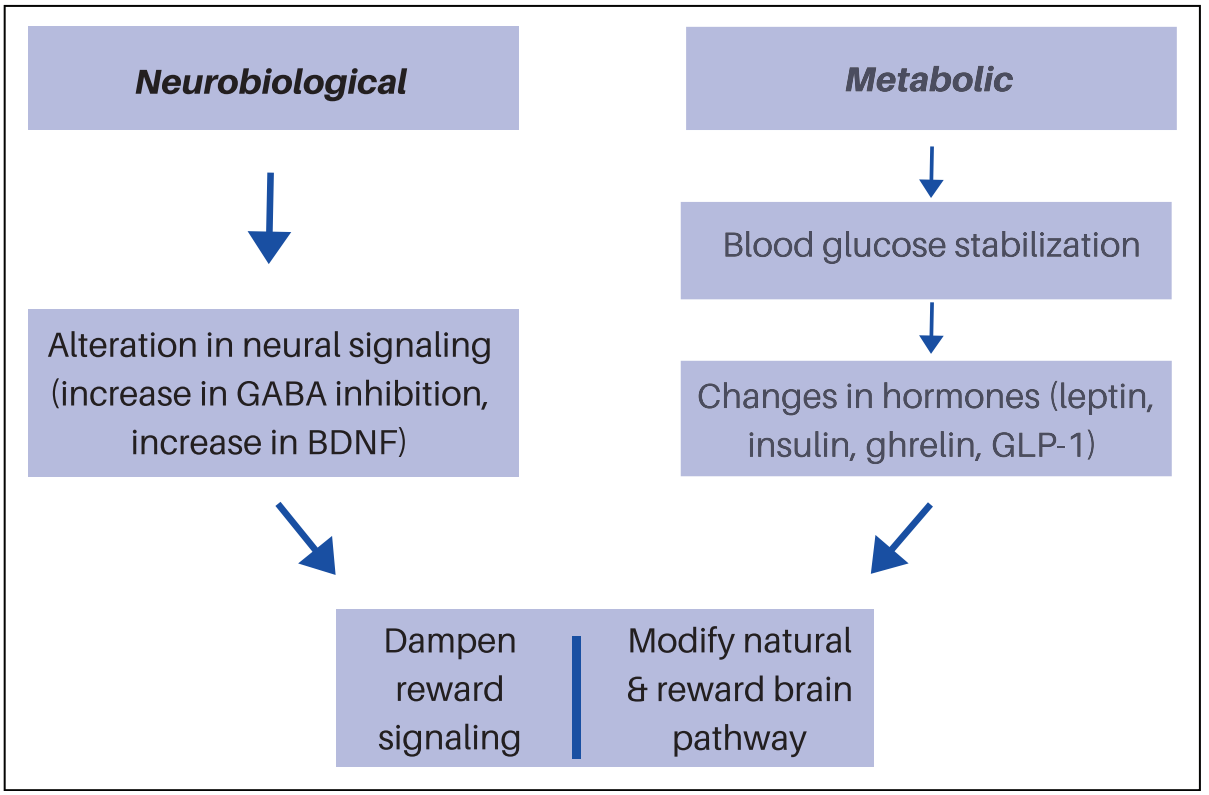

FIGURE 1. Potential mechanism of a low-carb ketogenic diet. Major mechanisms include neurobiological and metabolic pathways. Proposed neurobiological changes involve alteration in neurochemical signals, whereas proposed metabolic changes involve physiologic and hormonal changes, both affecting downstream reward pathways.

ultraprocessed foods leads to downregulation of dopamine D2 receptors, which corresponds to increased compulsive intake of ultraprocessed foods (but not chow) [24]. Hormones such as insulin, leptin, ghrelin and glucagon-like peptide (GLP)-1 modify natural and drug reward pathways in the brain [22]. An increase in hunger hormones can reduce satiety and also increase the reactivity of the dopamine system. These shifts signal the mesolimbic system to modify dopamine concentration through both direct and indirect pathways. For example, insulin increases dopamine reuptake in the presynaptic membrane and suppresses motivated behaviour [23]. Lennerz and Lennerz [21▪] propose that high glycemic index carbohydrates, such as corn and potatoes, trigger a rapid shift in blood glucose and insulin levels similar to the pharmacokinetics of addictive substances, which may also alter reward-related neural systems in a similar manner. See Fig. 2. In support of this idea, it is worthy to note typical binge foods listed in the literature are almost entirely ultraprocessed foods high in sugar [25]. A retrospective observational study of 74 patients showed that regardless of the type of eating disorder, those patients who engaged in binge eating binged on ultraprocessed foods 100% of the time [26]. Schulte *et al.* [20▪] found that a high glycemic index diet was the strongest component of processing associated with addictive eating behaviours.

A growing number of brain fMRI studies reveal that differences in functionally connected brain networks may contribute to binge eating behaviour, changes in reward processing and executive functioning. Decreases in resting state connectivity are seen in executive, default and salience networks in binge eating [27]. Diminished recruitment of prefrontal cognitive control circuitry is thought to play a role in development of binge eating. BED and ultraprocessed food addiction are associated with decreased inhibitory control and increased sensitivity to reward (particularly to ultraprocessed foods) [28]. Gearhardt *et al.* [29] have shown that those with high self-reported symptoms of food addiction had greater activation in the mesolimbic reward system in response to an ultraprocessed food cue and reduced activation in inhibitory regions in response to ultraprocessed food intake. The release of reward-associated neurotransmitters dopamine, opiates and endocannabinoids are implicated in processed food addiction [30]. Hence, both binge eating and particularly ultraprocessed food

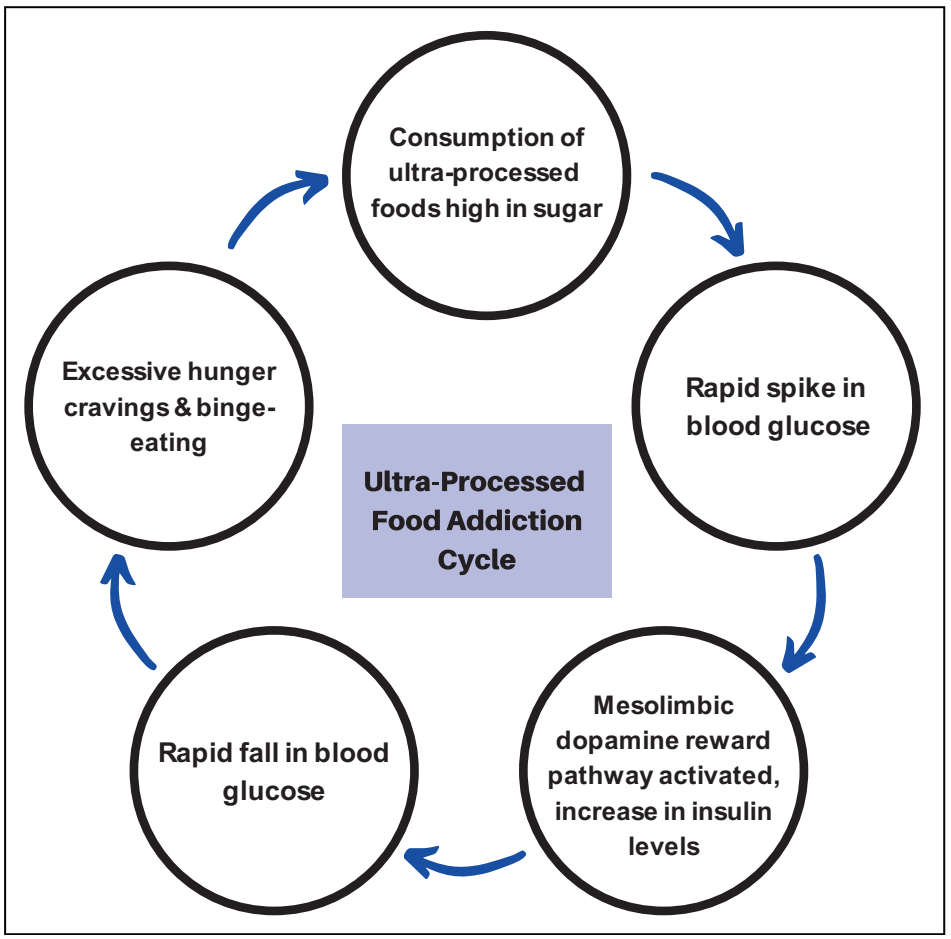

FIGURE 2. Ultraprocessed food addiction cycle. Ultraprocessed food (UPF) high in carbohydrates trigger a rapid shift in blood glucose and insulin levels. These shifts signal the mesolimbic system to modify dopamine concentration, which activate reward-related neural systems leading to compulsive intake of UPF.

addiction are associated with dysfunction in overlapping circuitry to substance addiction (Gearhardt *et al.*, in preparation; This study examines how highly processed foods have unnaturally high levels of refined carbohydrates combined with fat leading to high reinforcement, activation of reward-related systems and other addictive-like properties.)

A low carbohydrate ketogenic diet focused on whole foods, fats and adequate protein may provide beneficial effects ultimately on neural systems that bypass activation of the problematic cascade of effects that ultraprocessed foods activate. Drugs of abuse or foods considered to have addictive properties exert influence over the brain reward pathway directly through the action of dopamine within the system or indirectly by altering activity of other neurotransmitter systems, which modulates the activity of the mesolimbic dopaminergic pathway [31]. One such system involves the major inhibitory neurotransmitter gamma-aminobutyric acid (GABA), which is often used as a treatment target for substance addiction. Emerging evidence suggests that ketosis may alter the metabolism of excitatory amino acids, leading to an increase in GABA inhibition [18]. Indirectly, the ketogenic diet may play a role in altering neurotransmission and dampening reward signalling. In animal experiments, the ketogenic diet showed potential as therapy in dampening down the reward response in rats despite being injected with cocaine [32▪]. The ketogenic diet also increases expression of brain-derived neurotrophic factor (BDNF), which has been associated with lowered food intake. Diets high in sugar and refined carbohydrates have been shown to decrease BDNF expression and lead to hyperphagia [33]. Additional potential mechanisms of a low carbohydrate ketogenic diet include stabilization of blood glucose and prevention of unnatural blood glucose spikes due to the absence of highly processed sugar in the diet. The unnatural shifts in glucose and insulin are hypothesized to be key in triggering addictive effects of highly processed foods. This may be particularly important given that blood glucose levels are thought to trigger striatal dopamine release and high glycemic index foods

are consumed in an addictive manner [20▪]. Thus, reducing glucose spikes may be reducing addictive activation in the brain. Interestingly, foods with high fat found in a ketogenic diet devoid of carbohydrates are not consumed in an addictive manner [34▪]. The ketogenic diet also does not result in precipitous glucose declines or hypoglycemia, which may prime the reward centres of the brain to respond in addictive ways [35]. This dietary approach also includes a moderate amount of protein, which has been shown to dampen reward response to processed foods [36].

Ghrelin is a peptide hormone secreted by the stomach in response to a negative energy balance and increased levels have been linked to increased appetite in humans [37]. Ketone ester supplements have been shown to significantly reduce ghrelin and appetite [38]. This resulting increase in satiety may reduce how reactive the brain is to ultraprocessed food reward cues. Cholecystokinin (CCK) may also be involved in the improvement of symptoms following a ketogenic diet. This hormone is released postprandially from endocrine I receptors in the small intestine, with high circulating CCK levels linked to high levels of satiety and decreased food intake [39]. Typically, after weight loss that does not involve ketosis, circulating levels of CCK decrease [40]. However, sustained ketosis may raise CCK despite weight loss, such that the ability to modulate food intake is enhanced [41]. High circulating levels of PYY, a hormone released from both the small and large intestines postprandially, have been linked to high levels of satiety [42]. In a comparison of a low-carbohydrate, ketogenic diet to a low-fat diet, serum PYY levels were sustained at higher levels in those following the ketogenic diet [43]. The hormone leptin is also known to play a critical role in reducing hunger and has effects on dopamine and brain reward circuitry [44]. Individuals with obesity often have excess serum leptin levels, which is believed to be a surrogate for leptin resistance as a cause of impaired satiety [45]. Adhering to a ketogenic diet to achieve short-term weight loss is associated with acutely reduced levels of circulating leptin, potentially indicating restored leptin sensitivity [46]. In addition, individuals with food addiction symptoms report higher hunger levels than controls, with reductions in hunger associated with reduced food cravings [47,48]. Ketosis-induced appetite suppression may play a role in reducing cravings commonly reported in both BED and food addiction symptoms. A recent controlled study by Castro *et al.* [49▪] showed a reduction in food and alcohol cravings with a ketogenic diet in patients with obesity in addition to improvements in sleep, mood and quality of life. Additional treatment effects of this dietary intervention for other conditions have been explored; however, further study is needed to determine the exact relationship in those with binge eating or processed food addiction. This includes studying the potential role of reduction in oxidative stress and neuroinflammation, stabilization of brain networks and cerebral glucose hypometabolism [50▪].

A recent systematic review and meta-analysis found that the risk of type 2 diabetes mellitus (T2DM) triples in those with BED, suggesting that BED could lead to hyperinsulinemia or that hyperinsulinemia could promote satiety signalling changes leading to overeating or binge eating and hunger exacerbation. High carbohydrate foods that trigger greater insulin responses may play a role in both the maintenance of the disorder itself and the onset [51,52]. Consistent with the carbohydrate-insulin model of obesity that proposes consumption of refined carbohydrates actually triggering overeating, case series by Carmen, Sethi Dalai *et al.* reported compelling clinical experience on the successful treatment of binge eating and food addiction symptoms in three patients with comorbid obesity through the use of a ketogenic diet for at least 6 months. All patients experienced a significant decrease in frequency of binge episodes, fewer symptoms of depression, fewer food addiction symptoms, as well as a significant amount of weight loss (10–25% of initial body weight) leading to clinical improvements in metabolic health [53▪]. Evidence from this first case series supports the potential therapeutic utility of the removal of refined carbohydrates through a low carbohydrate ketogenic diet in this population and possibly others. A diet low in fat and high in carbohydrates dominated by processed carbohydrates may exacerbate feelings of hunger and enhance the likelihood of cravings. A low carbohydrate ketogenic diet encourages consumption of healthy fat, thus ultimately avoiding the exacerbation of hunger and overeating effects present in a standard American diet, and thus necessitating an exciting area for further study.

LIMITATIONS AND FUTURE DIRECTIONS

There are a number of limitations in using low carbohydrate ketogenic diets for the treatment of binge eating and ultraprocessed food addiction. For example, we do not have long-term data on the efficacy of the ketogenic diet or how high carbohydrate diets effect satiety signalling and neurobiological pathways in this population over years. A majority of studies are cross-sectional and case studies that limit any conclusions of causality. We also

do not have metabolic focused data predicting the emergence of binge eating or food addiction symptoms in these patients. Symptoms of ultraprocessed food addiction and binge eating may start at an early age in adolescence or early adulthood, necessitating any study of symptoms far earlier. There are no randomized controlled trials to date comparing diets containing ultraprocessed food to those without, or diets higher in fat such as a low carbohydrate ketogenic diet to those with lower fat or protein in those with binge eating or addiction disease. Evaluation of efficacy as well as any potential long-term adverse effects for others need to be evaluated.

With regard to binge eating, traditionally, dieting is thought to play a causal role with the concern that restrictive eating can cause negative psychological consequences, feelings of deprivation and potential relapse of disordered eating. Notably, the dietary restraint hypothesis has not been examined with all diets and needs further study. Studies analysing the effects of dieting in a more broadly defined sense, with calorie focus as opposed to food quality, have had mixed results, with some data supporting that very low calorie diets are effective in treating BED symptoms [12], whereas others showing that dietary restriction is ineffective [54]. However, several of these tested diets involve a large reduction in fat intake and very little research has been conducted in determining the effects with processed carbohydrate reduction. Although longitudinal studies are needed to validate the carbohydrate-insulin model of obesity, the implications of the findings are far-reaching and extend into the realm of mental health. Although the results of our case series by Carmen, Sethi Dalai *et al.* were encouraging, as they represent a potential shift from our previous understanding, these findings warrant longer follow-up and larger randomized controlled trials to characterize whether dietary restriction of carbohydrates is beneficial in treating obesity with comorbid eating disorders such as binge eating and ultraprocessed food addiction.

Future directions may focus on longer-term controlled studies comparing various diets within the eating disorder population struggling with binge eating and ultraprocessed food addiction symptoms. Studies can include targeted and validated scales, including The Yale Food Addiction Scale (YFAS) and the recently developed Highly Processed Food Withdrawal Scale (ProWS), as emerging evidence shows withdrawal from highly processed foods [55]. Future study could also include determining how the body responds overtime to repeated shifting from a carbohydrate burning state to a fat burning state and finding a mechanism to identify those more susceptible to withdrawal who would require additional support. Given metabolic and endocrine responses to foods may differ in the individual and its ensuing neurometabolic signaling effects, a one size fits all approach may not be feasible and warrant a personalized approach. The added dimension of our metabolic responses to food needs to be integrated into our understanding of the psychological model in the treatment of binge eating and food addiction disorders underscoring the need for future research and treatment paradigms.

CONCLUSION

Binge eating and ultraprocessed food addiction symptoms may be a result of changes in neurobiological and metabolic pathways triggered by specific foods, particularly processed foods with high levels of refined carbohydrates combined with fat. New keys to treating these modern-day illnesses of disordered eating may lie in avoiding unnatural levels of sugar in ultraprocessed foods, refined carbohydrates and high glycemic index foods. This would in turn prevent unnecessary blood glucose spikes and dips, insulin fluctuations and other metabolic hormones that play a large role in the development of binge eating/overeating, exacerbations of hunger and addictive-like neurochemical and behavioural responses. These conditions are associated with numerous metabolic abnormalities, including inflammation, insulin resistance, obesity and T2DM. The ketogenic diet has been shown to be an effective treatment for obesity, T2DM and paediatric epilepsy. Several advantages of a low carbohydrate ketogenic diet include beneficial effects on brain metabolism, appetite-satiety signalling, neurotransmission and stabilization of brain networks and blood sugar. Preclinical and clinical case evidence report clinical improvements in obesity, binge eating and food addiction symptoms utilizing a low carbohydrate ketogenic diet, and clinicians may consider these approaches especially if comorbid obesity is present. Further prospective controlled studies are needed to replicate the observed effects, establish long-term stability and ensure safety within the disordered eating population.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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