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Binge eating and obesity as reward–interoception disorders: Neuroendocrine and neuromodulation perspectives

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Abstract

Binge eating disorder and obesity are commonly approached through psychiatric, nutritional or metabolic frameworks, yet their clinical complexity increasingly suggests a deeper neurobiological dysregulation involving reward processing, interoceptive awareness, executive control and brain–body signaling. This Perspective proposes that binge eating and selected obesity phenotypes may be conceptualized as disorders of reward–interoception integration, in which highly salient food cues, dopaminergic motivational drive, altered hunger–satiety perception and impaired prefrontal inhibition may converge to increase vulnerability to loss-of-control eating. Within this framework, the insula, anterior cingulate cortex, salience network, mesolimbic reward circuitry and dorsolateral prefrontal cortex represent key neural nodes linking bodily signals, affective arousal, craving and behavioral regulation. Recent advances in glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 (GIP/GLP-1) receptor agonist therapies further support a brain–body model of ingestive behavior, suggesting that metabolic signals may be associated not only with appetite and satiety, but also with food craving, reward valuation and cue reactivity. In parallel, non-invasive neuromodulation, particularly prefrontal transcranial magnetic stimulation, offers a promising but still investigational strategy to potentially enhance inhibitory control and reduce craving-related vulnerability. The future treatment of binge eating and selected obesity phenotypes may benefit from an integrated neuropsychiatric approach combining incretin-based pharmacotherapy, neuromodulation, psychotherapy, clinical nutrition and digital craving monitoring. Moving beyond exclusively weight-centered models, this Perspective argues for a network-centered understanding of dysregulated eating as a condition of altered communication between reward, body, metabolism and executive control.

Keywords: Binge eating disorder; Obesity; Reward system; Interoception; Glucagon-like peptide-1; Glucose-dependent insulinotropic polypeptide; Transcranial magnetic stimulation; Food craving

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1. Introduction: From metabolic disease to neurobehavioral dysregulation

Obesity and binge eating disorder (BED) are frequently described through partially separated clinical languages: the former as a chronic metabolic disease and the latter as a psychiatric disorder of recurrent loss-of-control eating. However, this distinction may obscure the neurobiological continuity between dysregulated appetite, reward sensitivity, interoceptive processing and executive-control vulnerability. Obesity is not reducible to excess adiposity, nor is BED reducible to overeating. Both conditions may involve altered neural regulation of ingestive behavior, in which food cues may acquire increased motivational salience, satiety signals may become less behaviorally effective, and prefrontal inhibitory mechanisms may be less able to regulate craving-driven action.[1-3]

BED and obesity are therefore partially overlapping but not equivalent clinical entities. Many individuals with obesity do not present binge-eating episodes, and many patients with BED do not necessarily show severe or persistent obesity.

In the present article, the expression "selected obesity phenotypes" refers primarily to obesity accompanied by recurrent loss-of-control eating, high food-cue reactivity, poor satiety perception, marked craving, affect-driven eating or repeated relapse after dietary restriction. The proposed model is not intended to explain all forms of obesity, including metabolically healthy obesity, obesity primarily driven by endocrine, genetic, medication-related or socioeconomic determinants, or obesity occurring without clinically relevant dysregulated eating.

The relevant phenotype for a neuropsychiatric perspective is not weight excess alone, but the dynamic interaction among food craving, impaired satiety perception, impulsivity, affective arousal, cue reactivity, and loss of behavioral control. This interaction suggests that dysregulated eating may emerge when homeostatic, hedonic and cognitive-control systems become progressively desynchronized.[1,2]

Within this framework, BED and selected obesity phenotypes can be conceptualized as disorders of reward–interoception integration. The reward system assigns motivational value to palatable food; interoceptive networks translate bodily signals such as hunger, fullness and visceral arousal into conscious experience; executive-control circuits regulate action selection and inhibition; and metabolic-neuroendocrine pathways convey peripheral signals to the central nervous system. When coordination among these systems is weakened, eating behavior may become increasingly cue-driven, affectively charged and less clearly connected to bodily need.[3]

This Perspective proposes a selective and translational model rather than a comprehensive review. Its purpose is to reframe BED and obesity as brain–body conditions situated at the intersection of reward circuitry, interoceptive awareness, salience attribution, neuroendocrine signaling and neuromodulatory treatment targets. This approach shifts the focus from diagnostic categories to the neural systems through which craving, satiety, embodiment and self-regulation are integrated or disrupted.

The novelty of the present Perspective does not lie in the isolated claim that reward circuitry, interoception, executive control or gut–brain signaling are involved in dysregulated eating. Each of these domains has already been examined within incentive-sensitization, addiction-like, neurocognitive, salience-network, interoceptive and metabolic frameworks, as reflected in the literature discussed throughout the following sections. The proposed contribution is instead integrative and phenotype-oriented: it conceptualizes BED and selected obesity phenotypes as conditions in which reward valuation, interoceptive signal interpretation, inhibitory control and neuroendocrine-metabolic feedback become functionally desynchronized. This framework is intended to generate testable clinical phenotypes and research hypotheses rather than to replace existing models or to function as a validated diagnostic algorithm.

1.1. Conceptual scope and evidence selection

This article is a Perspective and not a systematic review. Evidence was selected to support a translational conceptual synthesis across five domains: reward neuroscience, interoception and salience-network research, obesity and BED neurobiology, incretin-based pharmacotherapy, and non-invasive neuromodulation. Priority was given to mechanistic studies, systematic reviews, meta-analyses, randomized controlled trials when available, and recent conceptual or translational reviews. Because the proposed model remains hypothetical, evidence is interpreted cautiously, and alternative explanations, contradictory findings and unresolved methodological limitations are explicitly considered throughout the manuscript.

The proposed reward–interoception integration model is summarized in Figure 1.

2. Reward circuitry and food craving: When eating becomes cue-driven

The transition from homeostatic eating to cue-driven eating is one of the central neurobiological events linking BED and selected obesity phenotypes. Homeostatic eating is organized around energy need and satiety feedback,

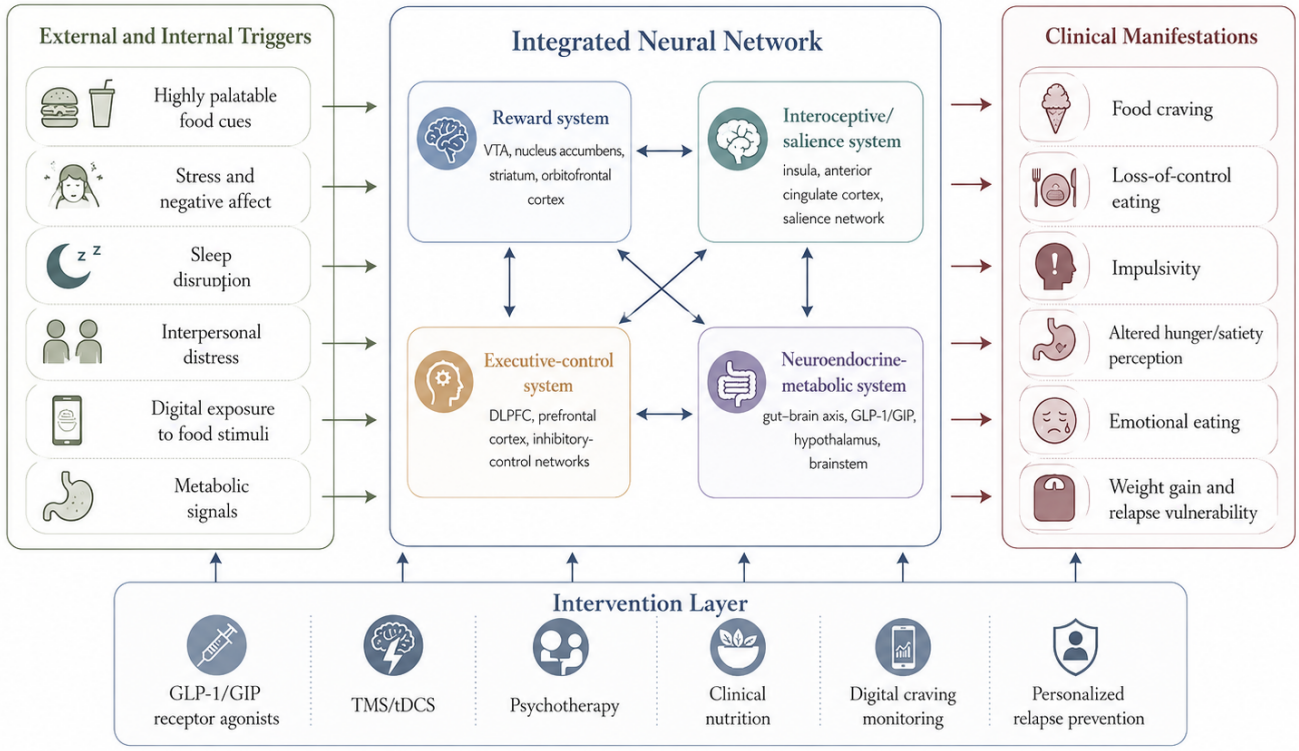

Figure 1. Reward–interoception integration model of binge eating and obesity. External and internal triggers may influence an integrated neural network involving reward, interoception/salience, executive control and neuroendocrine-metabolic signaling. Disrupted integration contributes to the clinical manifestations of BED and selected obesity phenotypes. Interventions may act across multiple network levels, including incretin-based pharmacotherapy, neuromodulation, psychotherapy, clinical nutrition, digital craving monitoring, and personalized relapse prevention. Solid arrows indicate directional influence; bidirectional arrows indicate reciprocal interaction.
Abbreviations: BED: Binge eating disorder; DLPFC: Dorsolateral prefrontal cortex; GIP: Glucose-dependent insulinotropic polypeptide; GLP-1: Glucagon-like peptide-1; tDCS: Transcranial direct current stimulation; TMS: Transcranial magnetic stimulation; VTA: Ventral tegmental area.

whereas cue-driven eating is shaped by motivational salience, learned associations and emotional anticipation of highly palatable food. In this condition, eating may become progressively less dependent on bodily need and increasingly governed by reward expectation, learned associations and impaired top-down inhibition.

The mesocorticolimbic reward system provides the principal neural architecture for this process. Dopaminergic projections from the ventral tegmental area to the nucleus accumbens and striatum participate in the generation of "wanting," a motivational state that is distinct from hedonic pleasure or "liking."[4] This distinction is clinically relevant, because patients may experience an intense drive toward food even when pleasure is transient, reduced or followed by guilt, shame and affective collapse. In BED, craving should therefore not be understood as simple appetite, but as a motivational-affective state in which incentive salience, emotional arousal and action tendency become coupled.

Food-cue reactivity further involves orbitofrontal, amygdalar, anterior cingulate and prefrontal regions. The orbitofrontal cortex contributes to the coding of reward value and expected pleasure, while the amygdala participates in emotional learning and cue–reward associations. Functional neuroimaging studies suggest that obesity may be associated with altered responses to both anticipated and consummatory food reward, supporting the view that palatable foods may acquire excessive neural and subjective value in vulnerable individuals.[5] At the same time, neurobehavioral evidence indicates that obesity-related eating patterns are often linked to striatal food motivation and lateral prefrontal systems implicated in self-control.[2]

This imbalance between reward drive and inhibitory control does not imply that BED or obesity are identical to substance addictions. The term "food addiction" may be useful as a dimensional analogy, especially when describing craving, loss of control and compulsive-like consumption;

however, it should not be used as a definitive nosographic equivalence. Empirical studies show that addictive-like eating constructs can identify clinically severe BED subgroups, but they also underline the need to distinguish food craving from drug craving, since food is biologically necessary, continuously available and embedded in affective, relational and metabolic regulation.[6] Thus, in a reward–interoception framework, binge eating may be better understood not as addiction in a strict categorical sense, but as a dysregulated motivational state in which food cues may capture attention, reward valuation may be amplified and prefrontal control may be insufficient to prevent loss-of-control eating.

3. Interoception, insula and embodied disconnection

Interoception can be defined as the nervous system's capacity to sense, interpret and integrate signals arising from within the body, including hunger, satiety, gastric distension, visceral discomfort, autonomic arousal and affective bodily states.[3,7] In BED and selected obesity phenotypes, dysregulated eating may therefore reflect not only excessive attraction to palatable food cues, but also a weakened capacity to transform internal bodily signals into coherent subjective guidance. From this perspective, the body is not absent from binge eating; rather, it is present in a dysregulated, poorly integrated and often misread form.

The anterior insula represents a central hub of interoceptive awareness. It integrates visceral, somatic, affective and cognitive information, contributing to the subjective feeling of the body as a lived organism rather than as a merely metabolic object.[7] Within this framework, hunger and fullness are not simple peripheral sensations, but brain-mediated bodily meanings. When insular processing or interoceptive interpretation is altered, the individual may have difficulty discriminating between physiological hunger, emotional tension, craving, gastric discomfort or affective emptiness. This may help explain why eating can occur in response to distress, reward expectation or cue salience even when homeostatic need is weak or absent.

The anterior cingulate cortex and the salience network further extend this model. The salience network, anchored in the anterior insula and dorsal anterior cingulate cortex, supports the detection of behaviorally relevant internal and external stimuli and contributes to the allocation of attentional and control resources.[3,7,8] In BED and obesity, highly palatable food cues may compete with, override or distort internal satiety signals. The subject does not simply "choose" food; rather, food becomes the most salient object within a neural field in which bodily need, affective arousal and action tendency are insufficiently differentiated.

This process may be conceptualized as embodied disconnection. The term does not imply a lack of body signals, but a disruption in the integration between bodily afference, emotional meaning and behavioral regulation. Evidence from disordered-eating research supports the relevance of altered interoceptive processing, including gastric interoception, hunger–satiety perception and body-signal interpretation in binge-eating phenotypes.[9] Thus, emotional eating may in some cases reflect difficulty distinguishing affective distress from bodily need: the individual eats not because the body clearly requires nourishment, but because interoceptive, affective and reward signals converge into an undifferentiated urgency. In this sense, BED and selected obesity phenotypes may reflect impaired translation of bodily signals into regulated action.

4. GLP-1/GIP signaling as a brain–body interface

The rapid clinical development of GLP-1 and dual GIP/GLP-1 receptor agonists has transformed the treatment of obesity, but its broader neuropsychiatric significance extends beyond weight reduction. These agents may be viewed as pharmacological probes of the interaction among appetite, satiety, reward valuation, metabolic signaling and brain function. In this sense, incretin-based therapies challenge the traditional separation between metabolic medicine, neurology and psychiatry, suggesting that ingestive behavior emerges from distributed brain–body communication rather than from isolated peripheral or psychological mechanisms.

GLP-1 receptors are expressed in multiple appetite-regulating and reward-related regions, including brainstem, hypothalamic and mesolimbic circuits. Preclinical and translational evidence indicates that central GLP-1 signaling may influence not only meal size and satiety, but also food reward, motivational salience and reward-driven consumption.[10] This is particularly relevant for BED and obesity phenotypes characterized by cue-driven eating, because the pathological target is not hunger alone, but the interaction between metabolic signals, craving, palatable-food valuation and impaired inhibitory control.

Semaglutide and liraglutide provide clinically important examples of this brain–body interface. In adults with obesity, once-weekly semaglutide 2.4 mg has been shown to suppress appetite, reduce *ad libitum* energy intake, improve control of eating and decrease food cravings.[11] These findings suggest that incretin-based treatments may be associated with changes in dimensions of eating behavior related to appetite, craving and perceived control

of eating, although they do not by themselves demonstrate direct normalization of reward processing or interoceptive integration. A recent systematic review further indicates that GLP-1 receptor agonists, particularly liraglutide and dulaglutide in preliminary studies, may reduce binge-eating frequency and associated clinical dimensions, although larger blinded controlled trials remain necessary before these agents can be considered established treatments for BED or bulimia nervosa.[12]

Tirzepatide adds another layer to this model. As a dual GIP/GLP-1 receptor agonist, it appears to affect ingestive behavior through mechanisms that include reduced energy intake, appetite, food cravings, tendency to overeat and food-cue reactivity in the environment.[13] These data suggest that GIP/GLP-1 co-agonism may affect ingestive behavior through peripheral, hypothalamic, brainstem and possibly reward-related pathways, although the relative contribution of mesolimbic and cortical mechanisms in humans remains insufficiently defined.

Nevertheless, caution is essential. BED is not simply obesity, and appetite suppression does not automatically resolve shame, affective dysregulation, impulsivity, relational vulnerability or the symbolic meaning of binge episodes. Incretin-based therapies may reduce the intensity of hunger and craving, but the subjective experience of eating remains embedded in emotional, interpersonal and behavioral regulation. Therefore, GLP-1/GIP therapies may be best considered within multimodal neuropsychiatric treatment rather than framed as stand-alone solutions. Their translational relevance may lie in encouraging clinicians and researchers to examine dysregulated eating as a brain–body condition in which metabolic signaling, reward sensitivity and self-regulation interact, while recognizing that these interactions require further mechanistic validation.

5. Neuromodulation and executive control: Probing top-down regulation

Non-invasive neuromodulation represents an investigational frontier for probing and potentially modulating the neural mechanisms of dysregulated eating. In a reward–interoception framework, its relevance does not lie in a direct "anti-obesity" effect, but in the possibility of experimentally modulating cortical systems involved in craving, impulsive action and cue-driven eating. The dorsolateral prefrontal cortex (DLPFC) is the most clinically relevant target in this context, because it participates in inhibitory control, decision-making, working memory, cognitive flexibility and top-down modulation of reward-related responses. When prefrontal regulation is insufficient, highly salient food cues may more easily capture attention and trigger loss-of-control eating.

Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) may modulate prefrontal excitability and influence the balance between reward drive and executive control. A meta-analytic review of rTMS in eating disorders and obesity suggested potential clinical utility, particularly in obesity-related outcomes and affective dimensions, but also emphasized the heterogeneity of samples, protocols, stimulation parameters and outcome measures.[14] Therefore, rTMS should not be presented as an established treatment for BED or obesity, but as a translational tool capable of testing whether prefrontal modulation can reduce craving vulnerability and improve behavioral regulation.

More specific evidence is now emerging in BED. A recent double-blind randomized controlled trial examined neuronavigated 10 Hz rTMS applied to the left DLPFC in individuals with BED and associated obesity. The study reported a greater reduction in binge-eating episodes in the active rTMS group compared with sham treatment, both at the end of treatment and at follow-up, although group differences were not observed across all secondary outcomes.[15] These findings are consistent with the hypothesis that DLPFC stimulation may influence clinically relevant loss-of-control eating, while also confirming the need for larger trials, longer follow-up, mechanistic biomarkers and more precise phenotypic stratification.

tDCS may provide a complementary line of investigation, but available findings remain heterogeneous and preliminary.[16] Future neuromodulation studies should therefore move beyond generic obesity samples and test phenotype-specific subgroups, such as high-craving/high-impulsivity BED, obesity with recurrent loss-of-control eating, or patients with relapse-prone cue reactivity. In this sense, neuromodulation should be integrated with psychotherapy, nutritional care and digital monitoring, not as an isolated procedure, but as a circuit-oriented strategy aimed at testing and potentially strengthening top-down regulation within a broader multimodal treatment model.

6. Psychotherapy and digital craving monitoring: Supporting regulation in real life

A neurobiological model of BED and obesity should not lead to a reductionistic treatment logic. Even when reward circuits, interoceptive networks, prefrontal control systems and incretin pathways are considered central, dysregulated eating still occurs within the lived context of emotion, shame, interpersonal stress, body experience and daily

exposure to food cues. For this reason, psychotherapy remains clinically important, not as an alternative to biological treatment, but as the clinical space in which self-regulation, embodied awareness and meaning-making can be reconstructed. Evidence indicates that psychological treatments are effective for BED, although long-term maintenance, mechanisms of change and integrated models of care remain important open questions.[17]

Within a reward–interoception framework, psychotherapy should be understood as a method for improving affect regulation, mentalization of hunger and satiety, recognition of triggers, tolerance of craving and processing of shame after loss-of-control eating. Clinical nutrition has a complementary role: it stabilizes meal patterns, reduces chaotic restriction–overeating cycles and provides behavioral and metabolic regularity. Psychological and behavioral interventions may target complementary dimensions, including binge-eating reduction, emotion regulation, meal regularity and relapse prevention. This distinction supports the need for multimodal rather than single-target treatment.

Digital craving monitoring may help translate this model into real-life clinical research and, potentially, clinical practice. Ecological momentary assessment and ambulatory methods allow repeated assessment of craving, affective arousal, impulsivity, sleep disruption, interpersonal stress, contextual exposure and loss-of-control risk in natural environments.[18] Such tools may be particularly useful because binge eating is not a static symptom, but a temporally dynamic process often preceded by changes in affect and followed by short-term emotional relief or subsequent distress.

In integrated care, digital trajectories may help determine whether reduced appetite during GLP-1/GIP therapy corresponds to improved regulation or merely pharmacological suppression. Similarly, craving peaks and relapse-risk windows may identify when additional psychotherapy sessions, nutritional adjustments, transcranial magnetic stimulation booster sessions or closer clinical monitoring are needed. Thus, psychotherapy and digital monitoring reconnect neurobiological treatment with lived experience, preventing the model from becoming a purely pharmacological or circuit-based account of dysregulated eating.

7. Alternative explanations and conflicting evidence

Several alternative explanations and sources of conflicting evidence must be considered. First, obesity is strongly shaped by environmental, socioeconomic, cultural, genetic, endocrine, medication-related and developmental determinants; consequently, the present model should be restricted to obesity phenotypes accompanied by clinically relevant dysregulated eating rather than generalized to obesity as a whole. Second, addiction-like models of overeating remain controversial because food is biologically necessary, heterogeneous in composition and embedded in social, affective and metabolic regulation.[6] Thus, although addiction-related constructs may help describe craving, loss of control and compulsive-like eating in some BED subgroups, they should not be interpreted as implying a direct equivalence between food intake and substance use disorders.

Third, findings on interoception in BED and obesity are not fully consistent across studies, assessment methods or clinical phenotypes. Interoception is multidimensional, and subjective interoceptive sensibility, behavioral interoceptive accuracy, hunger–satiety perception, and neural activity within the insula or salience network may not always converge.[3,7-9] Therefore, altered interoceptive processing should be considered a plausible vulnerability domain rather than a demonstrated causal mechanism. Fourth, emerging evidence on GLP-1 and GIP/GLP-1 receptor agonists supports clinically relevant effects on appetite, satiety, energy intake and, in some studies, craving-related dimensions; however, most available trials were not designed to directly test reward–interoception integration, food-cue learning or BED-specific psychopathology.[10-13] Reductions in craving or binge frequency should therefore not be automatically interpreted as proof that incretin-based therapies normalize reward or interoceptive circuitry.

Fifth, the evidence base for neuromodulation remains promising but methodologically heterogeneous. Studies of rTMS and tDCS differ in sample composition, stimulation target, stimulation parameters, sham procedures, outcome measures and follow-up duration.[14-16] As a result, non-invasive neuromodulation should currently be framed as an investigational or adjunctive strategy for probing and potentially modulating prefrontal control over craving, rather than as an established treatment for BED or obesity. Finally, altered activation in reward-related or interoceptive regions may reflect pre-existing vulnerability, compensatory adaptation, repeated dieting, weight cycling, developmental exposure, affective comorbidity or consequences of chronic overeating rather than primary causal dysfunction. The reward–interoception integration model should therefore be viewed as a hypothesis-generating framework that requires longitudinal, mechanistic and phenotype-stratified validation.

8. Toward an integrated neuropsychiatric model

The preceding sections converge toward an integrated neuropsychiatric model in which BED and selected obesity phenotypes are not explained by a single dysfunctional mechanism, but may be conceptualized through the progressive desynchronization of four interacting axes: reward, interoception, executive control and neuroendocrine-metabolic signaling. This model does not deny the metabolic reality of obesity or the psychiatric specificity of BED; rather, it proposes that both conditions may become clinically severe when brain–body communication loses coherence and eating behavior is increasingly organized by cue salience, affective urgency and impaired regulatory control.

The first axis is the reward axis. Highly palatable foods may acquire excessive motivational value through mesocorticolimbic mechanisms involving dopaminergic drive, incentive salience and learned cue–reward associations. In this context, eating becomes less dependent on metabolic need and more dependent on "wanting," anticipatory reward and environmental availability. The distinction between metabolic and hedonic drives is therefore essential: food intake is never regulated only by energy deficit, but by the continuous interaction between homeostatic signals and reward-based motivational systems.[1,19]

The second axis is the interoceptive axis. Hunger, fullness, visceral arousal and satiety are not merely peripheral events, but centrally interpreted bodily signals. When interoceptive processing or interoceptive interpretation is altered, the subject may have difficulty distinguishing physiological need from emotional tension, emptiness, anxiety or craving. The binge episode may thus be conceptualized as an episode of impaired integration: food cues become excessively salient, bodily awareness becomes ambiguous, and affective distress may be misrecognized as an urgent need to eat.

The third axis is the executive-control axis. The DLPFC and related control networks are involved in inhibiting impulsive actions, evaluating future consequences and regulating delay discounting. When these systems are insufficiently engaged, the individual may be able to recognize the maladaptive nature of binge eating while still having difficulty interrupting the behavioral sequence. The clinical phenomenon of loss of control may therefore reflect not only subjective distress, but difficulty in top-down modulation over reward-driven action tendencies.

The fourth axis is the neuroendocrine-metabolic axis. Hypothalamic, brainstem, gut–brain and incretin-mediated pathways regulate appetite, satiety, energy balance and metabolic adaptation. In obesity, chronic energy surplus and adiposity-related signals may feed back onto neural systems regulating appetite, reward and satiety. This may create a bidirectional loop in some patients: dysregulated eating may contribute to metabolic dysfunction, while metabolic dysfunction may feed back onto neural systems involved in appetite, reward and satiety.[9,19] In this sense, obesity may be understood as a chronic neurobehavioral condition in which metabolic consequences progressively reshape the nervous regulation of ingestive behavior.

This model has therapeutic implications, although these remain hypothesis-generating. Treatment may need to address interacting vulnerability domains, not only isolated symptoms. A patient with high craving and food-cue reactivity may be more likely to benefit from interventions focused on reward salience and relapse prevention; a patient with poor hunger–satiety awareness may be more likely to benefit from interoceptive and body-awareness work; a patient with high impulsivity may be considered for executive-control training, structured behavioral strategies or investigational neuromodulation; and a patient with severe metabolic dysregulation may require evaluation for incretin-based pharmacotherapy and nutritional stabilization.[9,13,14,16-19] Personalized intervention should therefore be understood as a research and clinical-development objective rather than as an already validated treatment-selection algorithm. The central clinical shift is from treating binge episodes or weight excess in isolation to examining the disrupted communication between reward, body, metabolism and executive control.

The translational implications of this model are summarized in Table 1, which links each mechanistic domain to a dominant substrate, a clinically observable phenotype, a potential therapeutic target, and candidate biomarkers/assessment tools.

9. Limitations, boundary conditions and testable predictions

Several limitations should be explicitly acknowledged. First, the reward–interoception integration model is conceptual and hypothesis-generating; it has not yet been validated as a diagnostic, prognostic or treatment-selection framework. Second, most available neuroimaging and behavioral studies are cross-sectional, limiting causal inference and leaving open the possibility that reward-related or interoceptive alterations reflect vulnerability, compensation or consequence rather than primary mechanisms. Third, obesity is heterogeneous and cannot be reduced to dysregulated eating or neural reward–interoception dysfunction. Fourth, interoception is

Table 1. Mechanistic domains, potential biomarkers and translational targets in the reward–interoception model

Mechanistic domain	Main neural/system substrate	Clinical phenotype/expression	Translational target / Therapeutic implication	Potential biomarkers/ assessment tools
Reward sensitization	VTA; nucleus accumbens; ventral/ dorsal striatum; orbitofrontal cortex; amygdala.	Food craving; cue-driven eating; attentional capture by highly palatable foods; "wanting" exceeding metabolic need; recurrent loss-of-control episodes despite satiety.	Craving-focused psychotherapy; cue-exposure strategies; relapse-prevention planning; GLP-1/GIP modulation as an adjunctive brain–body approach.	Food-cue fMRI; EMA craving peaks; attentional-bias tasks; wanting/liking paradigms.
Interoceptive dysregulation	Anterior insula; anterior cingulate cortex; salience network; visceral-afferent integration.	Altered hunger/fullness perception; confusion between bodily need and affective arousal; emotional eating; poor satiety recognition.	Interoceptive training; body-awareness work; mindfulness-informed strategies; psychotherapeutic reconstruction of embodied self-regulation.	MAIA or BPQ scores; hunger–satiety ratings; gastric interoception tasks; insula/salience-network connectivity.
Executive-control vulnerability	DLPFC; lateral prefrontal cortex; fronto-striatal inhibitory-control networks; decision-making circuits.	Impulsivity; weak response inhibition; difficulty interrupting binge sequences; preference for immediate relief over delayed goals; recurrent relapse after cue exposure.	rTMS/tDCS as investigational adjuncts; cognitive-control training; structured behavioral strategies; relapse-prevention scaffolding.	Go/No-Go or Stop-signal task; delay discounting; DLPFC activation/connectivity; executive-function measures.
Neuroendocrine-metabolic signaling	Gut–brain axis; GLP-1/GIP pathways; hypothalamus; brainstem; vagal-afferent and satiety circuits.	Appetite dysregulation; reduced satiety effectiveness; metabolic reinforcement of overeating; obesity with poor satiety perception and repeated overeating cycles.	GLP-1 receptor agonists and dual GIP/GLP-1 agonists; clinical nutrition; metabolic monitoring; integration with psychological treatment.	BMI trajectory; HbA1c; fasting insulin; leptin/ ghrelin; GLP-1-related markers; inflammatory markers.
Affective dysregulation and shame-related loops	Amygdala; anterior cingulate cortex; medial/ lateral prefrontal regions; stress-response systems.	Negative-affect eating; shame after binge episodes; affective collapse; anxiety/depressive arousal; interpersonal stress sensitivity; recurrent affect-driven relapse.	Psychotherapy focused on emotion regulation, shame processing, trigger recognition, mentalization and recovery of self-efficacy.	EMA negative affect; emotion-regulation scales; DASS-21; perceived stress; shame/ body-image measures.
Ecological relapse dynamics	Real-world interaction between neural vulnerability, digital exposure, sleep, stress, social context and eating opportunities.	Temporal craving peaks; relapse windows; binge episodes after stress, sleep disruption, interpersonal distress or digital food-cue exposure; poor early-warning detection.	Digital craving monitoring; ecological momentary assessment; personalized alerts; TMS booster scheduling or additional clinical contacts when risk increases.	EMA relapse timing; wearable sleep/activity markers; digital food-cue exposure; ecological risk signatures.

Notes: The table translates the proposed reward–interoception integration model into clinically interpretable mechanistic domains. It is intended as a conceptual and translational synthesis, not as a validated diagnostic algorithm, precision-medicine tool or treatment guideline. The proposed mappings between mechanisms, clinical phenotypes, biomarkers/assessment tools and therapeutic implications should be considered heuristic and require prospective validation before clinical implementation.
Abbreviations: BMI: Body mass index; BPQ: Body Perception Questionnaire; DASS-21: Depression Anxiety Stress Scales-21; DLPFC: Dorsolateral prefrontal cortex; EMA: Ecological Momentary Assessment; fMRI: Functional magnetic resonance imaging; GIP: Glucose-dependent insulinotropic polypeptide; GLP-1: Glucagon-like peptide-1; MAIA: Multidimensional Assessment of Interoceptive Awareness; rTMS: Repetitive transcranial magnetic stimulation; tDCS: Transcranial direct current stimulation; TMS: Transcranial magnetic stimulation; VTA: Ventral tegmental area.

multidimensional, and subjective, behavioral and neural measures may not converge. Fifth, incretin-based therapies and neuromodulation may influence clinically relevant dimensions of appetite, craving or inhibitory control, but their direct effects on reward–interoception integration remain insufficiently established. Contemporary reviews on reward and inhibitory-control mechanisms in BED, neurobiological treatment advances, GLP-1-related reward behavior and neuromodulation further support the need for cautious, mechanism-specific interpretation.[20-23]

Additional boundary conditions concern sex, developmental stage, hormonal status, inflammation and microbiota–gut–brain signaling. Sex- and gender-related differences in adiposity distribution, food craving, body dissatisfaction, hormonal modulation and response to weight-loss pharmacotherapy may moderate reward–interoception trajectories; therefore, future studies should stratify analyses by sex, gender, reproductive stage and developmental history.[24] Similarly, low-grade inflammation, hypothalamic and immune signaling, gut

microbial composition and microbiota–brain pathways may influence appetite regulation, mood, interoceptive processing and food reward.[25-27] These mechanisms broaden the present model by indicating that bodily signals reaching the brain are metabolic, endocrine, immune and microbial, rather than exclusively caloric or psychological.

The model also generates several testable predictions. First, individuals with BED and high food-cue reactivity should show stronger coupling between food-cue reward markers and ecological craving peaks than individuals with obesity without loss-of-control eating. Second, poor hunger–satiety discrimination should predict binge episodes beyond body mass index (BMI), depressive symptoms and negative affect. Third, reductions in binge risk during GLP-1/GIP therapy should be mediated by changes in appetite, craving or perceived control of eating more than by weight loss alone in hunger-dominant phenotypes. Fourth, DLPFC-targeted neuromodulation should show stronger effects in patients with baseline inhibitory-control deficits or reduced prefrontal regulation of food-cue responses. Fifth, multimodal phenotyping combining functional magnetic resonance imaging (fMRI), ecological momentary assessment, interoceptive tasks, metabolic/inflammatory markers and microbiome-related measures should predict treatment response better than BMI or binge frequency alone.

A provisional research-oriented clinical pathway can therefore be formulated as follows: first, identify whether obesity is accompanied by recurrent loss-of-control eating, marked craving or impaired satiety perception; second, screen the dominant vulnerability domain, including reward salience, interoceptive dysregulation, executive-control weakness, affective relapse dynamics or metabolic-inflammatory vulnerability; third, select candidate biomarkers or assessment tools such as Ecological Momentary Assessment (EMA), craving scales, interoceptive measures, inhibitory-control tasks, metabolic and inflammatory markers or microbiome-related indices; fourth, combine interventions according to the dominant phenotype; and fifth, monitor outcomes longitudinally using binge frequency, craving trajectories, satiety perception, metabolic markers, functioning and relapse risk. This pathway should be interpreted as a hypothesis-generating clinical-development framework, not as a validated algorithm for routine treatment selection.

10. Conclusion: Future therapeutic directions

Binge eating disorder (BED) and selected obesity phenotypes may be usefully examined through an integrated neurological and neuropsychiatric framework capable of connecting reward processing, interoceptive awareness, executive control and neuroendocrine-metabolic signaling. The most robust evidence supports associations among reward dysregulation, food-cue reactivity, impaired inhibitory control and dysregulated eating, as well as the clinical efficacy of incretin-based therapies for obesity-related outcomes. The most promising, although still developing, evidence concerns possible effects of GLP-1 and GIP/GLP-1 receptor agonists on craving, satiety, food-related motivation and cue reactivity, together with the possibility that neuromodulation of prefrontal circuits may experimentally modulate top-down control over loss-of-control eating.

The most speculative but theoretically generative hypothesis proposed in this Perspective is that BED and selected obesity phenotypes may be conceptualized as disorders of reward–interoception integration. This model does not replace metabolic, psychiatric or nutritional explanations; rather, it attempts to connect them within a network-based account of ingestive behavior. Future studies should therefore combine neuroimaging, endocrine and metabolic markers, interoceptive assessment, ecological craving monitoring, behavioral phenotyping and treatment-response prediction. Such designs may help identify clinically meaningful subgroups, including patients with predominant craving, impulsivity, poor satiety perception, affective dysregulation or recurrent relapse vulnerability.

Future research and clinical care for BED and selected obesity phenotypes may benefit from moving beyond exclusively weight-centered approaches toward phenotype-informed brain–body models, in which pharmacology, neuromodulation, psychotherapy, nutrition and digital monitoring are evaluated in relation to the patient's specific neurobehavioral and metabolic profile.

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Conflict of interest

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