

Binge eating disorder: from bench to bedside

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What makes us repeat behaviors compulsively that we ultimately regret? One intriguing behavior is that of binge eating—a pattern of food intake that is defined as recurring episodes of rapid, out-of-control overeating in which food is consumed in larger amounts than normal over a short period of time to the point of being uncomfortably full. Binge eating disorder (BED) has been accepted in *The Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, and is the most common eating disorder, with a lifetime prevalence of 1.4% to 3%. BED occurs without compensatory purging and is strongly associated with obesity but also occurs without obesity. Differentiating BED from obesity without BED can deconstruct the complex heterogeneity of obesity and identify more specific treatment targets. Understanding the pathophysiology of BED allows us to delineate and optimize mechanisms of efficacy underlying psychotherapeutic and pharmacological interventions; identify novel drug targets, including neurotransmitter and peptidergic targets; and identify cognitive, physiological, and neural biomarkers as treatment targets. In this set of translational articles on BED, we review preclinical animal models and the influence of dopaminergic, opioidergic, and peptidergic systems, and also translational studies on human epidemiology, genetics, cognitive and neuroimaging correlates, and clinical treatment studies.

Understanding how BED might also overlap with or differ from other eating disorders, impulsive- and compulsive-spectrum disorders, and substance and behavioral addictions is particularly relevant in light of the current trend toward dimensional psychiatry and understanding endophenotypes that may link seemingly diverse disorders. From a dimensional perspective, binge eating behavior overlaps across several eating disorders, including binge eating disorder, bulimia nervosa, and the

binge-purge subtype of anorexia nervosa, along with subsyndromal expressions in the general population with and without obesity. Similarly from a dimensional perspective, binge eating can be conceptualized beyond the simple phenomenon of eating, to identifying genetic, molecular, cognitive, and neural endophenotypes that may link this behavior of persistent, out-of-control, rapid consumption of a highly palatable food (or natural reward) with other behaviors within the impulsive-compulsive spectrum disorders, or substance and behavioral addictions. The general concepts of “food addiction” and “eating addiction” have been raised by previous reviews and are not without controversy^{1–6}; however, BED appears to have greater support for a relationship with disorders of addiction, although is not specifically the subject of this current review. This set of articles is particularly timely, as lisdexamfetamine, a pro-drug of dextroamphetamine that blocks monoaminergic transporter reuptake of norepinephrine and dopamine, was approved by the United States Food and Drug Administration to treat BED in adults in January 2015.

Together, preclinical reviews focus on binge eating rodent models, the role of dopamine and opioidergic mechanisms across rodent and human studies, and also an emerging literature on the influence of peptides. Avena and colleagues review the rodent model of sucrose binge eating: rodents exposed to food deprivation and access to sucrose solution show a rapid escalation of sucrose intake or bingeing, along with persistent dopamine release and delayed acetylcholine release in the nucleus accumbens, symptoms of withdrawal with food deprivation and cross-sensitization with amphetamine. The authors further discuss preclinical studies targeting orexin antagonism, modulation of dopamine receptors or suppression of dopamine synthesis, mu-opioid receptor antagonism, and GABA_B agonism. Chiara and Pietro focus on dissecting the role of the opioidergic system in BED, particularly focusing on the mu-opioid receptor, and relevant neural and cognitive processes. The authors emphasize the relevance

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of opioidergic mechanisms on the process of anticipatory incentive motivation that underlies hedonic binge eating of palatable foods across both rodent and human studies. Naef *et al* then focus on alterations in dopamine signaling, describing preclinical and clinical studies in obesity and binge eating and the influence of various rodent models on dopaminergic function. Whereas striatal dopamine concentration appears to be decreased in obesity, it is likely increased in binge eating. The authors further describe the relationship between neuropeptides and peripheral peptidergic signals and dopaminergic signaling and review the relevant literature on obesity and the more limited literature on binge eating, implicating ghrelin and glucagon-like peptide-1 receptor agonists.

Subsequent reviews then focus on human studies of BED, describing the epidemiology and genetics, cognitive and imaging correlates, and pharmacological and psychological treatment studies. These studies all use BED diagnostic criteria. First, Davis reviews the epidemiology of BED and common patterns of presentation and comorbidities, and describes preliminary emerging genetic studies that emphasize dopaminergic and opioidergic genes. BED is distinct from obesity without BED in phenomenology, disease course, severity, functional impairment, and comorbidities including mood, anxiety, and substance disorders. Voon discusses cognitive processes in BED as dissociable from obesity, and emphasizes the role of motivationally salient food cues that capture attention along with impairing motor response inhibition and underlying impairments in decisional impulsivity and behavioral inflexibility that may underlie decision making deficits in BED. Balodis *et al* then review human neuroimaging studies demonstrating decreased fronto-striatal processing to the anticipation and receipt of rewards and losses and inhibitory control, along with increased reactivity to food cues and palatable taste cues in the orbitofrontal cortex, insula, and striatum—regions implicated in reward and

motivation processing. Finally, McElroy *et al* review the randomized controlled trial evidence in BED to support efficacy of psychological interventions (eg, cognitive behavioral therapy and interpersonal therapy), along with the recently approved pro-drug lisdexamphetamine and the efficacy of topiramate, antidepressants, baclofen, and the mixed results for opioid antagonists. These treatment studies support preclinical and clinical pathophysiological studies, suggesting a potential role for dopaminergic and opioidergic mechanisms as treatment targets, along with possible roles for noradrenergic, serotonergic, glutamatergic, and GABAergic mechanisms.

Together these articles highlight a translational approach to understanding mechanisms underlying BED, leading to the optimization and identification of novel therapeutic targets.

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