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The Biology of Binge Eating

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Abstract

Objective—To examine the literature on binge eating to gain a better understanding of its biological foundations and their role in the eating disorders.

Method—Literature review and synthesis.

Results—Research using animal models has revealed several factors that contribute to the development and maintenance of binge eating. These factors, including stress, food restriction, the presence of palatable foods, and environmental conditioning, parallel many of the precursory circumstances leading to binge eating in individuals with bulimia nervosa and binge eating disorder.

Discussion—The animal literature has opened a new avenue to aid in the understanding of the neurobiological basis of binge eating. Future endeavors examining the genetic and environmental correlates of binge eating behavior will further contribute the understanding the biological foundations of binge eating and assist with establishing diagnostic criteria and the development of novel treatments for eating disorders marked by binge eating.

Introduction

Binge eating afflicts approximately 5% of U.S. adults at some time in their life (Hudson, Hiripi, Pope & Kessler, 2007). Binge eating constitutes a significant public health concern by virtue of its strong associations with other medical and psychiatric disorders, most notably obesity and depression. However, our understanding of the health consequences of binge eating and binge eating disorder (BED; e.g., the clinical manifestation of binge eating behavior) is limited, in part, because of problems inherent in the diagnosis of BED. First, the precise definition of a binge is unclear. Indeed, whether an individual considers a consummatory episode to be a binge may vary over time and with context. Second, the reliability of the assessment of binge eating is modest at best (Bulik, Sullivan & Kendler, 1998) with 5 year test-retest kappa being 0.34. Given these relatively nebulous boundaries, developing a more biologically-based profile of the behavior may assist with refining measurement, understanding phenomenology, and identifying genetic variants that may influence the trait. Toward this goal, in this paper we review what is currently known about the biology of binge eating.

What is a binge?

Binge eating is characterized by discreet episodes of rapid and excessive food consumption not necessarily driven by hunger or metabolic need (Brownley, Berkman, Sedway, Lohr & Bulik, 2007; Davis, Levitan, Carter et al., 2007). Individuals engaging in binge eating will eat until they feel uncomfortably full and may or may not compensate for the overabundance of

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food that they have consumed (Brownley et al. 2007; Davis, Levitan, Carter et al., 2007). Binge eating is often accompanied by feelings of loss of control and psychological distress (American Psychiatric Association, 2000; Brownley et al., 2007; Heatherton & Baumeister, 1991; Latner & Clyne, 2008). Not surprisingly, overweight and obesity, together with the associated physical and psychological health concerns, are commonly comorbid with binge eating (Brownley et al., 2007; Hudson et al., 2007).

Behavior versus disorder (definition of binge versus binge eating disorder)

The symptom of binge eating was first identified by Stunkard in 1959 (Stunkard, 1959); however, the syndrome of binge eating disorder (BED) has not yet achieved official diagnostic recognition and remains a syndrome in need of further study in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR (American Psychiatric Association, 2000).

The diagnostic criteria for BED are listed in Table 1. Similar to bulimia nervosa (BN), the definition of a binge eating episode requires the consumption of an unusually large amount of food coupled with a sense of feeling out of control. Also as in BN, the frequency criterion is twice per week, although this criterion is not well supported by the literature for BN and has not been validated for BED (Garfinkel et al., 1996;Sullivan, Bulik & Kendler, 1998). Where BN and BED diverge is that individuals with BED do not regularly engage in compensatory behaviors (i.e., purging, laxative abuse, excessive exercise), although the precise boundary between BED and non-purging BN is far from clear (Cooper & Fairburn, 2003;Fichter, Quadflieg & Hedlund, 2008;Latner & Clyne, 2008;Mond et al., 2006).

The BED criteria place additional qualifiers on the definition of a binge. These qualifiers are not validated in the literature and curiously hearken back to DSM III criteria for “bulimia,” which included criteria such as inconspicuous eating; termination of such eating episodes by abdominal pain, sleep, social interruption, or self-induced vomiting; awareness that the eating pattern is abnormal; and depressed mood and self-deprecating thoughts following eating binges.

Although such qualifiers were abandoned after DSM III for bulimia, they were resurrected for BED somewhat arbitrarily. As currently conceptualized, binge episodes are associated with at least three of the following criteria: 1) eating more rapidly than normal, 2) eating when not physically hungry, 3) eating until uncomfortably full, 4) eating alone because of shame, and 5) feeling disgusted with oneself, depressed or guilty after overeating (American Psychiatric Association, 2000). A final criterion stipulates that the individual must experience marked distress regarding binge eating. Given the concern with proliferation of categories in the DSM, experts have proposed guidelines to consider before adding another syndrome to the DSM (Blashfield, Sprock & Fuller, 1990). Although substantial work has been done on BED, not all of these guidelines have been adequately addressed.

The current diagnostic criteria are controversial partly because of the difficulty operationalizing a binge episode. For several reasons, researchers and clinicians are often unsuccessful in assessing and differentiating an *unusually large amount of food* from *overeating* (Cooper & Fairburn, 2003). First, assessors are inconsistent in recognizing bouts of overeating from grazing (i.e., eating continuously throughout the day instead of eating planned meals) and in deciphering what constitutes a truly large portion size from normal intake, overindulgence, or circumstantial eating (e.g., holiday). These inconsistencies make it difficult to determine the true number of binge episodes experienced by a patient or research participant. Second, researchers and clinicians (as well as patients) are unreliable in determining if loss of control was present (Cooper & Fairburn, 2003). Because of subjective differences in the definition, loss of control is difficult to measure. Some individuals may report loss of control after eating

a small amount of food (e.g., one cookie), whereas others may only experience a sense of loss of control after a much larger amount of food (e.g., a box of cereal).

Over the past decade, a variety of self-report inventories [e.g., Binge Eating Scale (Hawkins & Clement, 1980), Three Factor Eating Questionnaire (Stunkard & Messick, 1985), Body Shape Questionnaire (Cooper, Taylor, Cooper & Fairburn, 1986)] as well as interview methods [e.g., Structured Clinical Interview for the Diagnosis of DSM Disorders (First, Spitzer, Gibbons & Williams, 2001), Eating Disorders Examination (EDE) (Fairburn & Cooper, 1993), Questionnaire of Eating and Weight Patterns (Nangle, Johnson, Carr-Nangle & Engler, 1994)] have been developed to assess binge eating in adults. The EDE has a method for classifying types of overeating. An objective binge episode is one in which the amount eaten would be defined as relatively large (judged by the interviewer) and includes the patients' report of loss of control during the episode. A subjective binge episode is not viewed as large by the interviewer, but the patient still reports loss of control. For example, the patient may have eaten a regular size candy bar, but may have intended to only eat half of it. Alternatively, episodes in which the patient does not experience loss of control can be classified as either subjective or objective "overeating episodes". Despite these advances, uncertainties remain and continued efforts are needed to refine the definition of a binge and to develop valid and reliable diagnostic criteria and measurement tools for BED.

Given the highly subjective nature of many of the controversial elements surrounding the diagnosis of BED, it is no surprise that the debate over the inclusion of BED in the DSM continues. Understanding the biological foundations for binge eating via a thorough examination of what is known about analogous animal behaviors will help to elucidate the core components of BED. In the following sections, we review in detail animal models of binge eating and delineate their utility in clarifying the binge eating phenotype in humans.

Animal Models of Binge Eating

Overview—Binge eating in animals is characterized by behavior patterns similar to those seen in human binge eating. To be classified as a binge, animals must consume large quantities of food in a brief, defined period of time, and this quantity should exceed that which would be consumed by control animals under similar circumstances (Corwin & Buda-Levin, 2004). Binge eating behavior must be stable and maintained over long periods of time (Corwin & Buda-Levin, 2004). Crucial differences between animal and human binge eating include the fact that subjective feelings of distress or loss of control, which have been found in some (Engel et al., 2007; Stein et al., 2007) but not all (Wegner et al., 2002) studies linked prospectively to binge episodes in humans, are not easily assessed in animals (Corwin & Buda-Levin, 2004). As such, models designed to study binge eating in animals often exploit the precursory circumstances leading to binge eating in humans (e.g., dieting, exposure to palatable foods and fluids, stress) to elicit binge related behaviors (Boggiano et al., 2005; Chandler-Laney et al., 2007; Corwin & Buda-Levin, 2004; Hagan, Chandler, Wauford, Rybak & Oswald, 2003; Hagan et al., 2002; Specker, Lac & Carroll, 1994). In addition, animal models of eating disorders use food deprivation and restriction to mimic dietary restraint often seen in individuals with anorexia nervosa (AN), BN, and BED. A notable caveat and potential limitation is that establishing the equivalence of food deprivation between animal models and humans with restrictive eating disorders is not straightforward. Frequent snacking on sweet palatable foods, behavior that is significantly more common in individuals with BED than in non-binge eating obese or normal weight controls (Davis, Levitan, Carter, et al., 2007), is modeled in animals through exposure to palatable foods and fluids. Environmental stressors, daily hassles and negative affect have long been linked with binge eating in humans (O'Connor, Jones, Conner, McMillan & Ferguson, 2008; Smyth et al., 2007; Striegel-Moore et al., 2007). Not only is stress associated with the initiation of binge episodes, but it also increases the

reinforcing efficacy of foods that are commonly binged upon (Goldfield, Adamo, Rutherford & Legg, 2007; Greeno & Wing, 1994; Stice et al., 2001). These behaviors are more difficult to reproduce in animals because of the subjective nature of emotional states in rodents. Nevertheless, animal models of stress-induced alterations in food intake provide valuable information about the biological foundations of binge eating.

Food Deprivation—Food deprivation and food restriction reliably and consistently increase subsequent food intake in animals. Laboratory animals deprived of food for as few as two hours will consume significantly more calories upon the return of the food than animals that were not deprived (Cottone, Sabino, Steardo & Zorrilla, 2008). Rats maintained on a restricted feeding schedule, during which they receive 66% of the amount of food that free eating rats consume, increase their caloric intake by 42% compared with sated rats when allowed ad lib access to food. Increased consumption is evident within 2 hours of the return of the food and persists for up to 4 hours (Hagan et al., 2003). This increased consumption over a discrete period of time mirrors behaviors seen in humans who binge eat.

Dieting and food restriction have been demonstrated to increase the risk of binge eating in non-clinical populations as well as to prolong binge eating in individuals with BN and BED (Agras & Telch, 1998; Stice & Agras, 1998; Stice et al., 2001). In a recent study of 259 boys and girls ages 8 to 13 years old, dietary restraint prospectively predicted the onset of binge eating one year later (Allen, Byrne, La Puma, McLean & Davis, 2008). Still, some controversy exists as to whether food deprivation-induced overeating in animals is an accurate model of human binge eating. Animals in the aforementioned protocols do not show significant decreases in body weight; however, the rebound hyperphagic response to *ad libitum* food access provides convincing evidence that they are in an energy deficient state (Hagan et al., 2003). In contrast, most binge eating in humans is often not driven by physical hunger or metabolic need (Waters, Hill, & Waller, 2001; American Psychiatric Association, 2000). Indeed, most individuals suffering from BED are normal weight or overweight (American Psychiatric Association, 2000).

Several studies have used restriction/refeeding paradigms to emulate human binge eating more closely. Initially described by Hagan and Moss (1991), the restriction/refeeding protocol involves exposing animals to repeated fasting episodes accompanied by weight loss. These episodes are followed by periods of refeeding in which the animals are allowed to return to their normal body weights. Subsequent binge eating trials are then performed on sated, normal weight animals. When fasting episodes are sufficient to reduce an animal's body weight to 75–80% of free feeding levels, the animal will show significant binge-like eating in a sated state (Hagan & Moss, 1991; Specker, Lac & Carroll, 1994). Binge eating in this model is not dependent on the palatability of the test diet or additional environmental stressors. It is possible that the severe body weight loss elicits a physiological stress response within the animals that initiates the neurobiological changes necessary for the expression of binge eating. This model of binge eating is reminiscent of behaviors associated with BN-nonpurging (BN-NP) subtype in humans, which is differentiated from BED by the occurrence of the specific compensatory processes of fasting or excessive exercise and by a history of episodes of dieting and significant weight loss (Cooper & Fairburn, 2003; Santonastaso, Ferrara & Favaro, 1999).

More recent models of binge eating address this issue of severe prior weight loss by limiting weight loss during the restriction period to 7–9% below free feeding body weight. Body weights rapidly return to 95–105% of free feeding weights when the rats are returned to ad lib food access. However, restriction and refeeding in this protocol does not elicit significant binge-like eating. Intriguingly, it is only when paired with stressful stimuli and palatable foods that this restriction/refeeding schedule effectively induces significant binge-like increases in caloric intake in rodents (Artiga et al., 2007; Boggiano et al., 2005; Chandler-Laney et al., 2007; Hagan

et al., 2003; Hagan et al., 2002). The development of nuanced differences in rodent binge eating protocols has the potential to elucidate differential neurobiological and environmental correlates of BED and BN-NP to determine whether they are best conceptualized as different psychological disorders or just permutations of the same underlying psycho-biological processes.

Stress—Physiological and environmental stress plays a crucial role in animal models of binge eating. For example, rats with a history of caloric restriction alone do not show significant increases in food intake in the sated state; however, if exposed to footshock stress and then given free access to food they will significantly overeat palatable, preferred foods (Hagan et al., 2002). Specifically, rats exposed to three, 10-day restriction/refeeding cycles (4 days at 66% of free feeding intakes, 6 days of refeeding) and then exposed to a mild footshock stressor showed significant binge-like increases in caloric intake due to a selective increase in the intake of the palatable food (Hagan et al., 2002). This binge-like behavior was not evident after restriction/refeeding or stress alone conditions or in control animals. In fact, the stress alone group showed a decrease in caloric intake. This effect is highly replicable, resulting in 2–3 fold increases in caloric intake compared to control animals (Artiga et al., 2007; Boggiano et al., 2005; Chandler-Laney et al., 2007; Hagan et al., 2003; Hagan et al., 2002). Furthermore, the effect of stress on binge eating in these animals is highly specific. Stress must occur after a history of at least 3 restriction/refeeding cycles, must follow in close proximity to the last cycle, and palatable foods must be present. Binge eating in this paradigm is a stable trait and persists across at least 23 restriction/refeeding+stress cycles (Artiga et al., 2007).

Human eating behavior is similarly sensitive to the effects of stress, with the specific outcome depending on the nature of the stressor (physical or psychological) as well as the duration of the stressor (acute or chronic) and individual differences (see (Adam & Epel, 2007) for review). Although many people increase their food intake during stress, a subset of individuals actually decrease food intake during stress (Stone & Brownell, 1994). In part, these disparate effects reflect the nature of the stressor. Psychological (e.g., interpersonal, ego-threatening, and work related) stressors have been linked with an increase in food intake (Heatherton, Herman & Polivy, 1991) and inter-meal snacking (O'Connor et al., 2008); whereas, stress induced from the threat of physical harm or discomfort (and indexed as physiological symptoms of anxiety, illness, and fear of injury) decreases food intake (Heatherton, Herman & Polivy, 1991) and snacking behavior (O'Connor et al., 2008). In individuals with BED, elevated perceived stress and increased incidence of life stressors have been demonstrated to precede the onset of binge eating (Pike et al., 2006; Striegel-Moore et al., 2007).

Important individual differences can magnify the effect of stress on eating. For example, high levels of dietary restraint, emotional eating, external eating, and disinhibition; female sex; and obesity have been shown to exacerbate stress-induced eating (Nieuwenhuizen & Rutters, 2008; O'Connor et al., 2008; Ozier et al., 2008; Roberts, Troop, Connan, Treasure & Campbell, 2007). Notably, a history of dieting or food restriction and stress are two of the key etiological factors in eating disorders (Crowther, Sanftner, Bonifazi & Shepherd, 2001; Grilo, Masheb & Wilson, 2001; Polivy & Herman, 1985). Together, dieting and stress are powerful antecedents to binge eating in non-clinical populations (Heatherton, Herman & Polivy, 1991; Polivy & Herman, 1999; Polivy, Zeitlin, Herman & Beal, 1994; Wardle, Steptoe, Oliver & Lipsey, 2000); and, in patients with eating disorders, the combination of dieting and stress can prolong the maintenance of binge eating behaviors (Crowther et al., 2001; Grilo et al., 2001; Polivy & Herman, 1985; Stice et al., 2001).

Stress reactivity is another important individual difference that modifies the effect of stress on eating behavior. In a genetic mouse model of stress sensitivity, high stress reactive mice deficient in the corticotropin-releasing factor receptor-2 (CRFR2) showed a significant

increase in caloric intake following chronic, variable stress (Teegarden & Bale, 2007). Receptor deficient and wild type mice were given access to high fat, high carbohydrate, and high protein pellets and exposed to varied stressful stimuli (e.g., restraint stress, numerous cage changes, constant 24-hour light, being housed in another male's soiled cage, or 5 minutes of isoflurane anesthesia) for 16 days. Initial results showed an increase in food intake in both the wild type and receptor deficient mice due to a ceiling effect: both groups consumed 95% of their calories as the high fat diet. However, when access to the high fat diet was limited, CRFR2 receptor deficient mice ate significantly more calories while wild type mice significantly decreased their caloric intake (Teegarden & Bale, 2007).

High stress reactivity affects eating behaviors in humans, as well. Goldfield and colleagues (Goldfield, et al., 2007) assessed college-aged individuals for binge eating and stress reactivity and categorized them into four groups; high reactive binge eaters, low reactive binge eaters, high reactive non-binge eaters, or low reactive non-binge eaters. Participants then completed a computer simulation task in which they had to work for points to obtain palatable snack foods following either a stressful or neutral stimulus. Individuals in the high reactivity binge eating group earned more points for food after stress than the other groups. In fact, they worked 100% harder for snack food points (Goldfield et al., 2007).

Interactions between chronic negative affect and dieting have also been reported in the human population. In a passive-observational study of 631 adolescents, both dieting and negative affect were positively related to binge eating, and negative affect potentiated the relation between dieting and binge eating (Stice, Akutagawa, Gaggar & Agras, 2000). Although not specifically measuring stress, this observational study underscores the importance of assessing not only the main effects of food deprivation and affective measures, but also their interactive effects.

Taken together, these data suggest that stress can trigger binge-type eating in both rodents and humans. An interesting caveat emerges, however. The stress-induced increases in caloric intake described in these studies were generally due to a selective increase in the intake of palatable foods, indicative of increased motivation for reward rather than metabolic need in stress-induced binge eating.

Palatable food and fluids: intermittent exposure and parallels with addiction— Animal models of binge eating have been instrumental in highlighting the importance of palatable foods and fluids in the etiology of binge eating. As mentioned above, restriction and refeeding paired with stress elicits profound binge eating in rats. Notably, this binge eating is evident in the selective increase in palatable food intake, resulting in an overall increase in caloric intake (Boggiano et al., 2005; Chandler-Laney et al., 2007; Hagan et al., 2003; Hagan et al., 2002). When presented with chow alone, rats in the restriction/refeeding paradigm do not significantly increase their caloric intake following stress. However, the presentation of a mere morsel of palatable food will elicit binge eating of chow (Hagan et al., 2003).

In humans, strict dietary restraint and/or abstinence from eating forbidden, highly palatable foods have been shown to contribute to binge eating (Herman & Polivy, 1990; Polivy, 1996; Polivy & Herman, 1985; Polivy, et al., 1994). It is important to note, however, that not all individuals suffering from binge eating have a history of caloric restriction. In fact, several studies have reported that binge eating and weight concerns precede any attempts at weight control in individuals with BED (Abbott et al., 1998; Grilo et al., 2008; Manwaring et al., 2006; Mussell et al., 1995; Reas & Grilo, 2007). Others have intimated that binge eating may be more attributed to irregular meal patterns, haphazard meal planning and snacking on palatable foods than caloric restriction (Davis, Levitan, Carter, et al., 2007; Ledoux, Choquet & Manfredi, 1993). Furthermore, the presence of palatable foods, typically high in sugar and

fat, can trigger binge eating episodes (Rogers & Hill, 1989; Waters et al. 2001). Intermittent exposure to palatable foods in animal models of binge eating mimics dietary restraint in humans. Animals allowed intermittent exposure to palatable foods show significant binge-like increases in the intake of such foods. For example, rats that were food deprived for 2 hours and then allowed 10 minute access to chow followed by 10 minute access to a highly palatable sugar based diet consumed 42.9% of their daily caloric intake as the sugar based diet, consuming up to 34.4 kcals in 10 minutes. This equates to one 45 mg food pellet every 2.9 seconds (Cottone, et al., 2008). This effect was remarkable since animals given access to standard chow during the second 10 minute period ate little more than 1 kcal, or approximately 6 pellets over the 10 minute period (Cottone et al., 2008). Similarly, rats allowed daily 2 hour access to a palatable fat diet (Crisco) consumed 32% of their total daily calories from the fat. If further restricted to 2 hour access only three days a week, intake increased to 51% of their total daily calories (Corwin et al., 1998). In both of these examples, animals were minimally deprived and thus not binge eating in response to hunger or metabolic need. When paired with food deprivation, intermittent access to palatable sugar solutions leads to significant binge-like intake of the solution when the animal is returned to its cage. Rats maintained on a restricted feeding schedule during which they have access to chow and a 10% or a 25% sugar solution for 12 hours and food deprived for the remaining 12 hours will consume approximately half of their calories as sugar (Avena, Rada & Hoebel, 2008; Colantuoni et al., 2002), 21% of which is consumed within the first hour of exposure. Sugar intake in these animals increases with prolonged exposure.

Interesting parallels exist between the priming and intermittent exposure effects of palatable food on binge eating and of abused substances on drug use behavior. A morsel of palatable food can trigger binge eating in an animal undergoing a restriction/refeeding paradigm, and the presence of palatable foods high in sugar and fat triggers binge eating in humans. Similarly, drug taking behaviors can be reinstated in animals and humans recovering from drug addiction with a single exposure to the previously abused drug [see (Schmidt, Anderson, Famous, Kumaresan & Pierce, 2005; Shaham, Shalev, Lu, De Wit & Stewart, 2003; Shalev, Grimm & Shaham, 2002) for review]. In addition, in animals, prolonged intermittent exposure to sugar solutions leads to intake patterns similar to those seen in substance abuse models (i.e., escalation of intake and physical dependence) and to neurobiological changes that mimic drugs of abuse (Avena, 2007; Avena, Rada & Hoebel, 2008; Avena, Rada, Moise & Hoebel, 2006; Colantuoni et al., 2002; Rada, Avena & Hoebel, 2005). Likewise, prolonged exposure to rewarding stimuli such as palatable foods or drugs of abuse can lead to physical dependence, and when the stimulus is removed or its effects blocked through pharmacological intervention, physical symptoms of withdrawal often follow (see (Avena, 2007; Koob, 2000, 2006) for review, and “Neurobiology of Binge Eating” below).

Intake of palatable foods and fluids also alleviates the psychological and physiological consequences of stress through neurochemical pathways similar to those activated during addictive behavior. Specifically, intake of palatable or preferred food leads to the release of dopamine and endogenous opioid peptides within the central nervous system (Kelley et al., 2002; Kelley, Baldo, Pratt & Will, 2005). A similar neurochemical response is evident in addictive behaviors such as pathological gambling and substance abuse (Brewer & Potenza, 2008; Goodman, 2008; Lobo & Kennedy, 2006). Clinical parallels also exist—binge eating is accompanied by a loss of control and commonly followed by feelings of guilt, disgust and remorse which closely mimic the patterns seen in substance abuse (American Psychiatric Association, 2000). Similarly, impulsivity and impulse control disorders have been reported in both individuals who binge eat and individuals with substance use disorders (Brewer & Potenza, 2008; Fernandez-Aranda et al., 2008) and considerable comorbidity has been reported consistently between eating disorders marked by binge eating and substance use disorders (Bulik et al., 2004; Bulik, Sullivan, Carter & Joyce, 1997; Dawe & Loxton, 2004; Grilo et al.,

2008). Thus, excessive overconsumption of palatable foods and fluids as seen in binge eating may be indicative of an underlying neurobiological process similar to that seen in addiction (Avena, Rada, & Hoebel, 2008; Avena et al., 2006; Colantuoni et al., 2002; Rada, Avena & Hoebel, 2005).

Neurobiology of Binge Eating

The neurobiology of binge eating behavior mirrors that seen in substance abuse behavior. This is not surprising given that many of the antecedent environmental factors that contribute to the development of binge eating are similar to those seen in substance abuse and other addictive behaviors. Palatable foods and fluids and drugs of abuse exert their reinforcing effects through activation of natural reward pathways in the brain (Adam & Epel, 2007; Avena, Rada & Hoebel, 2008; Avena et al., 2006; Berridge, 1996; Colantuoni et al., 2002; Goldfield, et al., 2007; Johnson, 1995; Kelley et al., 2002; Kelley et al, 2005; Kelley, Schiltz & Landry, 2005; Kelley, Will, Steininger, Zhang & Haber, 2003; Rada et al., 2005; Spangler et al., 2004). Drug and food related cues induce similar conditioned gene expression and neuronal plasticity within the mesolimbic-cortical reward pathway as well as areas of the brain associated with learning and memory (Kelley, Schlitz & Landry, 2005). Adaptations within the natural reward pathways, specifically the endogenous opioids and dopamine, have been implicated in the transition from overeating to binge eating and from recreational drug use to drug abuse (Goodman, 2008; Koob, 2006; Koob & Le Moal, 2008).

Opioids—Endogenous opioids within the nucleus accumbens shell have been linked to the hedonic or reinforcing properties of food. Ingestion of sweet and fat foods and fluids increases opioid receptor binding within this region of the natural reward system (Kelley et al., 2002; Kelley, et al., 2003). Initial studies in animal models of binge eating showed that rats maintained on a food deprivation/refeeding schedule were more responsive to the hyperphagic effects of the kappa opioid agonist, butorphanol (Hagan & Moss, 1991). These data suggested that this model of binge eating led to alterations within the endogenous opioid system. Subsequent studies have supported this hypothesis. The opioid receptor antagonist, naloxone, completely blocks binge eating in rats maintained on a feeding and refeeding schedule followed by footshock stress (Boggiano et al., 2005). Moreover, butophanol enhances binge eating of palatable food in this model (Boggiano et al., 2005). Similarly, nalmefene, a mu and kappa opioid antagonist, significantly attenuated binge eating in rats conditioned to binge eat a chocolate flavored, high sugar diet (Cottone et al., 2008). Likewise, rats given intermittent access to a 25% glucose solution for 30 days showed increased opioid receptor binding in the cingulate cortex, hippocampus, locus coeruleus, and nucleus accumbens shell (Colantuoni et al., 2001).

Studies of physical and emotional withdrawal following opioid receptor blockade in binge-eating rats provide further evidence of binge-eating induced alterations within the endogenous opioid system that parallel those seen in substance abuse. Specifically, rats trained to binge on a 25% glucose solution for 30 days showed significant physical signs of opioid withdrawal (teeth chattering, tremor, head shakes) following injection with naloxone (Colantuoni et al., 2002). Naloxone administration also decreased the time these rats spent in the open arms of the elevated plus maze, indicating increased anxiety, an emotional side-effect of opioid withdrawal (Goodman, 2008).

Dopamine—Ingestion of palatable foods activates dopaminergic neurons within the nucleus accumbens and other reward centers (Kelley, Schlitz & Landry, 2005; Rada et al., 2005). Repeated stimulation of this system in an attempt to relieve the physiological or psychological effects of stress or negative affect has been linked to the development of binge eating and substance abuse (Koob & Le Moal, 2008). Evidence of binge-eating-induced alterations within

the dopaminergic pathways of the brain further supports the assertion that binge eating is an addictive process similar to substance abuse. In rats, prolonged binge-like intake of sugar solutions leads to increased dopamine receptor binding in the nucleus accumbens and striatum (Avena, Rada & Hoebel, 2008; Avena et al., 2006; Colantuoni et al., 2001; Rada et al., 2005). Moreover, rats trained to binge eat sugar display significantly decreased dopamine release within the nucleus accumbens after 36 hours of deprivation from sugar and chow compared to rats that did not binge eat the sugar (Avena, Bocarsly, Rada, Kim & Hoebel, 2008). Abstinence from chow and sugar in this model also increased signs of anxiety in the elevated plus maze. Escape from the aversive psychological and physical side-effects of abstinence has been associated with relapse to drug taking in substance abusing individuals (Koob & Le Moal, 1997, 2008). It has been posited that the same is true for binge eating. The desire to escape from aversive states perpetuates binge-eating in individuals with BED or BN and increases the likelihood of relapse to binge eating in individuals in recovery from BED and BN (Heatherton & Baumeister, 1991; Johnson & Larson, 1982).

In humans, alterations within the dopamine and endogenous opioid systems have been identified in individuals with BED and BN. For example, naloxone decreased the intake of palatable foods in individuals fitting the criteria for BN and BED but did not alter food intake in non-bingeing obese or normal weight individuals (Drewnowski, Krahn, Demitrack, Nairn & Gosnell, 1995). Similarly, opioid receptor binding within the insular cortex in individuals with BN is decreased compared to individuals with no symptoms of BN or binge eating (Bencherif et al., 2005). Disparities in dopamine receptor and dopamine transporter gene expression have also been linked to binge eating behavior in humans. For example, compared to non-binge eaters, a significantly higher frequency of binge eaters present with short alleles (7 or 9 repeats) of the variable number tandem repeats (VNTR) polymorphism in the 3′ untranslated region of the dopamine transporter (DAT1) gene (Shinohara et al., 2004). Furthermore, individuals with BED *and* this polymorphism are more sensitive to the appetite suppressing effects of the central nervous system stimulant, methylphenidate (Davis, Levitan, Kaplan, et al. 2007). This effect indicates that there is an alteration within the dopaminergic reward pathway in these individuals, but the exact nature of this permutation is still unknown (Davis, Levitan, Kaplan, et al., 2007). Interestingly, DAT1 polymorphisms are also implicated in substance abuse disorders (Guindalini et al., 2006; Jorm et al., 2000; Samochowiec et al., 2006). Decreased dopamine affinity at the dopamine D4 receptor due to a 7 repeat polymorphism in the third exon, encoding the third intracellular loop of the receptor, has been associated with both binge eating and high lifetime BMI in individuals with BN (Kaplan et al., 2008; Levitan et al., 2004). VNTR polymorphisms in the D4 receptor were also associated with greater and lesser craving for preferred foods after being presented with priming portions of these foods in healthy individuals and individuals with a history of binge eating, respectively (Sobik, Hutchison & Craighead, 2005).

Taken together, these data suggest that there may be differences in opioid and dopaminergic signaling pathways of healthy individuals compared with those with disordered eating; however, further research is needed to determine the direction and magnitude of these differences.

Reward and Hedonic Properties of Food—Given that dopamine and the endogenous opioid system are involved in the rewarding properties of food, it is plausible that individuals with BED and BN may respond differently to reward and the hedonic properties of food than individuals who are not prone to binge eating. Individuals with BED or obesity have been shown to have increased reward sensitivity when measured on the Sensitivity to Reward scale of the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (Torrubia, Avila, Molto & Caseras, 2002) and the Behavioral Activation scale of the Behavioral Inhibition/ Behavioral Activation questionnaire (Carver & White, 1994; Davis, Levitan, Carter, et al.,

2007). This increase in reward sensitivity may be related to decreased dopamine D2 receptor density in these individuals (Davis et al., 2008). Differences in food-related hedonics have been identified among individuals suffering from different forms of eating disorders. For instance, compared with individuals with BN, individuals with BED report greater enjoyment from the taste, smell, and texture of foods during a binge (Mitchell et al., 1999). Moreover, individuals with BN show less anhedonia in response to food than individuals with AN (Davis & Woodside, 2002). More research is necessary to determine if differences in reward sensitivity and taste hedonics exist between individuals with eating disorders and healthy individuals.

Conditioning—Learned associations between the rewarding properties of foods and the environment and conditions under which the food is consumed can contribute to the development of physiological and sensory cues for food consumption in the absence of hunger in laboratory animals (Weingarten, 1983) and binge eating in humans (Fedoroff, Polivy & Herman, 1997; Wardle, 1990; Weingarten, 1983). Eating that results from these learned associations is often not hunger driven but evidence of an acquired craving (Pelchat & Schaefer, 2000) or motivational process acquired through conditioning (Petrovich & Gallagher, 2007; Petrovich, Ross, Gallagher & Holland, 2007). This cue-elicited conditioned responding, based on research in drug priming and environmental conditioning in substance abuse, is one of the key contributors to relapse to binge eating or substance abuse (Koob & Le Moal, 2008; Self, 1998; Sobik, Hutchison & Craighead, 2005). Behavioral protocols used to assess drug craving and drug reward have also demonstrated evidence for food craving and food reward in laboratory animals. Specifically, research utilizing the conditioned place preference paradigm, in which a unique environment is associated with a rewarding substance such as a palatable food or drug of abuse, has provided evidence that 1) animals learn to associate palatable foods with specific environments; 2) animals will spend more time in an environment previously associated with palatable substances looking for the palatable food or "food seeking" because they find it reinforcing; and 3) "food seeking" in this instance is the result of opioid activation, indicative of reward motivated rather than hunger motivated behavior (Jarosz, Kessler, Sekhon & Coscina, 2007; Jarosz, Sekhon & Coscina, 2006). Repeated presentation of the food in the paired environment also leads to a progressive increase in food intake, even in sated rats (Jarosz, et al., 2007; Jarosz et al., 2006). Related studies have shown that placing rats in an environment previously associated with palatable foods can elicit neurochemical and gene expression changes similar to those seen after drug administration or palatable food intake (Kelley, Schlitz & Landry, 2005; Kelley, Will, Steininger, Zhang & Haber, 2003). Additionally, sensory cues, such as taste, sound and smell, can act as triggers to induce binge eating in rats. Rats trained to eat in response to an audible tone will eat more after hearing the tone, even if they are sated (Weingarten, 1983). Rats previously exposed to a feeding/refeeding protocol and then stressed with footshock will binge eat in response to just a taste of palatable food (Hagan, Chandler, Wauford, Rybak & Oswald, 2003).

Human data examining the effects of conditioned stimuli on feeding behaviors have provided valuable insight into the role of associative learning and environmental cues in the etiology of eating disorders. For instance, cravings for preferred foods in response to a visual cue (sight of the food) are significantly correlated with frequency of binge eating in individuals with a history of binge eating (Sobik, Hutchison & Craighead, 2005). In middle aged women (aged 55–65), eating in response to environmental or emotional cues is highly correlated with obesity (Hays & Roberts, 2008). Similarly, sensory cues in the form of sight, smell and taste increase the urge to binge eat and decrease reported willpower to refrain from binge eating in women with BN (Staiger, Dawe & McCarthy, 2000). Extinguishing binge eating as the conditioned response to food cues is extremely problematic. Unlike substance abuse where environmental and sensory cues associated with prior drug use can be avoided, cues associated with binge eating are not only omnipresent in daily life but they are also necessary for survival.

Conclusions

Binge eating is a complex behavioral phenomenon that closely mirrors substance abuse and addiction in its etiology and biology. Animal models of binge eating have helped to elucidate some of the biological systems driving binge eating behaviors. Many precursory circumstances that contribute to the development of binge eating in humans (such as a history of caloric restriction, stress, the availability if palatable foods, and conditioning to environmental and sensory stimuli) also elicit binge eating in laboratory animals. Similarly, data from animal models suggest that binge eating, like substance abuse, may result from maladaptive perturbations within the natural reward system. Additional research will further assist with determining the genetic correlates of binge eating in animal models, individual or interactive environmental factors that elicit binge eating in binge-prone rodents, and ultimately gene by environment interactions associated with rodent binge eating that may translate into models of binge eating in humans. Careful and programmatic interspecies modeling of these predisposing and eliciting genetic and environmental factors will assist with clarification of the neurobiological and environmental factors that underlie disordered eating and will also provide valuable insight into classification of eating disorders.

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Table 1

DSM-IV Diagnostic Criteria for Binge Eating Disorder (307.50)

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:

1. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances
2. The sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)

B. Binge-eating episodes are associated with three (or more) of the following:

1. Eating much more rapidly than normal
2. Eating until feeling uncomfortably full
3. Eating large amounts of food when not feeling physically hungry
4. Eating along because of being embarrassed by how much one is eating
5. Feeling disgusted with oneself, depressed, or very guilty after overeating

C. Marked distress regarding binge eating is present

D. The binge eating occurs, on average, at least 2 days a week for 6 months

Note: The method of determining frequency differs from that used for bulimia nervosa; future research should address whether the preferred method of setting a frequency threshold is counting the number of days on which binges occur or counting the number of episodes of binge eating

E. The binge eating is not associated with the regular use of inappropriate compensatory behavior (e.g., purging, fasting, excessive exercise, etc.) and does not occur exclusively during the course of anorexia nervosa or bulimia nervosa