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REVIEW ARTICLE

The epidemiology and genetics of binge eating disorder (BED)

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This narrative review provides an overview of the epidemiology of binge eating disorder (BED), highlighting the medical history of this disorder and its entry as an independent condition in the Feeding and Eating Disorders section of the recently published *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. Estimates of prevalence are provided, as well as recognition that the female to male ratio is lower in BED than in other eating disorders. Evidence is also provided of the most common comorbidities of BED, including mood and anxiety disorders and a range of addiction disorders. In addition, discussion of the viewpoint that BED itself may be an addiction – at least in severe cases – is presented. Although the genetic study of BED is still in its infancy, current research is reviewed with a focus on certain neurotransmitter genes that regulate brain reward mechanisms. To date, a focal point of this research has been on the dopamine and the μ-opioid receptor genes. Preliminary evidence suggests that a predisposing risk factor for BED may be a heightened sensitivity to reward, which could manifest as a strong dopamine signal in the brain's striatal region. Caution is encouraged, however, in the interpretation of current findings, since samples are relatively small in much of the research. To date, no genome-wide association studies have focused exclusively on BED.

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Introduction

Currently, more than half the adult population, in most developed countries, is overweight or obese – the first time in human evolutionary history that the global number of individuals with excess body weight has exceeded those who are underweight.[1,2] While the overall population prevalence of obesity has roughly doubled in the past few decades, there was an astonishing 4-fold increase in its morbid form (ie, a body mass index [BMI: weight(kg)/height(m^2)] > 40) between the years 1985 and 2002, compared to a more gradual increase at lower BMI categories.[3] The chronology of this weight-gain occurrence is particularly pertinent, considering that the first clinical reports of BED were published during the midst of this surge in the early 1990s.[†4] Such an exponential increase in morbid obesity suggests that the more weight one gains, the more likely it is that the trend will escalate over time. In other words, it may be that an "overeating sensitization" develops in some individuals, which contributes to more frequent and more excessive consumption and thereby a more rapid increase in weight.[7]

Not surprisingly, the two events described above also coincided temporally with pronounced changes in the food environment. For example, in the decades between 1970 and 1996, *per capita* consumption of augmented sugars in food and drink increased by a significant 23% in adults, similar to increases in the proportion of carbohydrates to total energy intake.[8] Compared to foods grown or raised in nature, the high reward-impact of ultraprocessed foods has been magnified multifold. Indeed, the advanced technology of the food-manufacturing industry is largely responsible for the prodigious addition of sweet, fatty, and salty taste enhancers in much of the food we eat on a daily basis.[9] There is now clear evidence that the chronic consumption of these calorically rich foods has enhanced their ability to sabotage healthy brain function and override well-regulated and adaptive ingestive behaviors.[10]

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[†]As early as 1955, a related syndrome was reported.[5] Found in certain obese individuals, it was referred to as night-eating syndrome and was characterized by "nocturnal hyperphasia, insomnia and morning anorexia" (p. 78).[5] This condition appeared to be most prominent during periods of stress and weight gain. The 1950s also saw a few isolated publications about so-called "food addiction" by Randolph,[6] but this putative condition also did not gain widespread acceptance for another 30 or 40 years.

In light of the relatively recent clinical recognition of BED, and its considerable temporal overlap with the environmental and economic events associated with the rise in obesity, BED has the requisite features of a "culture-bound syndrome" – that is, an illness with its emergence and occurrence in a specific ethnic and/or social context.[11] This perspective puts BED in rather sharp contrast to its clinical counterpart at the other end of the eating and body weight continuum. Importantly, anorexia nervosa has changed little in its biobehavioral characteristics for centuries, and has been found globally in a myriad of different cultures.[12]

BED can also be suitably conceptualized as an "evolutionary mismatch" condition arising from a maladaptive gene–environment interaction. This viewpoint asserts that certain human behaviors were fostered during the hunter-gatherer era, at a time when our genetic endowment was established, because they bestowed survival and reproductive advantages to the species.[13] However, in the face of rapid environmental changes – seen, for instance, in the proliferation of highly palatable, and greatly available, processed foods on the grocery shelves in most Western societies – these same behaviors became maladaptive and greatly over-expressed.[9] Specifically, it is strongly believed by evolutionary biologists that we evolved to desire highly palatable and calorically dense foods, and to eat beyond caloric need, since these strategies were the most adaptive in early environments where energy resources were sometimes of unknown quality, and were often unpredictable and scarce.[14] Simply stated, a strong hedonic response to food was an undeniable survival benefit until relatively recently in our evolutionary history.

In support of both the "culture-bound" and the "mismatch" viewpoints, population estimates suggest a roughly equal impact of biological and environmental factors in the risk for BED, although such evidence is still relatively scant. A U.S.-based case-control study of overweight/obese adults with and without BED calculated the heritability of this disorder as 57%[15] – a value that was similar to the 41% found in an earlier Scandinavian twin study of binge eating without compensatory behaviors.[16] A later twin study also investigated the heritability of BED, but this time at the symptom level rather than as an overall diagnosis, and found similarly that additive genetic effects accounted for 29–43% of the variance in individual symptom items.[17]

The Epidemiology of BED

Prevalence rates and demographic correlates

Relatively few studies have assessed the population prevalence of BED, and those that exist are based mostly on U.S. data. Not surprisingly, estimates tend to vary depending on the diagnostic assessment method that was used; that is, self-administered questionnaires versus interview-based protocols. Employing the latter methodology, lifetime rates were about 3% of the population[18,19] compared to a 6.6% point-prevalence rate with a self-report inventory.[20] Among the few exceptions to U.S. prevalence studies are World Health Organization adult data from 14 countries, mostly upper-middle and high income, where lifetime prevalence rates were estimated at 1.4% – considerably lower than equivalent U.S. data.[21] Even lower rates (0.6% and 0.5%, respectively) were found in 2 studies of high school and college students in Portugal,[22,23] in accord with U.S. evidence that the prevalence of BED is higher in mature adults than in younger individuals.[24]

There was some initial speculation that prevalence rates would increase with the BED modifications that appeared in the recently published *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5).[25] The more liberal diagnostic criteria for BED in DSM-5 specify a 3-month period for symptom duration, compared to 6 months duration in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV).[26] Based on predictions derived from existing DSM-IV data, however, Hudson *et al*[27] estimated only negligible increases of less than 0.2% for either lifetime or point prevalence of BED in future studies employing the newly revised standards.

Overall prevalence rates of BED are also moderated by sex/gender and by the BMI status of the sample. In the former case, as with other eating disorders such as anorexia nervosa and bulimia nervosa, there is a pronounced female bias, although the differences are typically not as large in BED[18,28] and vary from approximately a 2:1 to a 6:1 ratio.[29] While there is little doubt that some of these male–female differences can be attributed to sociocultural factors, there is also good evidence from animal models that some of the variance is accounted for by biologically-based factors. For instance, using numerous behavioral criteria for classifying binge-eating phenotypes in adult rats, occurrence rates were 2 to 6 times higher in the females compared to the males.[30] These authors concluded that at least some of the differences were the result of gonadal hormones on sex-differentiated behavior during development – effects such as increased reward responsiveness to food in females that tends to override homeostatic mechanisms. Importantly, however, and despite clear male–female differences in the proneness to binge-eating, few significant sex differences have been found in other aspects of the disorder, such as its developmental history,[31] or in the age of onset, the severity of symptoms, and the response to treatment.[32]

Given the absence of inappropriate compensatory behaviors in BED, it is not surprising that elevated body weight is strongly correlated with this disorder. For

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example, the lifetime occurrence of BED is substantially higher in samples comprising overweight and obese adults compared to the general population.[18,33] Similarly, the prevalence of this disorder is elevated in those waiting for bariatric surgery,[34,35] and in patients attending other weight-loss treatment facilities.[36] Studies suggest that between one-quarter and one-half of patients seeking surgical treatment for obesity meet the diagnostic criteria for BED.[35,37] The evidence is also relatively clear that both pre-surgical and post-operative binge-eating are inverse predictors of weight loss at follow-up.[38–40] The mechanisms whereby BED is linked to poor treatment success may be partly explained by psychological factors, as seen in the results of a large study of bariatric surgery candidates with and without BED. The former reported significantly greater dysfunctional negative emotions and fewer positive emotions than their weight- and demographically-matched female counterparts.[41]

Comorbid conditions

In addition to the physical comorbidities associated with BED, such as diabetes and metabolic syndrome – those largely occurring due to its strong links with overweight/obesity – BED is also linked with various co-occurring psychiatric disorders in the majority of patients. Lifetime mood and anxiety disorders are the most frequent conjoint disorders (close to 50%) in those with BED,[42] as they are with most psychiatric disorders including other eating disorders. The next most common comorbidities include a range of addiction disorders – and their sub-syndromal variants[42] such as alcoholism,[43] problem gambling,[44] and compulsive shopping.[45] Based on related risk-factor evidence, it is reasonable to speculate that impairments in impulse control found in BED and in addiction disorders are primary factors in both conditions.[7,46] Greater comorbidity rates have been found in those with child-adolescent onset of binge eating compared to individuals with onset in adulthood.[24] They have also been associated with more severe psychopathology and poorer daily functioning – although surprisingly not with more frequent binge eating or higher BMI.[42]

In recent years, it has been proposed that some cases of BED are themselves addiction disorders, based on evidence of their considerable symptom overlap with the so-called *food-addiction* construct – a proposed clinical entity based on parallels between the psychobiobehavioral responses to hyper-palatable, ultraprocessed foods, and to conventional substances of abuse such as cocaine and alcohol.[7] For research purposes, this putative syndrome is typically diagnosed by the Yale Food Addiction Scale (YFAS),[47] a self-report scale centered on the DSM-IV diagnostic criteria for substance dependence.[26] Indeed, 2 recent studies found that about 50% of obese adults diagnosed with BED also met criteria for YFAS food addiction.[48,49] In addition, in an earlier study of women diagnosed with BED, the investigators found that 92% of their sample met the DSM-IV[26] criteria for substance dependence when the word "food" was substituted for "drug" in the questions used in a structured telephone interview.[50]

Such investigations, and related work, have raised the question of whether – at least in some cases – the YFAS-inspired definition of food addiction simply reflects a more severe sub-type of BED. Some preliminary evidence supports this proposed viewpoint. For instance, a group of overweight men and women with BED was dichotomized according to whether they had co-occurring YFAS-diagnosed food addiction or not. Group differences were assessed on several variables related to demographic characteristics (age and BMI), patterns of overeating, personality risk factors, and comorbid clinical symptoms.[51] Results indicated that the 2 BED groups were equivalent in age and BMI. However, the group with food addiction was significantly much more likely to overeat for emotional and cue-driven reasons, they had more severe binge eating and food cravings, and they were more responsive to the rewarding properties of food. This group also had more addictive personality traits, was more impulsive, and had greatly elevated symptoms of depression compared to their non–food addict BED counterparts.

In summary, and based on an expanding amount of evidence, many scientists and clinicians subscribe to the view that some cases of compulsive overeating – a quintessentially defining feature of BED – share pronounced similarities with conventional addictions like substance abuse.[52,53] Not surprisingly, such discussions have inspired cautious conclusions that some forms of excessive overeating may be most appropriately viewed as an addiction to hyper-palatable foods. In other words, as the severity and compulsive nature of overeating increase over time, loss of control begins to resemble the physical dependence seen in those addicted to drugs, with the same concomitant symptoms such as powerful cravings and repeated relapses following efforts to abstain.

In concluding, it should also be noted that some argue that the term "food addiction" is a misnomer because it draws too strong a parallel with substance dependence.[54] Instead, they propose the term "eating addiction." Such a distinction in terminology appears more semantic than real. On the one hand, there is clear evidence that certain foods have properties similar to addictive substances in their ability to elicit specific brain and behavioral responses.[55] On the other hand, it is also well-established that the act of consuming a tasty meal is itself a hedonically rewarding experience.[56] Attempts to distinguish between food and eating – and which is most important in contributing to excessive and compulsive

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ingestion of a highly palatable diet – are in the same spirit as trying to separate the effects of nicotine from the act of smoking in those who are addicted to cigarettes. In the opinion of this author, in both cases we are describing 2 sides of the same coin.

The Genetics of BED

There is incontrovertible evidence that the risk for BED has a clear biological basis in forming individual risk. For instance, a large family study including overweight and obese individuals with and without BED, as well as their first-degree relatives, found that BED aggregated strongly in families independent of obesity.[57] Such results have prompted a growing interest in "brain and behavior" research, using both clinical and preclinical paradigms, to understand better the development and progression of BED. Much of this work has employed sophisticated neuroimaging techniques.[58,59] One must be cautious, however, when interpreting this evidence. Psychiatric case-control designs using this methodology only provide a "snap-shot" of the brain at a finite moment in time. It is therefore not possible to deduce if the observed physiology and/or anatomy are antecedent to the condition we are investigating, or a consequence of the behaviors that characterize individuals with the condition of interest. The limitation of neuroimaging technology is particularly relevant for behavioral conditions such as eating and addiction disorders where evidence of neuro-adaptations during the progression of the disorder are well-established.[60] A genetic approach to investigating the biological basis of, and the risk for, BED has the singular advantage of improving our ability to speculate on causal associations.

It has also become clear that inherent vulnerability factors interact with cultural and environment influences to promote maladaptive behaviors and subsequent pathology. For example, a compelling body of evidence suggests that certain foods – viz. processed foods high in sugar, fat, and salt – have an abuse potential similar to other concentrated and processed substances such as alcohol and cocaine.[9] A heightened preference for a calorically-rich diet can thereby increase the risk for overeating in individuals with this inherent predisposition. At the heart of these relationships is the central role of mesocorticolimbic dopamine in the regulation of rewarding behaviors, whether they are so-called "natural reinforcers" like food or pharmacologic reinforcers like cocaine.[61] Both the ANKK1 and the DRD2 dopamine receptor genes, for instance, have been significantly associated with addictions across multiple replicated studies.[62] The opioid system is also strongly implicated in the regulation of reward, and is known to foster eating behaviors by amplifying the hedonic properties of palatable food.[63,64] While the last few decades have seen a wealth of research on the genetics of obesity – and by implicit association the genetics of overeating – only a very few studies have been dedicated specifically to the etiology of BED. The following review will focus on case-control studies of BED and/or genetic studies investigating relevant symptom dimensions of BED, such as binge eating and food cravings.

The most commonly studied functional genetic marker of the brain dopamine system is the *Taq1A* polymorphism on the ANKK1 gene. There is reasonable evidence to suggest that carrying at least one copy of the minor A1 allele (ie genotypes A1/A1 and A1/A2) is associated with a 30–40% reduction in dopamine D2 receptors in the striatal area contributing to a diminished dopamine signal in the reward pathway.[65] A1 can thereby be seen as a "loss-of-function" allele. The A118G polymorphism of the μ-receptor gene (*OPRM1*) is a functional genetic marker of the brain opioid system.[66,67] By contrast to A1, the minor G allele has been associated with a "gain-of-function" as reflected by an increased responsiveness to a variety of rewarding stimuli, including palatable food.[68] The G allele has also been associated with stronger negative emotions to social separation and with greater positive emotions to social affiliation.[69] While the exact molecular function of the 118G allele is still unclear, evidence of its modulation of social reward is increasing.[70] Recent evidence of its positive association with neuroticism (a personality trait associated with anxiousness, worry, and stress-proneness) is also of interest, and suggests that this marker may contribute to more labile and pronounced emotional responses both to anticipated rewards, and to their removal – a phenotype that puts one at risk for various psychiatric disorders, including addictions.[67]

Because of the association of the 2 markers described above (*Taq1A* and *A118G*) with the functioning of brain reward mechanisms, an early study examined their conjoint influence in obese adults with and without BED.[71] A significant gene–gene genotype combination showed that of those with the gain–gain genotype (A1– and G+), 80% were BED participants, whereas only 35% of those with the loss–loss genotype (G– and A1+) were from the BED group. These findings suggest that BED may be a subtype of obesity characterized by a hyper-reactivity to reward and to the hedonic properties of food. A more recent study examined 5 functional markers of the dopamine D2 receptor genes (*DrD2/ANKK1*) in a group of obese adults with and without BED.[72] Results indicated that the BED group was significantly related to the *Taq1A* and the *C957T* genotypes that reflect enhanced dopamine neurotransmission (viz. A2/A2 and T/T, respectively). Allelic analyses also indicated that the T allele of *C957T* was significantly overrepresented in the BED group compared to the non-BED obese counterparts. In addition, sub-phenotypes of BED such as binge eating, emotional

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eating, hedonic eating, and food cravings were also higher in the A2/A2 genotype, while the T/T genotype was only significantly related to the measure of binge frequency and severity.

A recognition that complex human traits and behaviors are under multigenetic control has fostered the current view that common disorders may be better conceptualized in quantitative terms than as discrete qualitative entities.[73] From the perspective of genetic analyses, it has been suggested that relevant genetic variants can be summated into a composite index that reflects a polygenetic liability for the disorder in question – a potentially more powerful approach to uncovering important genetic risk factors, because individual polymorphic loci typically tend only to account for a small proportion of phenotypic variance and therefore may not reach statistical significance in studies with relatively small clinical samples.[74] Using such an approach, and including 6 functional markers on 4 dopamine genes – ANKK1, DRD2, DAT1, and COMT, we found that the BED group showed a significantly higher multilocus genetic profile score than the obese non-BED counterparts, implying greater brain dopamine signaling strength in the striatum and a higher responsiveness to reward among the participants with BED.[75] These findings mesh with other psychobehavioral evidence that BED is a reward-reactive subtype of obesity.[71,72]

The role of serotonin (5-HT) involvement in modulating disordered eating has been widely studied for many years, especially in the context of anorexia nervosa. Relatively few studies in this area have focused on BED, and even fewer of these on the possible role of serotonin genes in the development of this disorder. One early study genotyped the 5-HTTLPR polymorphism of the serotonin transporter gene (5HTT) and found that both the Long/Long genotype and the Long allele were significantly more frequent in a sample of women with BED compared to controls,[76] although these findings have not been replicated in subsequent research.[77] While a more recent study found no 5-HTTLPR effect on the severity of binge eating in the general population, it was observed that women with the Short/Short genotype had great anxiety and a tendency for higher impulsivity – traits associated with the personality profile of those with BED.[78]

And finally, because of evidence that melanocortins – peptide hormones that are expressed in the hypothalamus and have an important role in regulating appetite – have strong links with obesity,[79,80] some recent work has investigated whether the melanocortin 4 receptor gene (*MC4R*) has a role in the etiology of binge eating. While most of the studies have produced null results,[81,82] one such study included more than twice as many patients with bulimia nervosa in the same group as those with BED and only included non-obese participants[83] – a design that may have compromised the ability to detect effects specific to BED. More promising results have come from a study of adults with European ancestry where the C allele of the rs17782313 *MC4R* marker was associated with higher scores on a trait measure of food cravings, and suggested that this variable partially mediated the relationship between the genetic variant and BMI.[84]

Summary and Conclusions

In the 35 years since the first clinical reports of BED appeared in the literature, we have gained a good understanding of its prevalence and major demographic characteristics – especially its association with obesity and its conceptualization, in severe cases, as a form of addiction. Evidence of its clinical comorbidities and the psychopathology characteristics, such as anxiety, depressed mood, and impulsiveness that link compulsive overeating to other psychiatric conditions, is also well-established. Less clearly delineated is the neuroscience of BED and the innate risk factors that predispose to this condition. To date, the limited genetic research on BED has indicated the involvement of both dopamine and μ-opioid receptor genes in the etiology of this disorder. It has been tentatively concluded that a risk for compulsive overeating may be a strong responsiveness to the hedonic properties of food, and a heightened preference for sweet and fatty cuisine. These particular traits were deemed highly adaptive in an environment characterized by uncertain and often scarce energy resources – one that described most of our evolutionary history. They are, however, mismatched to our current environment with its superfluity of highly palatable, calorically dense, and nutritionally impoverished foods.

An important issue in future BED research – given its strong links with other compulsive behaviors such as substance abuse and gambling addiction – is to include the appropriate control groups, or what have sometimes been called "super-controls." This is of particular relevance to genetic research in BED given the evidence from population-based transmission studies that *common* biological factors contribute to the excessive use of a broad range of addictive drugs and activities, and that these influences do not differ between men and women.[85] In case-control designs, a control participant should be similar to the cases except that it is absent of the condition under investigation. Since it is known, for example, that polymorphisms of the dopamine receptor genes are associated with a number of impulsive-addictive/compulsive disorders including BED,[86] it is important to screen potential control participants for a broader range of conditions than simply for disordered eating.

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