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Neurobiology of anorexia and bulimia nervosa

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Abstract

Anorexia nervosa (AN) and bulimia nervosa (BN) are related disorders of unknown etiology that most commonly begin during adolescence in women. AN and BN have unique and puzzling symptoms, such as restricted eating or binge-purge behaviors, body image distortions, denial of emaciation, and resistance to treatment. These are often chronic and relapsing disorders, and AN has the highest death rate of any psychiatric disorder. The lack of understanding of the pathogenesis of this illness has hindered the development of effective interventions, particularly for AN. Individuals with AN and BN are consistently characterized by perfectionism, obsessive–compulsiveness, and dysphoric mood. Individuals with AN tend to have high constraint, constriction of affect and emotional expressiveness, ahendonia and asceticism, whereas individuals with BN tend to be more impulsive and sensation seeking. Such symptoms often begin in childhood, before the onset of an eating disorder, and persist after recovery, suggesting they are traits that create a vulnerability for developing an ED. There is growing acknowledgement that neurobiological vulnerabilities make a substantial contribution to the pathogenesis of AN and BN. Considerable evidence suggests that altered brain serotonin (5-HT) function contributes to dysregulation of appetite, mood, and impulse control in AN and BN. Brain imaging studies, using 5-HT specific ligands, show that disturbances of 5-HT function occur when people are ill, and persist after recovery from AN and BN. It is possible that a trait-related disturbance of 5-HT neuronal modulation predates the onset of AN and contributes to premorbid symptoms of anxiety, obsessionality, and inhibition. This dysphoric temperament may involve an inherent dysregulation of emotional and reward pathways which also mediate the hedonic aspects of feeding, thus making these individuals vulnerable to disturbed appetitive behaviors. Restricting food intake may become powerfully reinforcing because it provides a temporary respite from dysphoric mood. Several factors may act on these vulnerabilities to cause AN to start in adolescence. First, puberty-related female gonadal steroids or age-related changes may exacerbate 5-HT dysregulation. Second, stress and/or cultural and societal pressures may contribute by increasing anxious and obsessional temperament. Individuals with AN may discover that reduced dietary intake, by reducing plasma tryptophan availability, is a means by which they can modulate brain 5-HT functional activity and anxious mood. People with AN enter a vicious cycle which accounts for the chronicity of this disorder because caloric restriction results in a brief respite from dysphoric mood. However, malnutrition and weight loss, in turn, produce alterations in many neuropeptides and monoamine function, perhaps in the service of conserving energy, but which also exaggerates dysphoric mood. In summary, this article reviews findings in brain chemistry and neuroimaging that shed new light on understanding the psychopathology of these difficult and frustrating disorders.

Keywords: Anorexia; Bulimia

1. Introduction

Anorexia nervosa (AN) and bulimia nervosa (BN) are related disorders of unknown etiology that most commonly begin during adolescence in women (DSM-IV; Table 1). They are frequently chronic and often disabling conditions that are characterized by aberrant patterns of feeding behavior and weight regulation, and deviant attitudes and perceptions toward body weight and shape. In AN, an inexplicable fear of weight gain and unrelenting obsession with fatness, even in the face of increasing cachexia, accounts for a protracted course, extreme medical and psychological morbidity, and standardized mortality rates exceeding those of all other psychiatric disorders. BN usually emerges after a period of food restriction, which may or may not have been associated with weight loss. Binge eating is followed by either self-induced vomiting, or by some other means of compensation for the excess of food ingested. Although abnormally low body

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Table 1

DSM IV, Diagnostic criteria for anorexia nervosa

A Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected.)
B Intense fear of gaining weight or becoming fat, even though underweight.
C Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight.
D In postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles. (A woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration.)
Specify type:
Restricting type: during the current episode of anorexia nervosa, the person has not regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas)
Binge-eating/purging type: during the current episode of anorexia nervosa, the person has regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas)

DSM IV, Diagnostic Criteria for Bulimia Nervosa

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 during a similar period of time and under similar circumstances
(2) a 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 Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, enemas, or other medications; fasting, or excessive exercise
C The binge eating and inappropriate compensatory behaviors both occur, on average, at least twice a week for 3 months
D Self-evaluation is unduly influenced by body shape and weight
E The disturbance does not occur exclusively during episodes of anorexia nervosa
Specify type:
Purging type: during the current episode of bulimia nervosa, the person has regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas
Non-purging Type: during the current episode of bulimia nervosa, the person has used other inappropriate compensatory behaviors, such as fasting or excessive exercise, but has not regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas

weight is an exclusion for the diagnosis of BN, some 25% to 30% of bulimics have a prior history of AN.

Because AN and BN present most often during adolescence in women, they are often theorized to be caused by cultural pressures for thinness [1] since dieting and the pursuit of thinness are common in industrialized countries. Still, AN and BN affect only an estimated 0.3% to 0.7% and 1.5% to 2.5%, respectively, of females in the general population [2]. This disparity between the high prevalence of pressures for thinness and the low prevalence of eating disorders (EDs), combined with clear evidence of AN occurring at least several centuries ago [3], the stereotypic presentation, substantial heritability, and developmentally specific age-of-onset distribution, underscores the possibility of contributing biological vulnerabilities.

Considering that transitions between syndromes occur in many, it has been argued that AN and BN share at least some risk and liability factors [4,5]. In fact, AN and BN are cross transmitted in families. [6,7] Moreover there is an increased prevalence of AN and BN as well as subthreshold forms of ED in relatives, consistent with the possibility of a continuum of transmitted liability in at risk families manifesting a broad spectrum of eating disorder phenotypes [7]. Twin studies can differentiate genetic from environmental effects by comparing concordance for a trait, or disorder, between identical (monozygotic; MZ) and fraternal (dizygotic; DZ) twins. Twin studies of AN and BN suggest there is approximately a 50 to 80% genetic contribution to liability [4,8–11] accounted for by additive genetic factors. These heritability estimates are similar to those found in schizophrenia and bipolar disorder, suggesting that AN and BN may be as genetically-influenced as disorders traditionally viewed as biological in nature.

2. Clinical symptoms and puzzling behaviors

The DSM-IV diagnostic criteria for AN and BN focus on eating behavior and body image distortions. Because of their unusual and prominent nature, these symptoms tend to capture much attention. The pathogenesis of the disturbed eating behaviors is poorly understood [5,12]. Individuals with AN rarely have complete suppression of appetite, but rather exhibit an ego-syntonic resistance to feeding drives while simultaneously being preoccupied with food and eating rituals to the point of obsession. Individuals with AN severely restrict food intake, particularly fats and carbohydrates, but rarely stop eating completely; rather they restrict their caloric intake to a few hundred calories a day. They tend to be vegetarians, have monotonous choices in food intake, select unusual combinations of foods and flavors, and have ritualized eating behaviors. Similarly, BN is not associated with a primary, pathological increase in appetite; rather, like individuals with AN, individuals with BN have a seemingly relentless drive to restrain their food intake, an extreme fear of weight gain, and often have a distorted view of their actual body shape. Loss of control with overeating in individuals with BN usually occurs intermittently and typically only some time after the onset of dieting behavior. Restrained eating behavior and dysfunctional cognition relating weight and shape to self-concept are shared by all types of patients with EDs.

AN and BN individuals commonly have clusters of other puzzling symptoms. Excessive exercise and motor restlessness are common in AN [13]. While not well studied, excessive exercise is thought to be associated particularly with the purging subtype of AN, as well as with a constellation of anxious/obsessional temperament. Individuals with AN often have resistance to treatment [14]. In part this is due to the ego syntonic nature of the disorder, which is demonstrated by the patient's denial of being underweight and refusal to accept the seriousness of the medical consequences of the disorder. Consequently, few control trials of any therapy have been performed, in part, because it has been difficult to enlist cooperation of individuals with AN, and in part because psychological and pharmacological strategies that have been successful in other disorders appear to be less effective in this illness.