Eating Disorders

P. SÖDERSTEN AND C. BERGH
Karolinska Institute, Sweden

I. INTRODUCTION
II. PREVALENCE, INCIDENCE, AND PROGNOSIS
III. PSYCHOPATHOLOGY
IV. ENDOCRINE AND PHYSICAL EFFECTS
V. NEUROTRANSMITTERS
VI. TREATMENT
VII. CAUSES
VIII. SUMMARY

There are three classifications of eating disorders, anorexia nervosa (AN), bulimia nervosa (BN), and eating disorders not otherwise specified, as defined by the Diagnostic and Statistical Manual of Mental Disorders. AN can be further divided into two subtypes, restricting and binge-eating/purging types, and BN can be divided into two subtypes as well, purging and nonpurging types. The regulation of body weight is a main public health concern today because of the great increase in obesity, and it is now estimated that the medical consequences of too much food are as devastating as those of too little food worldwide. The focus here, however, is on the eating disorders listed above and their prevalence, incidence, prognosis, psychopathology, endocrine and physical effects, treatment, and causes.

I. INTRODUCTION

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), eating disorders are classified broadly into three types: anorexia nervosa (AN), bulimia nervosa (BN), and eating disorders not otherwise specified (EDNOS). There are two subtypes of AN, restricting and binge-eating/purging types, and two subtypes of BN, purging and nonpurging types. The main symptom of AN is the refusal to maintain a normal body weight, so that the body mass index (BMI) is reduced to ≤ 17.5 (kg/m^2) from a normal of 19–24 for women and 20–25 for men. Because of their restricted food intake and their low body weight, anorexics do not menstruate and amenorrhea is a diagnostic criterion of AN. According to the DSM-IV, anorexics fear gaining weight and perceive their body as unrealistically large. Bulimic patients are of normal weight; their main behavioral disorder is that they eat large amounts of food in a brief period of time and subsequently display compensatory behavior to maintain their body weight. These behaviors include vomiting, the use of laxatives, and excessive exercise. Patients suffering from an EDNOS have some of the symptoms characteristic of AN and/or BN but not all these symptoms.

Other types of disordered eating behavior or eating behaviors that cause medical problems, e.g., obesity, are not included in the DSM-IV as eating disorders because they may not be associated with a psychological or behavioral syndrome. However, it is estimated that at least 20% of obese patients display a pattern of eating behavior that is similar to that of patients with BN, although they do not compensate for the increased intake of energy and hence become obese. Binge-eating disorder, i.e., intake of large amounts of food in a short period of time but no other signs of BN, may be viewed as an EDNOS.

In addition to the symptoms mentioned above, anorexic patients are often overactive physically and always hypothermic. These symptoms are obvious in most clinical settings and are likely to be included among the diagnostic criteria in future editions of the DSM. Likewise, patients with bulimia can display physical hyperactivity and deficiencies in thermoregulation.

II. PREVALENCE, INCIDENCE, AND PROGNOSIS

The specific condition of AN has been recognized for several hundred years, although it is debated whether the different types of emaciation that have been described during the course of medical history are equivalent to the present DSM-IV description of the condition. It is not surprising that AN has been observed for a long time in medical practice, because of its conspicuous physical marker, i.e., the low BMI. By contrast, the specific diagnosis of BN is only 20 years old. Most likely the condition was brought to medical attention only recently because bulimic patients are of normal weight and display no obvious external markers.

The prevalence of AN has remained constant, at approximately 1%, for as long as it has been documented. The patients are typically 14–19 years old at the onset of the disorder and approximately

95% are female. The prevalence of BN is approximately 1–1.5%, the patients are 20–25 years old at the onset of the disorder, and the majority are females and have a history of AN. However, the probability that a young woman may develop an eating disorder symptom, such as binge-eating or vomiting, during a restricted period of her life is as high as 5–25%. On the other hand, there is some evidence that the incidence of both AN and BN has increased somewhat during the past 40 years. The incidence of EDNOS, however, has most likely increased markedly.

The prognosis of patients with eating disorders is poor. Anorexics typically have less than a 50% chance of recovery in 10 years and 25% of the cases become chronically ill. Sadly, the mortality rate is high; as many as 6–15% may die within 10 to 20 years after the onset of the disorder. A low BMI is regarded a poor prognostic factor; with a BMI ≤ 13, the risk of becoming chronically ill approaches 100%, and with a BMI ≤ 10, the risk of dying approaches 50%. Bulimics have been reported to have a better prognosis, but at least one-third of the patients continue to binge-eat and purge 10 years after the onset of the disorder.

III. PSYCHOPATHOLOGY

Patients with AN suffer from concomitant psychopathology. This is not surprising, however, because animal studies have shown that food deprivation alters the concentration, synthesis, and turnover of the neurotransmitters that are involved in reward, mood, and emotion, e.g., dopamine. It is commonly recognized that humans subjected to experimental starvation develop the psychopathological symptoms found in patients with AN. These symptoms include depression, anxiety, and obsessive thoughts and actions. Patients with BN show a similar psychopathology, and periods of self-induced starvation are common among bulimics. Also, 10–20% of patients with AN show bulimic behavior and are, therefore, classified as a subgroup of AN, binge-eating/purging type. Although it has been argued that AN and BN are separable disorders and that EDNOS constitute several different disorders, the similarities between these disorders with regard to behavior and psychopathology are more conspicuous than are the differences. Moreover, there is a general consensus that the psychopathology of eating disorders is enhanced by food restriction. The most parsimonious interpretation, therefore, is that psychopathology emerges from the physical condition of eating-disorder patients. The alternative hypothesis, i.e., disordered eating behavior is an epiphenomenon of an underlying psychopathology, is not supported by any existing evidence. This hypothesis has been proposed in many versions, the most recent being that AN develops because of an underlying obsessive–compulsive disorder. Contradicting this view is the observation that obsessive-compulsive behaviors in AN patients are markedly reduced when the patient's body weight increases. Also, it is unclear how an obsessive personality trait translates into a disordered pattern of eating behavior. Most patients with eating disorders have been examined in a state of illness and, therefore, making a distinction between the potential effects of trait and those of state is not possible. Although patients show reductions in most psychopathological symptoms by the time of clinical discharge, there are no reports of patients who are free of all of their psychopathological symptoms. Consequently, these remaining symptoms may be an effect of a partially effective method of treatment rather than a personality trait of the patient.

IV. ENDOCRINE AND PHYSICAL EFFECTS

A. Reproduction

Reduction of food intake and a subsequent loss of body weight cause cessation of menstruation and amenorrhea in AN. Many patients do not experience menarche and therefore suffer from primary amenorrhea. The physical hyperactivity of anorexia may also contribute to their amenorrhea. Thus, amenorrhea is common among normal-weight elite female athletes; in fact, as many as 65% of those engaging in long-distance running are affected. Physical hyperactivity and reduction of food intake, therefore, both contribute to cessation of menstruation. An associated decrease in the level of pituitary gonadotropins and an increase in prolactin and pro-opiomelanocortin-derived hormones are also secondary to the reduced food intake and low body weight. Neither induction of menstrual cyclicity nor restoration of any of these hormonal imbalances has thus far been found useful in restoring the eating behavior of anorexics.

Approximately 50% of bulimics have menstrual disturbances. It is doubtful, however, that menstrual irregularities, including polycystic ovaries, predispose a woman for an eating disorder. Animal experiments suggest instead that the ovarian dysfunction in patients with eating disorders is caused by their disordered eating behavior.

Dieting and/or physical hyperactivity can cause functional hypothalamic amenorrhea, i.e., reduced pulsatile secretion of gonadotropin-releasing hormone (GnRH), and can therefore disrupt the menstrual cycle in women as well as testicular function in men. Consequently, the secretion of gonadal hormones (estradiol and progesterone in women and testosterone in men) is impaired. Puberty, therefore, is delayed.

Thus, the disturbances in reproductive neuroendocrine function in eating-disorder patients are secondary to reduced or altered intake of food and physical hyperactivity. Reproductive quiescence or disturbance induced in this way is reversible.

B. Adipose Tissue

Leptin is a 15 kDa protein secreted by adipocytes that was first thought to inhibit food intake and play a role in preventing excessive weight gain. However, it has become apparent that reduced leptin facilitates the adaptation to starvation by entraining a complex set of behavioral and neuroendocrine responses that favor survival during periods of limited energy availability. The concentration of leptin is directly proportional to the body fat mass. In anorexia, fat mass is gradually decreased, and leptin levels therefore decrease in parallel. The increase in physical activity that also occurs in anorexia causes a further decrease in fat mass and therefore leptin. It has also been suggested that physical hyperactivity per se might influence leptin levels independent of its effect on fat mass. In addition, experiments on animals suggest that leptin reduces physical activity. The inhibition of pulsatile GnRH secretion and menstrual cyclicity that is caused by both food restriction and excessive physical activity can be reversed by the administration of leptin. Changes in peripheral leptin levels may therefore provide a signal to the brain essential for the adaptations that occur during periods of food shortage and/or abundance.

In view of the fact that many studies have shown that leptin inhibits the food intake of animals, the low levels of leptin and low intake of food in anorexic patients are paradoxical. However, the role of leptin in food intake in humans has been examined only in the obese and has been found to have a minor inhibitory effect. The eating behavior and body weight of anorexics are, of course, radically different from those of the obese, including those who show a bulimic pattern of eating behavior. Yet it has been recently reported that both anorexics and bulimics have low levels of leptin. These findings argue against a direct role of leptin in the eating behavior of patients with eating disorders.

C. Other Hormonal and Physical Effects

Most likely, all of the other endocrine and physical changes that occur in eating-disorder patients are also the result of periods of dieting or continuous dieting; that is to say, the hormonal changes in starvation are the same independent of the way in which starvation is induced. Thus, hyperprolactinemia, hypercortisolism, bradycardia, hypotension, and hypothermia follow starvation in anorexia just as they do in starvation induced by enforced shortage of food. Other indirect effects of a restricted availability of food are reduced gastrointestinal motility and gastric emptying, constipation, and early satiation. Although most of the endocrine and physical effects in eating-disorder patients are reversible, some are not. Thus, reduced bone mass follows long periods of starvation and estrogen depletion. Physical activity is necessary for the development of bone mass, and the high physical activity in AN may counteract the effect of low food intake and low levels of circulating estrogens. However, normal-weight women with a history of AN will have a permanent reduction in bone mass, and osteoporosis may be a consequence in women with frequent periods of relapse. In BN, permanent dental damage may occur due to recurrent episodes of vomiting.

Interestingly, patients with AN rarely catch infections. This phenomenon is well known but has yet to be explained.

Patients suffering from type 2 diabetes have an increased prevalence of BN. The intriguing possibility that BN may be a risk factor for the development of diabetes deserves investigation.

V. NEUROTRANSMITTERS

The neural mechanisms controlling food intake are currently the subject of intensive investigation. Although pharmacological studies have shown that many neurotransmitters affect food intake in laboratory animals, these results have not yet allowed the formulation of a model for the development of either AN or BN.

A. Peptides

Work in animals has failed to demonstrate a factor that initiates feeding under physiological conditions. By contrast, gastrointestinal secretions during a meal

are known to cause a physiologically relevant inhibition of food intake. The mechanisms of inhibitory control are localized mainly in the caudal brainstem, and neural systems related to initiation of behavior, including ingestive behavior, are localized in the forebrain, particularly in the ventral striatum. As animals, including humans, eat meals, forebrain and brainstem control mechanisms must interact in the onset and termination of ingestion, but there is no information on how this occurs. The octapeptide cholecystokinin (CCK-8) is in all probability a physiological satiety signal. Inhibition of food intake by CCK-8 is mediated by the vagal nerve and occurs as a result of interplay among CCK, dopamine, and glutamate receptors in the brainstem satiety relay system in the nucleus of the solitary tract. Little is known about how these brainstem mechanisms interact with the neural networks in the forebrain, which are activated by food deprivation before an animal starts ingesting food.

The arcuate nucleus of the hypothalamus lies outside of the blood–brain barrier and senses the leptin signal from adipose tissue. High leptin levels down-regulate the synthesis and release of Neuropeptide Y (NPY) in the arcuate nucleus. Numerous studies over the past 15 years have demonstrated that an infusion of NPY into the brain of experimental animals stimulates food intake, carbohydrate intake in particular. Closer inspection of the behavioral effect of NPY shows, however, that NPY also causes an increase in physical activity and an increase in the intake of water. The effect on water intake is at least as marked as the effect on food intake. Thus, contrary to the common notion that NPY is a potent stimulator of food intake, i.e., an orexigen, its behavioral effect is far from specific.

The hypothalamic circuit activated by hypoleptinemia following fat depletion, and, conversely, the circuits activated by hyperleptinemia following fat repletion have been outlined in impressive detail in animal studies. The theoretical framework of these studies remains much the same as in the early days of regulatory physiology, i.e., that body weight is controlled by precise negative feedback loops. The increase in the incidence of eating disorders and particularly the marked increase in obesity suggest, however, that negative feedback of food intake in humans is easily disrupted. In addition, the rather small effect of most weight-reducing pharmacological treatments and the almost immediate relapse that occurs after the termination of such treatments suggest that food intake in humans has redundant controls.

Animal studies, therefore, have thus far had limited bearing on the understanding on human eating disorders. For example, there is no unequivocal evidence that CCK-8 has any relation to the enhanced feeling of satiety that anorexic patients experience during meals. And the low level of leptin and the associated increase in brain levels of NPY that occur in anorexia, as in starving animals, are not followed by an enhanced intake of food. Interestingly, however, NPY has a much smaller effect on food intake in food-deprived animals than in nondeprived animals. In view of the effects of leptin and NPY on behaviors other than food intake, e.g., water intake and physical activity, the absence of a stimulatory effect on food intake in anorexics is not surprising. In an anorexic state, NPY may cause enhancement of physical activity to facilitate the search for food rather than stimulating the actual intake of food. Food deprivation has long been known to stimulate physical activity, not only in mammals, but in other animal species as well.

B. The Hypothalamus–Pituitary–Adrenal Axis and Dopamine and Noradrenalin

Food deprivation activates the secretion of corticotropin-releasing hormone (CRH) by the hypothalamus and so acts as a stimulus for the activation of the hypothalamus–pituitary–adrenal (HPA) axis. As a consequence, patients with eating disorders have elevated plasma levels of cortisol. CRH is a well-known appetite suppressant per se, but the activity of the HPA axis can also influence food intake indirectly. Corticosterone, the rat adrenocortical equivalent to cortisol, stimulates the release of dopamine in the ventral striatum. This is the brain's reward pathway, which consequently is sensitized by food deprivation and also by enhanced physical activity. Adrencortical activation of the mesolimbic dopaminergic pathway provides an underlying substrate for the experience of reward, enjoyment, and pleasure that is typical in the beginning of an episode of self-imposed dieting or enhanced physical activity in humans. If dieting runs out of control, as occurs in AN, patients often say they must diet or run excessively, not for an experience of reward or enjoyment, but because they must get away from their feelings of anxiety and depression. Apparently, the neural substrate of reward is activated during the course of anorexia in a way not unlike the way the system is activated during the development of biologically based addictions.

Forebrain dopamine has long been thought of as an inhibitor of food intake, but recent work suggests that its main role is to initiate the behavioral sequences necessary to gain access to various rewards, while not affecting the consumption of those rewards. In addition, dopamine interacts with other transmitter systems, e.g., opioid peptides and benzodiazepines, to assign hedonic qualities to the ingestion of food.

Food restriction also activates the noradrenergic cell group in the locus coeruleus in the brainstem, the neural substrate for selective attention. CRH may mediate this effect as well.

C. Serotonin

Serotonin is one of the best-known anorexic neurotransmitters. Thus, it was demonstrated 40 years ago that peripheral administration of serotonin inhibits food intake by activating a stretch receptor in the muscular wall of the stomach, thereby stimulating a vagally mediated satiety message to the brain. Subsequently, it has been found that intracerebral administration of serotonin also inhibits food intake. These observations provide the basis for the use of serotonergic agonists in the treatment of obesity.

Given this background, it is surprising that selective serotonin reuptake inhibitors (SSRIs), which facilitate the activity at serotonergic synapses, have been used to treat AN. It is somewhat less surprising that SSRIs are used in bulimia but the risk that the patients might develop anorexia is obvious. Other well-known effects of serotonin, e.g., inhibition of pubertal development, gonadotropin secretion, sexual behavior, and induction of hypothermia, are also incompatible with the use of SSRIs in anorexia.

VI. TREATMENT

A. Evaluation of Treatment

There are few if any reports of effective treatments for patients with eating disorders. Over the past 20 years, it has been reported many times that fewer than half the anorexic patients who have been treated recover and that recovery occurs over a prolonged period of time and only after repeated episodes of treatment. There is some evidence that treatment of patients who are younger than 17 years, who have had the disorder for less than a year, and who have not been treated extensively before may recover after treatment with a family-based method. However, similar modestly ill patients have also been shown to recover spontaneously with time.

There is no evidence that older patients with AN benefit from currently available treatments. In fact, the possibility that they may has not been properly examined. Thus, treatment interventions have not been evaluated against a no-treatment or minimal intervention control group in randomized controlled trials (RCTs). It is commonly argued that such comparisons are difficult for ethical reasons, but unless such studies are performed we will never know the effect of such a treatment. Of the few RCTs performed to date, none have shown a major effect of treatment. Furthermore, it has been reported recently that treatment by specialist units is not a predictor of outcome at follow-up 5 years later. This latter situation should encourage investigators to examine the effect of current methods of treatment using RCT methodology.

It is generally thought that the situation for patients with BN is better because cognitive behavioral therapy is effective in this group of patients. This type of therapy aims at changing the way the patient thinks about his or her condition. However, only half of the patients respond to such treatment and the evidence suggests that other types of individualized treatment are equally effective.

Pharmacological treatment has no beneficial effect in AN but treatment with anti-depressants offers some help in BN. Although SSRIs are thought to be useful in BN, their effect is not as great as that of cognitive behavioral therapy and is therefore rather minor.

Follow-up studies have shown that relapse is a significant problem in weight-restored anorexics. Thus, 30–50% of the patients have been reported to relapse within a year after their weight has been restored. There are no reliable figures for relapse of bulimic patients. The existing studies are difficult to interpret because many of the patients were given additional treatment during the follow-up period.

In most studies, the patients are only in partial remission at clinical discharge. Thus, many of them display eating-disorder symptoms or psychopathological symptoms; i.e., they may suffer from an EDNOS. The problem, therefore, remains as to whether these residual symptoms are signs of trait-dependent patient characteristics or simply the effect of a less than optimal method of treatment. This issue is of considerable importance because most of the currently available diagnostic tools do not allow a clear distinction to be made between state- and trait-dependent psychopathological symptoms.

B. Treatment with Serotonin Agonists

The recent discussion on the possible role of serotonergic mechanisms in BN offers an example of the problem of distinguishing trait from state. Thus, it has been suggested that elevated levels of 5-hydroxyindole acetic acid in the spinal fluid and reduced 5-HT_{2A} receptor binding in the frontal cortex of bulimic patients in remission are signs of trait-dependent patient characteristics. Although these patients did not fulfill the DSM-IV criteria of BN, none of them were free of eating-disorder symptoms or other psychopathological symptoms. Therefore, most of these patients were merely in partial remission and suffered from an EDNOS. Experimental reduction of 5-HT levels by giving patients a diet free of the 5-HT precursor tryptophan has offered better support for the possible role of 5-HT in bulimia. Thus, patients in complete remission with a history of bulimia have been reported to develop symptoms such as feeling fat and fear of losing control over eating immediately after intake of such a diet.

Surprisingly, because of the difference in eating behavior, it has been suggested that the 5-HT_{2A} receptor may also be altered in patients with a history of AN or at risk of developing AN. The results thus far have been inconsistent. The evidence for the use of serotonergic agonists in the treatment of eating disorders is, therefore, weak. Not surprisingly, such drugs have minor effects.

In addition, the hypothesis has been advanced that treatment with SSRIs may prevent relapse in weight-restored anorexics. Some relapse prevention has been reported, but the main result in these studies has been a rapid relapse in both SSRI- and placebo-treated groups or a marked dropout rate. Thus, although it is well known that 5-HT has a role in the control of eating behavior in experimental animals, its possible involvement in eating disorders in humans remains unclear.

VII. CAUSES

It is commonly stated that eating disorders have multifactorial causes or unknown etiologies. This may reflect the fact that there are only partially effective methods of treatment available and that these methods may target the wrong symptoms.

Obviously, a reduced intake of food is necessary for a loss of body weight and therefore for the development of AN. Also, as mentioned above, reduced availability of food causes an increase in physical activity and it is known that those who are physically active, i.e., elite athletes and ballet dancers, are at risk of developing AN or an EDNOS. Thus, we know that dieting and physical activity are risk factors for the induction of self-starvation, a subsequent loss of the control of food intake, and, eventually, therefore, AN.

It has been demonstrated that animals will run in running wheels if offered the opportunity and that they will run progressively more if the supply of food is restricted. As food availability is further restricted in this situation, the animals will eventually lose control over body weight. This situation, activity-based anorexia (ABA), is virtually identical to the development of AN in humans with the exception that if the animals are allowed *ad libitum* access to food, they stop running, eat, gain weight, and return to a normal physiological state. By contrast, AN develops despite the continuous presence of food. Yet, animals that have developed ABA are conspicuously similar to patients with AN. For example, hypothermia is obvious in both conditions and it has been recently reported that when animals in a state of ABA are treated with external heat they run less, eat more, and gain weight. Similarly, it was noticed in the first description of AN that heat treatments enhance recovery. Treatment with heat, therefore, is likely to become part of a future effective treatment perhaps not only of AN but of other eating disorders as well.

In the first descriptions of AN it was noted that patients were restless. This physical hyperactivity was considered paradoxical because it was argued that the patients would be better off if they were less active and conserved energy. Also, the physical hyperactivity appeared "agreeable" to the patient, i.e., rewarding. In later clinical descriptions, it was noted that losing weight is "enjoyable, pleasurable, and rewarding" to a patient. These clinical observations are compatible with the research on the neural pathways of reward discussed briefly above. Thus, reduced food intake and(or) enhanced physical activity activate the mesolimbic dopaminergic reward pathway in the brain. Interestingly, both dieting and physical activity also activate the locus coeruleus noradrenergic pathway of selective attention. During conditions of reduced food intake and enhanced physical activity, the substrates for reward and attention are activated, thus providing an optimal situation for learning. Therefore, it can be hypothesized that AN develops because it is rewarding to reduce one's food intake and that it is maintained by conditioning to the stimuli that provided the reward.

This hypothesis offers an explanation for the development and maintenance of AN that is compatible with established neurophysiological principles. Because of the symptomatic similarities between anorexics and bulimics and because most bulimics have a history of anorexia, it is possible that AN and BN develop in similar ways. However, it must be added that the marked sex difference in eating disorders await an explanation. Based on the present hypothesis, an attempt to set up an effective treatment for eating disorders should include a method for teaching patients how to eat and how to reduce their physical activity. Although there are no pharmacological methods for reduction of physical activity, it is possible that a supply of external heat might be used.

It seem likely that most of the current methods of treating patients with eating disorders fail because most of them do not rely on sound physiologic hypotheses or are incompatible with basic neurophysiology, e.g., the frequent use of SSRIs. The hypothesis outlined above is offered as a starting point but is likely to be replaced by a better hypothesis as soon as our understanding of the neurobiology of ingestive behavior, physical activity, and temperature regulation has increased beyond its present state.

VIII. SUMMARY

A considerable amount of information has accumulated about the hypothalamic control of food intake and body weight through negative feedback signals from gastrointestinal and adipose tissues. Thus far, this information has had little influence on the management of patients with eating disorders. These patients still have a poor prognosis and there are few if any effective methods of treatment. Most pharmacological treatments have failed. Also, there are only a few investigations of the effect of treatment interventions that meet the criteria of random assignment and proper control. The effect of most of the methods that are currently used is, therefore, unknown. This situation is most likely caused by the absence of realistic explanations of why eating disorders develop and how they are maintained. Future attempts should take into consideration the possibility that eating disorders might be disorders of physical activity as much as they are disorders of eating behavior or mental disorders. Most endocrine and physical changes observed in patients with eating disorders are consequences rather than causes of self-imposed starvation that is maintained by conditioning to cues in the patient's environment.

Glossary

activity-based anorexia (ABA) Animals run excessively and lose control over body weight if very little food is provided and they enter a state of ABA, which is conspicuously similar to self-starvation in humans.

anorexia nervosa An eating disorder with severe, self-imposed starvation and commonly associated with a high level of physical activity and hypothermia.

body mass index An indicator used to define nutritional status and derived from the formula: weight divided by the square of height (kg/m^2). The acceptable range is 19–24 in women.

bulimia nervosa An eating disorder with episodes of excessive food intake, followed by compensatory methods to maintain a normal body weight.

eating disorder not otherwise specified An eating disorder that does not fulfill the diagnostic criteria of anorexia nervosa or bulimia nervosa.

5-hydroxytryptamine A neurotransmitter long known to inhibit food intake; it is the focus of many treatment interventions aimed at normalizing disordered eating behavior. Also known as 5-HT or serotonin.

neuropeptide Y A neuropeptide thought to increase food intake.

orexigen A compound that stimulates or increases food intake.

randomized controlled trial The standard method of random assignment to a treatment and a control condition necessary for the proper evaluation of medical interventions.

selective serotonin reuptake inhibitors Widely used antidepressants that enhance serotonin availability at synaptic sites thought to be altered in patients with eating disorders.

See Also the Following Articles

Appetite Regulation, Neuronal Control • Cholecystokinin (CCK) • Gastrointestinal Hormone-Releasing Peptides • Ghrelin • Leptin • Neuropeptide Y (NPY)

Further Reading

Agras, W. S., Walsh, T., Fairburn, C. G., Wilson, G. T., and Kraemer, H. C. (2000). A multicenter comparison of cognitive-behavioral therapy and interpersonal psychotherapy for bulimia nervosa. *Arch. Gen. Psychiatry* **57**, 459–466.

American Psychiatric Association (1995). "Diagnostic and Statistical Manual of Mental Disorders" 4th ed. American Psychiatric Association, Washington, DC.

Ben-Tovim, D. I., Walker, K., Gilchrist, P., Freeman, R., Kalucy, R., and Esterman, A. (2001). Outcome in patients with eating disorders: A 5-year study. *Lancet* **357**, 1254–1257.

Bergh, C., Eklund, S., Eriksson, M., Lindberg, G., and Södersten, P. (1996). A new treatment of anorexia nervosa. *Lancet* **348**, 611–612.

Bergh, C., and Södersten, P. (1996). Anorexia nervosa, self-starvation and the reward of stress. *Nat. Med.* **2**, 21–22.