# A CRH2-CRH1 Theory of Anorexia and Bulimia

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**Abstract.** I present a biological theory of anorexia nervosa (AN) and bulimia nervosa (BN). AN and BN are caused by stress-induced corticotropin-releasing hormone (CRH) that chronically activates the CRH2 and CRH1 receptors, respectively. The physiological role of CRH2 is to trigger responses to excess states, recruiting serotonin to reduce food intake and gut activity and promote white adipose tissue growth. The role of CRH1 is to respond to deficiency states, promoting food intake. I show that chronic activation of the two receptors can explain the symptoms and properties of the two disorders. In particular, refusing to eat, binge eating, purging behavior (e.g., vomiting, usage of laxatives), and claiming to be too fat are rational responses to concrete biological signals. The theory is supported by strong evidence and points to several novel treatment directions.

**Keywords.** Anorexia nervosa; bulimia nervosa; CRH1; CRH2; serotonin;

## 1 Introduction

Anorexia nervosa (AN) and bulimia nervosa (BN) are the two major eating disorders [1, 2]. The diagnostic criteria for AN include reduced food intake that leads to significant low body weight, "intense fear of gaining weight" or behaviors that oppose weight gain, mainly purging (intentional vomiting, usage of laxatives and diuretics) and excessive exercise, and "disturbed perception of body weight" (e.g., lack of insight on current low weight). The criteria for BN include recurrent binge eating episodes (eating larger amounts than normal in a short time, with a sense of lack of control over eating), and purging behavior, exercise, or fasting. Many AN patients also show binge eating.

Like almost all psychiatric disorders, the etiology of AN and BN is currently not understood [1, 2, 3, 4]. Patient behavior is known to be influenced by biological factors rather than being a personal choice [3], but there is no theory explaining what these factors are.

Here I present the first theory that explains AN and BN (T*AB). The theory is complete is the sense that it explains their etiology, symptoms, and pathophysiology. T*AB is supported by strong empirical biological evidence, and implies several novel treatment directions.

**Theory overview.** AN and BN result from chronic stress-induced release of corticotropin-releasing hormone (CRH). This can be due to stress experienced by the patient, or to (epi)genetic parental transmission of the effects of past stress. Moderate levels of CRH activate the CRH1 receptor, whole main role is to respond to energy-deficient states by increasing blood glucose and food intake and stimulating the sympathetic nervous system (SNS). High CRH levels activate the CRH2 receptor, whose role is to support energy excess states by reducing food intake, storing glucose in tissue, and restraining the SNS. CRH2 recruits serotonin (SER) to achieve its function, mainly for suppressing gut motility and food intake.

The effects of CRH on food intake trivially explain the food intake aspects of AN and BN. Regarding purging behavior, it is done in order to reduce the nausea induced by excessive gut SER and CRH2. Excessive exercise in AN is done in order to recruit epinephrine (EPI) and norepinephrine (NEP), both suppressed by CRH2. Patients claim to be too fat because they feel that something is wrong with their adipose tissue, which stems from excessive SER and CRH activity that mimics inflammatory responses. T*AB is supported by strong evidence regarding CRH, SER, and the autonomic nervous system in animal models and patients, and by established patient data.

# 2 Theory

## 2.1 CRH, CRH1, CRH2, serotonin

**General.** CRH is best known for its role in the hypothalamic-pituitary-adrenal (HPA) axis, where stress induces CRH release from the hypothalamus paraventricular nucleus (PVH), CRH acts on CRH1 receptors in the pituitary to stimulate ACTH release, which induces glucocorticoid (GC, cortisol in humans) release from the adrenals. CRH is also synthesized in other body tissues, including the skin, gut, the reproductive and immune systems [5], brain [6], and adipose tissue [7].

CRH acts via two G protein-coupled receptors, CRH1 and CRH2, which both bind Gs (to stimulate cAMP, PKA) and also Gi/o and Gq [8]. The affinity of CRH to CRH1 is greater. Following ligand binding, the receptors show sustained signaling from endosomes, allowing chronic signaling beyond the original release event [8]. CRH2 is also activated by urocortins, a family of ligands that do not have a major role in AN and BN.

**CRH1.** The role of CRH1 is well known. Besides its stimulation of GC release, it activates the SNS [9], to increase blood glucose, promote food intake, and induce other sympathetic responses (e.g., increased heart rate, lipolysis, thermogenesis). Note that it is not accurate to view CRH1 as triggering the response to all types of stress, but as responding to *deficiency*

states, including low glucose, low temperature (cold), and low oxygen (hypoxia) [10]. Acute social stress increases the metabolic demands from the body, creating a deficiency stress state.

**CRH2.** CRH2 is known to oppose many CRH1-induced effects, including appetite, anxiety and depression [9]. In particular, its food intake suppression function is overwhelmingly supported [11]. It also suppresses adrenal EPI release done as part of the counter-regulatory responses to insulin-induced hypoglycemia [12], opposes thermogenesis [13], and promotes glucose uptake by tissue, including skeletal muscle [14] (at least partly insulin-independently), heart [15], brain [16] and adipose tissue [17]. This effect occurs mainly in high glucose levels, and can utilize insulin via direct action on beta cells [18]. In the gut, CRH2 slows gastric transit [19].

**Serotonin.** SER is present in most body tissues, including the gut, brain, heart, lung, skeletal muscle, adipose tissue, and the reproduction system [20]. The SER system is complex, and for our purposes it suffices to highlight the following facts. First, CRH2 recruits SER, promoting its synthesis [21] and release from dorsal raphe neurons [22] and gut enterochromaffin cells [23]. SER reciprocally activates PVH CRH neurons, via SER2c [24]. Second, SER is well-known to suppress food intake, an effect mediated by SER2c [25]. Eating carbohydrates enhances the synthesis and release of hypothalamus SER, which suppresses carbohydrate intake [26]. Third, the food intake suppression function of CRH2 is done, at least in part, via SER2c [27].

Fourth, SER is a major gut agent. The gut contains most of the body's SER, and SER is present in both mucosal enterochromaffin cells and in the enteric nervous system [28]. The former support reflexes that increase local motility to enhance absorption after feeding [29], while the latter slow gastric emptying and suppress intestinal motility [28] in response to glucose [30]. Gut glucose induces gut SER release via SER3 on gut vagal sensory neurons [31].

Finally, SER promotes insulin-independent glucose uptake by tissue [32], including adipose tissue [33], skeletal muscle [34] and liver, where it promotes glycogen synthesis [35]. plasma SER and blood glucose levels show a positive correlation [36], and raphe obscurus and raphe pallidus SER activity diminish following insulin-induced hypoglycemia [37]. Most relevant to AN, SER promotes lipogenesis in white adipose tissue (WAT) and opposes its browning and thermogenesis [38, 39, 40].

SER has 14 different receptors, and can also produce results in the opposite direction to the above, depending on conditions [41]. What is important for our purposes here is that it is clearly recruited by and cooperates with CRH2 in fulfilling its function. A full theory of SER function will be presented elsewhere.

**Summary.** T*AB posits that *the role of CRH2 is to trigger responses to excess stress*, including high glucose and heat, but also prolonged social stress. As part of this role, it suppresses the responses to deficiency stress, including EPI release, thermogenesis, and food intake. This account of the role of CRH2 is a novel contribution of the present paper. To achieve its role, CRH2 recruits SER, which suppresses food intake, slows gut motility, responds to high glucose, and promotes its gut absorption and storage in tissue. In particular, SER promotes the growth of white adipose tissue but opposes brown adipose tissue.

## 2.2 Anorexia nervosa (AN)

According to T*AB, *AN is caused by excessive CRH release that chronically activates CRH2 in the brain and other tissues*. Since the affinity of CRH1 to CRH is higher than that of CRH2, there would be tissues in which CRH1 is chronically activated as well. The symptoms induced by these fundamental biological effects are most likely enhanced by modern cultural and media influences. This section explains how stress, including social stress, can cause this state, and shows that this simple premise can explain the defining characteristics of the disorder. Other data are presented in the evidence section.

**AN core cause: stress.** As described above, CRH is recruited in states of metabolic deficiency or excess. This includes social stress (e.g., maternal separation, conspecific aggression, social defeat, sexual trauma), which produces a deficiency state because the organism initially needs more energy to address the situation, and is well-known to induce CRH release [42]. If the problem is not quickly resolved, CRH release continues and can chronically activate the lower affinity receptor CRH2.

Stress that occurs during sensitive developmental periods, such as early life and adolescence, can yield persistent changes in protein expression via epigenetic marks [43]. Moreover, epigenetic changes can be multigenerational, passed from parents to offspring [44]. It is well-supported that early life stress can persistently increase CRH, e.g., CSF CRH in non-human primates [45], and mRNA in rodents [46].

Thus, prolonged social stress (and other types of stress), especially during early life or adolescence, can create the optimal conditions for AN. Indeed, social pressure and stress are known to be precipitating factors for AN, and social difficulties are very common [4]. Traumatic experiences are common in moderate-severe AN patients, with 50% being at the cutoff threshold for PTSD (without being diagnosed) [47]. In one report, almost half of AN patients have suffered childhood sexual abuse [48].

**Food intake.** Suppression of food intake is one of the major functions of CRH2, cooperating with SER2c. The AN patient's brain receives a strong signal of nutrient excess, even if the real state is that of deficiency. CRH2 opposes the main agents that promote food intake, GCs and EPI, and CRH opposes neuropeptide Y, which is elevated in AN but whose effect is not that strong [2]. Adiponectin reflects the status of adipose tissue and is indeed elevated in underweight AN patients, but it is not a strong appetite stimulator [2]. Thus, there is no strong physiological biological signal that can offset the erroneous message conveyed by excessive CRH2 in AN.

**Purging behavior.** Chronic CRH2 induces chronically high SER in AN. In the gut, SER is known to induce nausea and the vomiting reflex, mainly via SER3 but also via other receptors [49]. This is consistent with SER's role in suppressing food intake and gut motility. CRH itself has also been hypothesized to be responsible for the cyclic vomiting syndrome [50]. Thus, excessive CRH-induced gut SER explains the urge to vomit in AN.

CRH is produced by colon enterochromaffin cells [51], and triggers inflammation via mast

cell activation [52]. Mast cells can uptake, store and secrete SER and CRH [53]. CRH2 specifically increases gut inflammation following stressors [54]. SER also promotes gut inflammation [28]. Since the state of the gut (as that of any other tissue) is continuously reported to the brain via sensory neurons, AN patients experience a constant feeling that there is something wrong in the gut. Since gut carbohydrates induce SER release, this uncomfortable feeling is relieved when the gut is empty. This explains general purging behaviors in AN, and provides another explanation for food avoidance.

**Body image.** White adipose tissue has a population of mast cells [55], whose activation promotes chronic low inflammation and macrophage accumulation [56]. Since CRH greatly potentiates mast cell activation [57], and mast cells secrete SER and CRH [53], AN adipose tissue involves a continuous inflammation-like state, as in the gut. This state is reported to the brain via interoception pathways [58], a feeling that patients verbalize as "I am too fat" (they could say "something is wrong with my fat stores", but this sounds strange, as opposed to the former, which is generally accepted by society). Even though patients are not too fat, some processes that make people fat, namely SER-induced glucose uptake and lipogenesis, are indeed chronically active in their WAT.

**Binge-eating type.** AN patients are defined to be either of the restricting type or the binge-eating/purging type, depending on whether they have engaged in recurrent binge eating or purging episodes during the last 3 months [1].

According to T*AB, the basic active AN state involves CRH levels that are high enough to activate the lower affinity receptor CRH2. If CRH levels diminish for any reason but do not get to full recovery level, or if CRH2 gets desensitized, CRH would strongly activate the CRH1 receptor, which promotes food intake. This, along with other signals stemming from the person's state of deficiency, explains binge eating episodes. Indeed, more than 40% of the restrictive type show binging and purging at some point [59].

### 2.3 Bulimia nervosa

According to T*AB, BN is caused by CRH release that chronically activates the CRH1 receptor. CRH1 strongly promotes food intake, explaining binge-eating episodes. Since the effects of CRH on mast cell inflammation and transit time in the gut can be promoted by both CRH1 and CRH2 [60], chronic CRH1 explains purging behavior in BN in the same manner as in AN.

## Evidence

This section presents strong evidence supporting T*AB.

**Sex differences.** AN and BN show female dominance (10:1 and 3:1 respectively). This has two reasons. First, estrogen excites PVH CRH neurons [61], and increases CRH synthesis [62]. One reason for this is that CRH is needed for birth, and increases 100-1000x in maternal serum

from the 2nd pregnancy trimester onwards [63]. Second, testosterone decreases PVH CRH expression via androgen response element [64], reducing CRH secretion [65].

The ratio in AN is higher than that in BN because estrogen mainly acts on CRH2 [66, 67]. One reason for this is that the temperature of women is affected by the menstrual cycle, and estrogen serves to lower it [68].

**Age of onset.** AN usually erupts during early adolescence. This occurs because this is the period in which estrogen is dramatically increased, enhancing CRH secretion and CRH2 signaling as explained above. This biological reason is enhanced by the increased vulnerability to social stress during adolescence.

**Heritability.** AN and BN have a substantial heritable component [3]. As explained above, stress can yield transgenerational changes in protein expression via epigenetics [43, 44].

**Menstruation.** Female amenorrhoea used to be a defining characteristic of AN. Currently, it is thought to be secondary to malnutrition. However, it can also be directly explained by the fact that CRH2 suppresses gonadotropin hormone-releasing hormone, and thus the hypothalamus-pituitary-gonadal (HPG) axis [67]. This account also explains why a substantial part of AN patients show prodromal menstrual issues [69].

**Exercise.** AN patients very commonly engage in excessive exercise, which is usually attributed to a desire to lose weight. In T*AB, excessive exercise is a form of self-treatment. Intense exercise stimulates the release of EPI and NEP [70], which are suppressed by CRH2 and are important for real-world stress resilience [71]. In addition, exercise relieves social stress by reducing SER release [72]. Again, this AN behavior is a rational response to the biological problem, not a psychiatric obsession done in order to reduce weight.

**HPA axis: CRH, GC.** There is considerable direct evidence for increased CRH secretion in AN. CSF CRH was reported to be 1.6x higher in patients, with a blunted ACTH and GC response to a CRH challenge [73]. CSF CRH was elevated in underweight AN patients with hyper cortisol, and normalized following recovery [74]. The HPA axis is hyperactive in AN, and this is due to CRH [75]. Patients show basally higher cortisol levels, with a blunted ACTH response to CRH [76] and a blunted GC response to social stress [77].

AN and BN are highly comorbid with depression and anxiety, both of which known to be associated with high CRH [78]. In particular, the central amygdala contains a large population of CRH-releasing neurons whose activity is associated with threat-induced stress and anxiety [79].

**CRH2 genetics.** An association between AN and a single nucleotide variant in the CRH2 gene has been reported [80]. Recall, however, that according to T*AB, most of the genomic effects would be via epigenetics.

**Comorbidities.** There is high comorbidity of AN with psychiatric conditions such as anxiety disorders (especially obsessive-compulsive disorder) [81] and autism [82], both known to be associated with stress. This can explain obsessions (including perfectionism) and social impair-

ment in AN.

**Serotonin.** Higher plasma SER [83], higher CSF 5-HIAA (SER metabolite) [84], decreased SER2a PET binding [85, 86], increased SER1a (suppressive autoreceptor) binding in many cortical areas [87], and decreased SER transporter (SERT) PET binding in parietal cortex [88] all indicate elevated SER activity in AN. Importantly, tryptophan depletion, which decreases the amount of synthesized SER, has been reported to reduce anxiety in patients [89], giving rise to the idea that starvation is done in order to reduce SER activity [90].

Some genetic alterations in AN were initially reported regarding SER2a and SERT, but they have not been replicated in more recent GWAS [91].

Drugs that antagonize some SER receptors are commonly given as treatment in AN, see Treatment below.

**NEP, EPI levels.** T*AB predicts reduced levels of EPI and NEP, due to direct inhibition by CRH2. Indeed, low plasma NEP has been reported [83, 92], even in remitted weight-recovered patients [93]. Lower levels of the NEP metabolite MHPG were also reported, more significantly in AN than BN [94]. One of these papers reported somewhat higher EPI levels [83], which is most likely due to the fact that their cohort had more binge-eating than restrictive AN patients. Desensitization of the NEP system (via orthostatic tests) has been reported in BN patients with normal weight [95], and blunted cardiovascular EPI responses to mental stress has been reported in women with BN [96].

**Heart rate.** Low heart rate is probably the most consistent physical finding in underweight patients [97]. This is readily explained via CRH2 suppression of EPI and NEP.

**Heat responses.** Half of AN patients were reported to engage in intentional exposure to extreme cold at least monthly [98]. The authors attribute this behavior to a desire to control shape and/or weight. According to T*AB, this behavior is, like exercise, a form of self-treatment done in order to increase EPI/NEP release. Patient hands, face and feet temperature is lower than in controls [99], and they have lower cold-activated brown adipose tissue [100], indicating an impaired sympathetic thermogenesis response.

**Glucose, insulin.** AN patients show chronic prolonged mild hypoglycemia (with normal fasting glucose) [101], and higher insulin sensitivity [102]. Hypoglycemia in AN can be explained via adipose tissue depletion, but also by reduced function of the SNS. Indeed, patients show a markedly decreased plasma EPI response to insulin-induced hypoglycemia [103].

**Growth hormone (GRH).** AN patients show increased levels of GRH, coupled with decreased levels of its target, IGF1 [2]. These data are consistent with desensitization of the GRH receptors. GRH release is stimulated by mild hypoglycemia and by ghrelin, whose release is stimulated by an empty stomach. Both of these occur in AN and explain the GRH data.

**Gut.** AN patients show decreased gastrointestinal tract motility [1]. This is not always due to starvation, because 20% of AN patients turned to get treatment for prodromal gut symptoms [69].

**Skin.** CRH activates mast cells, which are strongly present in human skin [55]. Hence, T*AB predicts that AN patients would show skin sensitivity. Indeed, patients suffer from itch, and engage in scratching and self-injury [104].

# Treatment

This section discusses possible pharmacological treatments for AN and BN. Psychological treatments can certainly help, and are not discussed here.

**CRH.** The best treatment for both AN and BN would be to normalize brain and peripheral CRH levels. However, there are currently no approved drugs that directly induce this effect. Note that antagonizing CRH2 (for AN) or CRH1 (for BN) may switch patients to the other disorder.

CRH can be used in tests for the disorder. The combined DEX-CRH test, and the ACTH response to CRH, can both indicate chronically high CRH release.

**Somatostatin (SST).** SST directly opposes CRH receptor-mediated stress responses and CRH2 suppression of food intake [105], and stimulates food intake in animal models. It also suppresses growth hormone release. SST inhibits gut secretory responses induced by SER [106], and opposes insulin secretion [107], which may be good in AN because it would allow blood glucose to increase.

Several SST analogs (including octreotide, lanreotide, and pasireotide) are currently approved for treating various conditions, including acromegaly (excessive GRH), pancreatitis, diabetic retinopathy, diabetic nephropathy, pain, inflammation, and cancer [107]. Octreotide's brain penetration is not high, but there are methods to enhance it [108]. SST drugs should still suppresses CRH and SER in the periphery, including in the gut, pituitary, adrenal gland, adipose tissue, and pancreas, and they may act on some hypothalamic nuclei.

SST drugs reduce adrenal EPI release, so in AN there may be a risk of reducing heart rate even more than the usual slow rate. However, SST drugs are reported to stimulate NEP release [109], which should compensate for EPI. In any case, heart rate is easy to monitor and handle (e.g., via small NEP or EPI doses augmenting SST).

In light of these data, treatment of acute AN using SST needs to be seriously examined.

**Tryptophan hydroxylase inhibitors.** Another promising direction, alone or in combination with SST, is to use tryptophan hydroxylase (TPH) inhibitors [110]. Telotristat etiprate suppresses peripheral SER synthesis by inhibiting TPH1, the rate limiting enzyme for peripheral SER synthesis. It is approved for humans in combination with SST analogs for treating cancer-related diarrhea. This drug might be very helpful in AN, because it is highly possible that the main factor in the fear of eating exhibited by patients is SER-induced negative events starting at the gut, more than central effects.

It is also possible that ondansetron (Zofran), a SER3 antagonist routinely used to relieve nausea and vomiting [49], would help in AN.

**Atypical antipsychotics.** Atypical antipsychotics are SER2a antagonists, and can be expected

to alleviate some of the symptoms of AN. Indeed, a UK survey found that olanzapine is the most common drug treatment for AN [111]. However, because these drugs do not act on the important targets, their effects are quite limited [112].

**SSRIs.** Selective SER reuptake inhibitors (SSRIs) increase brain SER levels. Some SSRIs may be helpful in BN, because SER opposes the CRH1 mode. Because this SSRI effect can include decreased CRH production, SSRIs might also help in AN under some conditions. SER is a major promoter of the disorder, but its main effect is in the gut and adipose tissue, which are less affected by SSRIs. Due to the causative involvement of SER in AN, care should be taken in the usage of SSRIs for treatment.

# 3 Discussion

This paper presented the first complete biological theory of AN and BN. T*AB is complete in the sense that it explains the etiology, symptoms, and pathology of these disorders. A complete theory does not have to be correct, but being complete is the minimal requirement from a theory.

**AN and CRH.** It is widely acknowledged that AN is currently not understood, and no biological theory has been formulated to fully explain it. T*AB focuses on stress (mainly social stress) and CRH. Given the well-known link of AN and BN with both of these, and given that the food intake suppression effects of CRH2 have been well-known for more than 20 years [9], it is surprising that a CRH2-based AN theory has not been proposed yet. CRH has been discussed in AN, but this has virtually always been in the context of HPA activity.

A possible explanation for this might be the general view of CRH2 as being anxiolytic, as opposed to the anxiogenic CRH1. Thus, it was perhaps not natural to link CRH2 with AN, which clearly involves anxiety. The new theory of CRH2 presented in this paper resolves this apparent paradox, by noting that deficiency stress is different from excess stress, and by assigning CRH2 to the latter. CRH1 is assigned to the former, and this provides an immediate parallel theory for BN.

**The evidence.** This paper has brought evidence supporting every aspect of T*AB (CRH, SER, EPI, NEP, gut, skin, epidemiology, various properties) except direct evidence for SER- and/or CRH-induced adipose tissue inflammation. The evidence for AN is larger than that for BN, reflecting the relative interest of researchers in the two disorders.

**Other eating disorders.** AN and BN are the major eating disorders, but there are additional ones, including binge-eating disorder (BED), pica, rumination, and avoidant/restrictive food intake disorder. These disorders were not dealt with here in order to keep the presentation simple. BED is defined via binge-eating episodes without purging behaviors (as in BN). BED can be explained via chronic activation of CRH1 in areas that control feeding (mainly the brain), without strong activation in the gut. That this can happen is natural, in light of the fact that TPH2 controls SER synthesis in the enteric nervous system and brain, while TPH1 controls it in enterochromaffin cells [28]. These are two different systems.

**Serotonin.** Depression is treated today by SSRIs, which increase brain SER levels. As a result, SER is commonly associated with positive emotions. Thus, readers may question the negative role SER has in T*AB. The T*AB answer is that SSRIs improve depressive symptoms because they mimic a state of healthy excess in which the organism's needs (food, sex) have been met. Hence, they reduce deficiency-related stress responses, including CRH activation of CRH1. However, in AN, SER is associated with excess-related stress and CRH2, and is a negative factor. Indeed, SSRIs are known to induce a large variety of gut side effects when used for treating depression.

The negative role of SER in AN has been recognized a long time ago, yielding a proposal that starvation is done in order to decrease SER activity [90]. T*AB agrees with this insight and shows how it fits within a complete theory.

**Behavior is rational.** According to T*AB, the major drivers for eating and purging behaviors in AN and BN are molecular, not psychological. While sociocultural constructs such as "being thin is better than being fat" and social media-promoted body image probably promote pathogenesis by increasing social stress, only a minor fraction of people are ill with AN. The parsimonious account is that the fundamental cause is biological.

The T*AB account is that metabolic body signals erroneously convey the message that the person has eaten too much, even if the objective state is that of deficiency. The major causal factor in the "intense fear of eating" in AN is not fear of gaining weight. The cause is the stress-inducing activations in the brain, gut and adipose tissue that are exacerbated by eating and by a non-empty stomach. Reduced eating and purging behaviors are a form of self-treatment meant to reduce the highly uncomfortable feeling accompanying these activations. Patient behavior is a rational response to their biological situation. This view can by itself reduce patient stress, and can serve as a basis for novel pharmacological treatments.

# List of Abbreviations

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ACTH: adrenocorticotropic hormone.
AN: anorexia nervosa.
BED: binge-eating disorder.
BN: bulimia nervosa.
CRH: corticotropin-releasing hormone.
CRH1, CRH2: CRH receptors 1 and 2.
EPI: epinephrine.
GC: glucocorticoid.
GRH: growth hormone.
HPA: hypothalamic-pituitary-adrenal (axis).
NEP: norepinephrine.
PVH: hypothalamus paraventricular nucleus.

SER: serotonin.
SER1a, SER2a, SER2c, SER3: SER receptors 1a, 2a, 2c, 3.
SERT: SER transporter.
SNS: sympathetic nervous system.
SSRI: selective serotonin reuptake inhibitor.
SST: somatostatin.
T*AB: The theory of AN and BN presented here.
TPH: tryptophan hydroxylase.
WAT: white adipose tissue.

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