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Review

Night eating syndrome: an overview

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Abstract

Objectives The purpose of this review is to outline the nosographic characteristics of NES and the most reliable ethiopathogenetic theories in relation to the most recent evidence in the literature.

Key findings The night eating syndrome (NES) is a disorder occurring at the stated time, that does not meet the criteria for any specific eating disorder. NES is characterized by a reduced feeding during the day, evening hyperphagia accompanied by frequent nocturnal awakenings associated with conscious episodes of compulsive ingestion of food and abnormal circadian rhythms of food and other neuroendocrine factors. Frequently it is associated with obesity and depressed mood. We highlight the therapeutic possibilities of some drugs, especially selective serotonin re-uptake inhibitors (SSRIs), which reduce the hyperactivity of the serotonin transporter in NES and significantly improve the clinical picture of this disease.

Conclusions Night eating syndrome is of importance clinically because of its association with obesity. The recognition and effective treatment of NES may be an increasingly important way to treat a subset of the obese population. Treatment of the syndrome, however, is still in its infancy. One clinical trial has reported efficacy with the SSRI sertraline. Other treatments, such as the anticonvulsant topiramate, phototherapy, and other SSRIs, may also offer future promise. Particularly useful would be studies involving brain scans (magnetic resonance imaging or single-photon emission computed tomography) of patients with NES compared with the healthy population, to investigate more thoroughly the possible alterations involved in the pathogenesis of NES.

Introduction

The night eating syndrome (NES) is categorized in the diagnostic and statistic manual (DSM) IV[1] as an 'eating disorder not otherwise specified', although, along with binge eating disorder, NES is now considered a disorder worthy of being an entity separate from its clinical nosographic dealing with the specific diseases of food patterns, including its close links with obesity.

The purpose of this review is to outline the nosographic characteristics of NES and the most reliable ethiopathogenetic theories in relation to the most recent evidence in the literature.

Diagnosis

Basically, NES is not the same as binge eating disorder, although individuals with NES are often binge eaters. People with binge eating disorder eat large amounts of food at different times of day, while those with NES eat the majority of their food at night, but do not always binge. Individuals with NES feel like they have no control over their eating patterns and often feel shame and guilt over their condition. NES affects an estimated 1.5% of the population and is equally common in men and women, according to the National Institute of Mental Health.[2]

NES, also called the 'nocturnal eating syndrome', is a very specific disorder in which the affected individual wakes up several times during the night and is unable to fall back to sleep unless they eat something. Another characteristic of this disorder is that foods eaten during these waking episodes are often highly caloric in content and unhealthy. These eating episodes usually occur in secret and any evidence is often hidden from others.[2] The night eating behaviour seems totally beyond the affected individual's control. For these individuals, 35% or more of their calories are eaten after dinnertime.[3]

Eating disorder specialists use the term 'night eating syndrome', coined in 1955 by Stunkard *et al*.,[4] for patients exhibiting nighttime eating. The criteria for NES include the consumption of 50% or more of daily calories after the evening meal, eating after waking from sleep and morning anorexia.[4] Furthermore, Stunkard and colleagues in 1996 revisited this definition to specify over 50% of input energy occurs after 1900 h, accompanied by initial insomnia or sleep disturbance and permanent daytime anorexia.[5]

Also NES is associated with a greater incidence of anxiety, depression, low self-esteem and a strong sense of guilt for the loss of control associated with compulsive over ingestion of food during the night. For a diagnosis of NES it is necessary that the symptoms are present for at least three consecutive months.[5]

Subsequently other controlled studies added other NES criteria.[6] Such studies revealed a surprising coherence of the behavioural and neuroendocrine patterns of persons selected on the basis of morning anorexia, evening hyperphagia and insomnia. Persons selected on the basis of these minimal criteria were found to manifest not only sleep-onset insomnia but also, quite unexpectedly, nighttime awakenings during half of which food was ingested. This distinctive circadian pattern of behaviour was associated with a similarly distinctive pattern of mood disturbance. Contrary to the usual pattern found in depression, the mood of the night eaters fell during the evening.

Allison *et al*.[7] proposed new criteria for diagnosis of NES. This research established two core criteria: (1) the consumption of at least 25% of daily caloric intake after the evening meal and/or (2) evening awakenings with ingestions at least twice per week. Five descriptors have been added to the core criteria, three of which are required for the diagnosis of NES. Additionally, persons must be aware of their nocturnal ingestions, they must experience distress or impairment in functioning and they must have experienced the signs and symptoms for the past three months.[7] These criteria help standardize the definition of NES. Additional aspects of the nosology of NES yet to be fully elaborated include its relationship to other eating and sleep disorders. Assessment and analytical tools are needed to assess these new criteria more accurately.[7] These nosographical criteria for NES have been proposed for inclusion in the diagnosis of axis I of the next edition of the DSM V of the American Psychiatric Association and they have been further confirmed in several studies using self-report, structured interviews and rating scales.[8]

In this way the NES can be clearly distinguished from other related diseases such as binge eating disorder or sleep-related eating disorder (SRED). The authors conclude that a clearer connotation nosographic allows a better definition for the prevalence, association with obesity, assessment of the frequent comorbidity and a more effective determination of the underlying biological implications.[7] Therefore, NES appears to be a combination of an eating disorder, a sleeping disorder and a mood disorder.[9,10]

O'Reardon *et al*.[11] compared the eating and sleep–wake patterns of persons with NES with those of matched control subjects. The pattern of cumulative energy intake of the night eaters suggests a phase delay in energy consumption relative to sleep–wake times. NES may involve a dissociation of the circadian control of eating relative to sleep.

Alteration in the timing of food intake, typical of NES, is related to abnormal neuroendocrine patterns. The blood levels of cortisol, albeit measured in a limited number of studies, are on average higher with lower circadian fluctuations, and the production of thyroid-stimulating hormone appears to be increased[6,12] similar to stress-related disorders.[13] Several studies also show that people with NES have lowered levels of melatonin, which is the naturally occurring hormone that regulates the body's circadian rhythms that control the biochemical, physiological and behavioural 24-h cycles such as sleep and many others.[6] It is believed that the decreased melatonin is a big contributor to disturbances of sleep and the onset of NES. Additional factors that contribute to NES and its night binging are leptin[6] (a hormone that is believed to suppress appetite and speed up metabolism), certain medications and highly restrictive and prolonged dieting among obese individuals. The regulation of ghrelin,[14] an endogenous ligand receptor growth hormone that affects not only food but also control induction of sleep, is altered in NES.[12,15]

The main neuroendocrine systems involved are those of glucocorticoids, melanocortin and serotonin. Patients with NES appear, although only small samples of patients have been observed, to have not only higher levels of glucocorticoids than the general population but also an alteration of the normal circadian rhythm of release into the circulation of these hormones.[6,16] The high average levels of glucocorticoids promote food intake by acting positively on the system of age-related protein (AgRP) in the hypothalamus. Besides the alteration in the circadian rhythm, glucocorticoids may promote a desynchronization in the normal rhythms of food intake in patients with NES, through action on AgRP.[17]

There is also known to be an interaction between glucocorticoids and leptin, a hormone produced by adipocytes, which limits the appetite.[18] In fact, leptin reduces the secretion of glucocorticoids by increasing the negative feedback of glucocorticoids on corticotropin-releasing hormone.[19] Among the night eaters, leptin does not reach normal levels during the hours of the night and therefore is unable to reduce the release of glucocorticoids, which then continue to stimulate food intake, favouring the crisis of binging at night, typical of patients with NES.[6]

Melanocortins seems to be involved in the genesis of NES, although the data are still doubtful, because, even in small samples,[6] the melanocortins, such as leptin, has low levels at night.[20] The melanocortin is essential in controlling appetite and energy homoeostasis through agonism with α-melanocyte-stimulating hormone (α-MSH) and in sleep regulation.

The serotonin system is involved in the pathogenesis of NES. In fact, serotonin controls appetite and food intake. In an imaging study[21] using single-photon emission computed tomography (SPECT) with ^{123}I-ADAM, six patients with NES compared with six healthy controls, showed higher levels of the serotonin transporter (SERT) in the temporal lobe midbrain. The increase in serotonin reuptake due to high availability of SERT induces an alteration in serotonergic transmission, which could contribute to the genesis of NES, affecting both food intake and circadian rhythms.

Although there are various similarities between NES and major depression (presence of changes in appetite, night awakenings, affective symptoms, positive response to SSRIs), the brain SPECT with ^{123}I-ADAM,[22,23] it is significant that only in NES are found higher rates of SERT availability in midbrain and temporal lobes. In other eating disorders, such as bulimia nervosa and binge eating disorder, studies of brain imaging with SPECT,[24,25] did not find higher levels of SERT at the central level. Albeit in the small samples of patients studied, differences in SERT availability between NES, major depression and other disorders of eating behaviour suggest a different pathogenesis.

The adjustment of a hormone secreted by the stomach, ghrelin, which acts as an endogenous ligand of grown hormone, and that affects not only the control of food intake but also the induction of sleep, is altered in NES.[12,15]

Emotional factors, such as depression, anxiety, stress, boredom, low self esteem and skewed body image, play a significant role in NES and they are the catalysts that lead to night binging on comfort foods that have high caloric values due to their carbohydrates and fat content.[26] Often patients with NES (and patients with other eating disorders) exhibit significant comorbid psychopathology such as depression. Patients with NES often have higher scores on the Beck Depression Inventory Scale and the Zung Depression Scale compared with controls,[26] with a chance of lifetime incidence of major depression of 55%.[27] Often in patients with NES the decline in mood occurs in the evening and at night, in the opposite way to the typical experience in clinical depression.[28] There are also frequent symptoms related to a condition of anxiety[29,30] and worthlessness.[31] Together with the reduction in the mood, they also have intense feelings of shame and embarrassment regarding these frequent crises of night eating and often also tend to hide this from their family and doctor. Usually it is the insomnia or feeling of fatigue and tiredness that occur during the day that is reported to the doctor. Often patients report symptoms related to comorbidity before the NES, such as depression or the significant increase in weight, and then the frequent nocturnal awakenings with feeling of intense fatigue and tiredness during the day. At this point it is essential to the diagnosis that the doctor investigates the possibility of nocturnal food ingestion.

For possible confirmation of diagnosis, two assessment tools have proved profitable. The purpose of the first study was to evaluate the Night Eating Questionnaire (NEQ) as a measure of severity of the NES.[32] The 14-item NEQ assesses the behavioural and psychological symptoms of NES. The NEQ was evaluated in three samples: 1980 persons who completed the NEQ on the Internet; 81 persons diagnosed with NES; and 194 bariatric surgery candidates. Study 1, using principal components analysis, generated four factors (nocturnal ingestions, evening hyperphagia, morning anorexia and mood/sleep) and an acceptable alpha.[32] Confirmatory factor analysis suggested that 99% of covariation among factors is accounted for by a higher-order construct. Study 2 found convergent validity of the NEQ with additional measures of night eating, disordered eating, sleep, mood and stress. Study 3 compared scores from obese bariatric surgery candidates with and without NES and found appropriate discriminant validity of the NEQ. The NEQ appears to be an efficient, valid measure of severity for NES.[32] The second study took the form of a semi-structured interview, the NES and Inventory (night eating sydrome history and inventory), characterized by an assessment of food intake for 24 h, including the recall of food and snacks and sleep patterns.[11,33] This second study showed that among obese adults with type 2 diabetes, NES was reported more frequently than binge eating disorder, which, in turn, was less common than expected.[33]

Epidemiology

The prevalence of NES is estimated at just over 1% in the general population, between 6 and 14% in obese patients[34–37] and between 3.8 and 9.7% according to various studies in patients with diabetes of any type. The presence of NES in diabetics is an important predictor of change in glycosylated haemoglobin (HbA1c > 7), obesity, depressed mood and two or more complications of diabetes and also of poor adherence to diet, exercise physical and control of blood glucose.[33,38]

Regarding the distribution between the sexes, NES is much more common in females than in males.[39] Grilo *et al.*[39] examined the frequency of nighttime eating and its correlation in men and women with binge eating disorder. A sample of consecutively evaluated adults (45 men and 162 women) with binge eating disorder were assessed with semi-structured interviews and a battery of behavioural and psychological measures. Overall, 28% ($n = 58$) of the participants reported nighttime eating. A significantly higher

proportion of men (42%) than women (24%) reported nighttime eating. Overall, participants who reported nighttime eating had a significantly higher body mass index, but otherwise differed little from those who did not report nighttime eating. Men and women without nighttime eating differed little on behavioural and psychological measures, whereas women with nighttime eating had significantly higher levels of eating, weight and body-shape concerns than men with nighttime eating.[39]

Lundgreen *et al*.[30] assessed the prevalence of NES and binge eating disorder among overweight, obese, weight-loss-seeking individuals with serious mental illness. Sixty-eight consecutive overweight (body-mass index (BMI) $\geq$ 25 kg/m^2) and obese (BMI $\geq$ 30 kg/m^2) individuals with serious mental illness (mean age = 43.9 years; mean BMI = 37.2 kg/m^2; 67.6% Caucasian, 60.3% female) who were enrolled in a group behavioural weight-loss treatment program were assessed at baseline for NES and binge eating disorder with clinician-administered diagnostic interviews. Using conservative criteria, 25.0% met the criteria for NES, 5.9% met the criteria for binge eating disorder, and only one participant met the criteria for both NES and binge eating disorder. Lundgreen *et al*.[40] reported that obese individuals with serious mental illness, compared with previously studied populations, are at significantly greater risk for NES, but are not at greater risk for binge eating disorder. Stress, sleep patterns and medication use might account for the high prevalence of NES found in this population.

This study confirmed the findings of a previous study, also performed by Lundgreen *et al*.,[41] assessing the prevalence of NES and its comorbid psychopathology in a psychiatric population. The NEQ was administered to 399 patients in two psychiatric outpatient clinics. Those scoring above 20 on the questionnaire ($n = 205$) were assessed for NES with a semi-structured telephone interview. Chart reviews of all participants were performed to determine their psychiatric diagnoses and medications. Forty-nine participants (12.3%) met the criteria for NES.

Greater rates of substance use disorders were found among patients diagnosed with NES than among those without the syndrome. Obese patients were more likely than non-obese patients to manifest NES. This study showed that NES is prevalent among psychiatric clinic outpatients and is likely to co-occur with substance use disorders and obesity.[31]

Differential Diagnosis

The presence of episodes of nocturnal feeding is not a peculiarity of NES, but can also occur in other abnormal eating behaviour, such as bulimia nervosa or binge eating disorder, though rarely, however, without day anorexia. NES differs from binge eating disorder and bulimia nervosa in that the food is not consumed in large quantities and is not accompanied by typical compensatory behaviour.[39,42] NES is more a change in the timing of food intake, which disrupts the regularity of sleep, rather than a large quantity of food being consumed at a single time.[9]

Identifying abnormal nocturnal eating is critically important for patient care and public health. Obesity is a global pandemic and a leading cause of preventable mortality in the USA, with more than 100 000 deaths annually. Normally, nighttime energy homoeostasis is maintained, despite an absence of food intake, through appetite suppression and alterations in glucose metabolism that result in stable energy stores. Two conditions break this nighttime fast and are associated with weight gain as well as medical and neuropsychiatric comorbidities. SRED is characterized by isolated nocturnal eating, whereas NES is a circadian delay in meal timing leading to evening hyperphagia, nocturnal eating and morning anorexia (Table 1).[43]

SRED is a little-described syndrome combining features of sleep disorders and eating disorders. The behaviour consists of partial arousals from sleep followed by rapid ingestion of food, commonly with at least partial amnesia surrounding the episode the following day. A study provided an estimate of the prevalence of SRED.[44] The Inventory of Nocturnal Eating, a self-report questionnaire addressing nocturnal eating and sleep disturbance, was administered to: outpatients ($n = 126$) and inpatients ($n = 24$) with eating disorders; obese subjects ($n = 126$) in a trial of an anorexic agent; depressed subjects ($n = 207$) in an antidepressant trial; and an unselected group ($n = 217$) of college students. SRED was operationally defined as nocturnal eating, with a self-reported reduced level of awareness, occurring at least once per week. Almost 5.0% (33/700) of the sample described symptoms consistent with SRED. The inpatient eating disorder group had nearly twice the prevalence (16.7%) of the outpatient eating disorder sample (8.7%), which had nearly twice the prevalence of the next highest group, the student sample (4.6%). Subjects with SRED endorsed more symptoms consistent with sleep disorders and had higher levels of

Table 1 Differential diagnosis between night eating syndrome and sleep-related eating disorder

	NES	SRED
Nocturnal ingestion	+	+
Morning anorexia	+	+
Alterations level of consciousness	–	+
Amnesia of nocturnal event	–	+
Possible ingestion of harmful or toxic substances	–	+
Frequent association with sleepwalkers	–	+
Frequent comorbidity with PLMD, RLS or OSA	–	+

NES, night eating syndrome; OSA, obstructive sleep apnoea; PLMD, periodic leg movement disorder; RLS, restless legs syndrome; SRED, sleep-related eating disorder. +, present; –, absent.

depression and dissociation than those without nocturnal eating.[44] Therefore, SRED is more common than is generally recognized, especially in those with a daytime eating disorder. Sleep disorder symptoms are often associated with SRED, as are depression and dissociation. Evaluation of individuals with eating disorders should include assessment for sleep-related eating.[44]

Patients with SRED, during episodes of nocturnal feeding, may swallow unconsciously, not only foods high in calories, but also compounds or liquids that are inedible or even toxic.[45] SRED is often associated with other sleep disorders such as the periodic leg movement disorder, restless legs syndrome or obstructive sleep apnoea.

NES occurs when the coordination of these two drives (eating and sleep disorder) is dysregulated, resulting in the disordered eating of a daytime eating disorder combined with the disordered sleep of a sleep disorder.

The most prominent cited distinction between NES and SRED is the level of consciousness during nighttime eating episodes. Whereas those with NES eat after attaining full awareness, those with SRED often report that they are 'half asleep, half awake' or even fully asleep during nocturnal episodes and may have impaired recollection of the event the following morning.[46]

The difference between NES and SRED may be that patients with the latter are sleep-walkers who happen to eat, whereas patients with NES are those with binge eating disorder who happen to eat at night. On the other hand, many of those patients with alterations in level of consciousness during nocturnal eating (and thus diagnosed with SRED) may also have night eating with full alertness, either during other episodes in the same night or at other periods during the course of the nocturnal eating disorder. In this way, rather than being two distinct disorders, pure SRED and NES may reflect opposite ends of a continuum of impairment of consciousness during nocturnal eating.[47] Although these diagnostic issues remain unresolved on clinical and scientific bases, the recent revision of the International Classification of Sleep Disorders (ICSD) has effectively eliminated the distinction between the two disorders (Table 2).

The diagnostic criteria for SRED in the revised ICSD do not specify a level of consciousness during episodes of nocturnal eating and, thus, incorporates NES into the classification of SRED.

Table 2 Definition and diagnostic criteria for sleep-related eating disorder[a]

A. Recurrent episodes of involuntary eating and drinking occur during the main sleep period.
B. One or more of the following must be present with the recurrent episodes of involuntary eating and drinking:
1. Consumption of peculiar forms or combinations of food or inedible or toxic substances.
2. Insomnia related to sleep disruption from repeated episodes of eating, with a complaint non restorative sleep, daytime fatigue, or somnolence.
3. Sleep-related injury.
4. Dangerous behaviour performed while in pursuit of food or while cooking food.
5. Morning anorexia.
6. Adverse health consequences from recurrent binge eating of high caloric food.
C. The disturbance is not better explained by another sleep disorder, medical or neurologic disorder, mental disorder, medication use or substance use disorder (hypoglycaemic states, peptic ulcer disease, reflux oesophagitis, Kleine–Levin syndrome, Kluver–Bucy syndrome, and nighttime extension of daytime anorexia nervosa (binge/purge subtype), bulimia nervosa and binge eating disorder).

[a]From The International Classification of Sleep Disorders: Diagnostic and Coding Manual, 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005:174–175.

Treatment

NES is treatable but it is not easy since, in most instances, the patients are unaware of their condition and are, therefore, resistant to treatment.

In this respect, treatment for NES, because of the complexity of diagnosis, has to be done on an individual basis, combining mental health therapy, education on diet and nutrition, possibly medication to reduce stress, time spent in a sleep laboratory for observation and a great deal of support. This particular disorder is showing signs of responding favourably to antidepressants such as SSRIs. These have been found useful due to their effect on the serotonin levels in the brain. Serotonin promotes calm and helps counteract cravings and is involved in the production of melatonin, which aids sleep. This ties in with a theory that by binge eating mainly on high carbohydrate foods, the NES sufferer is (subconsciously) self-medicating, as when carbohydrates are eaten, they allow an amino acid called tryptophan to cross the blood–brain barrier to be used in the production of serotonin.

However, current trials on pharmacological treatments of NES are still at a preliminary stage. Some data in the literature suggest that three types of drugs seem likely to be effective in reducing episodes of NES: (1) dopaminergic drugs such as pramipexole; (2) anticonvulsants such as topiramate; (3) selective serotonin reuptake inhibitors (SSRIs).

Pramipexole, used at low dose (0.125 mg before bedtime), in a recent double-blind, placebo-controlled study,[38] was effective in treating SRED, improving sleep quality and reducing nocturnal activity. Provini *et al*.[48] assessed the safety, tolerability and efficacy of pramipexole, a dopamine D3-receptor agonist, in the treatment of SRED. Eleven consecutive patients with SRED in the absence of concurrent daytime eating disorders underwent actigraphic recording

and subjective sleep diary evaluation for a week before, and every week for 2 weeks of treatment with, pramipexole 0.18–0.36 mg or placebo, administered in a double-blind crossover randomized sequence. The primary outcomes of the trial were actigraphic measures of night sleep parameters (sleep efficiency, motor activity mean and median, number and duration of wake episodes), secondary outcomes were the number of good sleep nights per week, number and duration of nocturnal awakenings per night, and visual analogue preference score. Pramipexole was well tolerated without any patient withdrawing from the study. Pramipexole reduced nighttime activity median ($P = 0.02$) and increased the number of nights of good sleep per week ($P = 0.02$). All other measurements remained unaffected. Pramipexole at low doses was well tolerated, improving some measures of sleep quality and reducing median night activity in SRED.[48]

For topiramate, an antiepileptic drug used as a mood stabilizer in bipolar disorder, there is also sufficient evidence of its effectiveness in treating SRED and NES. A recent study,[49] showed the efficacy and tolerability of topiramate in the treatment of SRED. This was a retrospective chart review of consecutive patients treated in an open-label trial of topiramate for SRED in a sleep disorders clinic. Patients were diagnosed according to the second edition of the International Classification of Sleep Disorders. Patients with a Clinical Global Impressions of Improvement (CGI-I) rating of 'very much improved' or 'much improved' were considered treatment responders. Thirty subjects were prescribed topiramate, of whom 25 had at least one postbaseline follow-up appointment. The mean age of these 25 patients was 44 $\pm$ 12 years, 76% were female, and the mean age at onset of SRED was 25.2 $\pm$ 12.8 years. The mean dose of topiramate was 135 $\pm$ 61.6 mg (range, 25–300 mg) over a mean period of 11.6 $\pm$ 11.4 months (range, 1–42 months). Over two-thirds of the patients (17/25 or 68%) were considered topiramate responders. Twenty-eight percent (7/25) of the patients lost more than 10% of body weight. Adverse events were reported by 84% (21/25) of patients. Nearly half (7/17 or 41%) of the responders discontinued topiramate after a mean of 12.4 months. In this open-label retrospective trial, topiramate was found to be very effective in reducing nocturnal eating in patients with chronic SRED. The tolerability of topiramate was an issue in some patients. Given the promise of this approach, but the limitations of this study, prospective, a double-blind study of topiramate in a larger sample of patients with SRED is warranted.[49]

Even a naturalistic and not-controlled study[50] in a small number of cases (four patients, of which two had NES and two had SRED) has highlighted the effectiveness of topiramate, with an average dose of 200 mg, but in three of the four patients already at 100 mg/day there was a good improvement of symptoms. In all patients, topiramate reduced the number of food crises occurring at night, improved sleep quality and favoured the loss of weight (11.1 kg mean weight reduction in 6–12 months).

More evidence of efficacy in the treatment of NES is shown, however, for some SSRIs such as paroxetine, fluvoxamine, and especially sertraline. This effect appears to be independent of the concomitant effects on mood. An initial report[40] showed complete remission of episodes of nocturnal feeding in three cases, and in one case with paroxetine, and fluvoxamine. Four patients with NES were treated with an SSRI, which was effective in controlling the episodes of nocturnal eating. This is the first published case report of successful treatment with SSRIs in NES.[51]

Furthermore O'Reardon *et al.*[52] showed the efficacy of the SSRI sertraline in the treatment of NES. Seventeen patients meeting the criteria for NES received sertraline in a 12-week open-label, nonblind trial. The outcome was assessed by four primary measures, namely, the number of nocturnal awakenings, the number of ingestions, total daily caloric intake after the evening meal, and an overall rating of change from the Clinical Global Impression of Improvement scale (CGI-I). An intent-to-treat analysis revealed highly significant improvements across all four primary outcome measures for all 17 subjects. Five subjects achieved full remission of symptoms (CGI-I score of 1 = very much improved) and lost a significant amount of weight over the course of the study (-4.8 ± 2.6 kg, $P < 0.05$), indicating that sertraline may be beneficial in the treatment of NES.[52]

A recent double-blind, placebo-controlled study in 34 patients with NES has confirmed the efficacy of sertraline.[53] Thirty-four outpatients diagnosed with NES were randomly assigned to receive either sertraline ($n = 17$) or placebo ($n = 17$) in an 8-week, double-blind, flexible-dose (50–200 mg/day) study. A mixed effects linear regression model was used to analyse change in the primary outcome measure, Clinical Global Impression (CGI) improvement rating. Secondary outcomes included changes in night eating symptoms, the number of nocturnal awakenings and ingestions, total daily calorie intake after the evening meal, CGI severity ratings, quality of life ratings, and weight. Sertraline was associated with significantly greater improvement than placebo. Twelve subjects in the sertraline group (71%) were classified as having responded (CGI improvement rating ≤ 2, indicating much or very much improved) versus only three (18%) in the placebo group. There were also significant improvements in night eating symptoms, CGI severity ratings, quality of life ratings, frequency of nocturnal ingestions and awakenings, and calorie intake after the evening meal. Overweight and obese subjects in the sertraline group ($n = 14$) lost a significant amount of weight by week 8 (mean = –2.9 kg, SD = 3.8) compared with overweight and obese subjects receiving placebo ($n = 14$) (mean = –0.3 kg, SD = 2.7). In this 8-week trial, sertraline was effective in the treatment of NES and was well tolerated.[54]

The effectiveness of SSRIs in the treatment of NES may be due to their direct action of stimulating serotonin (5-HT) 5-HT1A receptors on neurons of the nuclei of the hypothalamus sovrachiasmatici, deputizes to the synchronization of circadian rhythms of sleep and feeding behaviour.[9,55] Normally, in humans, the circadian rhythms of sleep and food are synchronized so as not to interrupt sleep at night with the need to feed. It is possible that sertraline, and possibly other SSRIs, can be effective in the treatment of NES by facilitating a more physiological circadian rhythm of food intake,[56] for the direct effect on neurons of the suprachiasmatic nucleus.

A recent pilot study[21] using SPECT in patients with NES showed high levels of serotonin transporter (SERT) gene in the midbrain, compared with healthy controls. Six night eaters underwent SPECT imaging using the radiopharmaceutical ^{123}I-ADAM. Uptake, compared with that of the cerebellum, was obtained for the midbrain, basal ganglia and temporal lobes; uptake ratios in night eaters were compared with those of six healthy controls. Night eaters had significantly greater SERT uptake ratios in the midbrain than healthy controls. These findings, in conjunction with the therapeutic response of NES to sertraline, indicate that the serotonin system is involved in the pathophysiology of NES.[21]

These high levels of SERT may cause alterations in circadian rhythms of food-intake and neuroendocrine functions. SSRIs, by reducing the reuptake of serotonin, would favour the restoration of physiological circadian rhythms. This implies that the reduction of the SERT by SSRIs could increase postsynaptic serotonin transmission and significantly improve the clinical picture of NES. NES should therefore be regarded as a function of high activity of SERT and their blockers, SSRIs, should be considered the treatment of choice.[57]

This above study[57] suggests a biobehavioral mechanism for NES. This mechanism was explored by reviewing neuroimaging of brain SERT and treatment with SSRIs. SERT binding is elevated in the midbrain of night eaters, causing dysregulation of the circadian rhythm of both food intake and neuroendocrine function. The administration of SSRIs blocks the reuptake of serotonin and restores the circadian rhythm of both food intake and neuroendocrine function. This hypothesis implies that reduction of SERT activity should increase postsynaptic serotonin transmission and relieve NES. This is precisely the effect of SSRIs. NES is a function of elevated SERT, and blocking of SERT with an SSRI resolves NES. This model of NES attests to the validity of the diagnosis of NES and the criteria by which it is identified, and it provides an explanation of the mechanism.[57]

Therefore, SSRIs should be considered the drug of choice for the treatment of NES, not only because of evidence in the literature but also since they display the best pharmacological profile with fewer adverse events. Topiramate should be reserved for cases resistant to treatment with SSRIs. Also, if the drug used is shown effective in reducing clinical symptoms of NES, it should be continued for at least a year. The drug trials so far have proved effective enough but still involve a small number of studies, not all randomized controlled trials, and a small number of patients. Further studies are therefore desirable and should be randomized controlled trials, which include a satisfactory number of patients and a sufficiently long period of follow-up for evaluation of drug treatment and outcomes.

Nonpharmacological Treatments

There are also references in the literature, albeit a minimum number, to non-pharmacological treatments for NES. A few years ago, a paper presented a case report of treatment with bright-light therapy,[48] at doses of 10 000 lux for 30 min daily for 10 days repeated after a month with 12 days of treatment in an obese patient with NES. This treatment induced a marked reduction in the crisis of binging at night. Such data, however, were the most repeated. As for other forms of non-pharmacological treatment of NES, one very recent paper[58] described the treatment of 25 patients (19 females and 6 males) with cognitive behavioral therapy (CBT). Assessment was performed by the NES Scale (NESS), body weight and the number of nocturnal ingestions food. After 10 sessions the number of nocturnal ingestions decreased on average from 8.7 to 2.6 per week, the weight reduced from an average of 82.5 to 79.4 kg and the score of the NESS from 28.7 to 16, 3 (all $P < 0.001$).

Conclusions

Night eating syndrome is of importance clinically because of its association with obesity. Its prevalence rises with increasing weight, and about half of those diagnosed with it report a normal weight status before the onset of the syndrome. The recognition and effective treatment of NES may be an increasingly important way to treat a subset of the obese population. Treatment of the syndrome, however, is still in its infancy. One clinical trial has reported efficacy with the SSRI sertraline. Other treatments, such as the anticonvulsant topiramate, phototherapy, and other SSRIs, may also offer future promise.

Particularly useful would be studies involving brain scans (magnetic resonance imaging or SPECT) of patients with NES compared with the healthy population, to investigate more thoroughly the possible alterations involved in the pathogenesis of NES.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorder*, 4th edn. Washington, DC: American Psychiatric Association, 2000.
2. Vetrugno R *et al*. Nocturnal eating sleep-related eating disorder or night eating syndrome? A videopolysomnographic study. *Sleep* 2006; 29: 949–954.
3. Fassino S *et al*. Sleep and eating disorders: a review. *G Ital Psicopatologia* 2005; 11: 354–362.
4. Stunkard AJ *et al*. The night-eating syndrome: a pattern of food intake among certain obese patients. *Am J Med* 1955; 19: 78–86.
5. Stunkard AJ *et al*. Binge eating disorder and the night eating syndrome. *Int J Obes* 1996; 20: 1–6.
6. Birketvedt G *et al*. Behavioral and neuroendocrine characteristics of the night-eating syndrome. *JAMA* 1999; 282: 657–663.
7. Allison KC *et al*. Proposed diagnostic criteria for night eating syndrome. *Int J Eat Disord* 2010; 43: 241–247.
8. Stunkard AJ *et al*. Development of criteria for a diagnosis: lesson from the night eating syndrome. *Compr Psychiatry* 2009; 50: 391–399.
9. O'Reardon JP *et al*. Night eating syndrome: diagnosis, epidemiology and management. *CNS Drugs* 2005; 19: 997–1008.
10. Vinai P *et al*. Psychopathology and treatment of night eating syndrome: a review. *Eat Weight Disord* 2008; 13: 54–63.
11. O'Reardon JP *et al*. Circadian eating and sleeping patterns in the night eating syndrome. *Obes Res* 2004; 12: 1789–1796.
12. Goel N *et al*. Circadian rhythm profiles in women with night eating syndrome. *J Biol Rhythms* 2009; 24: 85–94.
13. Stunkard AJ *et al*. The night eating syndrome: a progress report. *Appetite* 2005; 45: 182–186.
14. Van Der Lely AJ *et al*. Biological, physiological, pathophysiological and pharmacological aspects of ghrelin. *Endocr Rev* 2004; 25: 426–457.
15. Allison KC *et al*. Neuroendocrine profiles associated with energy intake, sleep and stress in the night eating syndrome. *J Clin Endocrinol Metab* 2005; 90: 6214–6217.
16. Geliebter A *et al*. Cortisol following a stress test and dexamethasone suppression test (DST) in relation to psychopathology in the night eating syndrome. *Appetite* 2002; 39: 77.
17. Lu XY *et al*. Diurnal rhythm of agouti-related protein and relation to corticosterone and food-intake. *Endocrinology* 2002; 143: 3905–3915.
18. Gaillard RC *et al*. Cytokines, leptin and the hypothalamo-pituitary-adrenal axis. *Ann N Y Acad Sci* 2000; 917: 647–657.
19. Arvaniti K *et al*. Effects of leptin and corticosterone on the expression of corticotropin-releasing hormone, agouti-related protein and proopiomelanocortin in the brain of ob/ob mouse. *Neuroendocrinology* 2001; 73: 227–236.
20. Rogers NL *et al*. Assessment of sleep in women with night eating syndrome. *Sleep* 2006; 29: 814–819.
21. Lundgren JD *et al*. ADAM-SPECT imaging of serotonin transporter binding in patients with night eating syndrome: a preliminary report. *Psychiatry Res Neuroimaging* 2008; 15: 214–220.
22. Lundgreen JD *et al*. Differences in serotonin transporter binding affinity in patients with major depressive disorder and night eating syndrome. *Eat Weight Disord* 2009; 14: 45–50.
23. Newberg AB *et al*. 123I-ADAM binding to serotonin transporters in patients with major depression and healthy controls: a preliminary study. *J Nucl Med* 2005; 46: 973–977.
24. Tauscher J *et al*. [123I] beta-CIT and single photon emission computed tomography reveal reduced brain serotonin transporter availability in bulimia nervosa. *Biol Psychiatry* 2001; 49: 326–332.
25. Kuikka JT *et al*. Reduced serotonin transporter binding in binge eating women. *Psychopharmacology (Berl)* 2001; 155: 310–314.
26. Gluk ME *et al*. Night eating syndrome is associated with depression, low self-esteem, reduced daytime hunger and less weight loss in obese outpatients. *Obes Res* 2001; 9: 264–267.
27. de Zwaan M *et al*. Night-time eating: a descriptive study. *Int J Eat Disord* 2006; 39: 224–232.
28. Boseck JJ *et al*. The application of ecological momentary assessment to the study of night eating. *J Eat Disord* 2006; 40: 271–226.
29. Pawlow LA *et al*. Night eating syndrome: effects of brief relaxation training on stress, mood hunger and eating patterns. *Int J Obes Relat Metab Disord* 2003; 27: 970–978.
30. Striegel-Moore RH *et al*. Night eating syndrome in young adult women: prevalence and correlates. *Int J Eat Disord* 2005; 37: 200–206.
31. de Zwann M *et al*. Night time eating: a review of the literature. *Eur Eat Disord Rev* 2003; 11: 7–24.
32. Allison KC *et al*. The night eating questionnaire (NEQ): psychometric properties of a measure of severity of the night eating syndrome. *Eat Behav* 2008; 9: 62–72.
33. Allison KC *et al*. Binge eating disorder and night eating syndrome in adults with type 2 diabetes. *Obesity* 2007; 15: 1287–1293.
34. Rand CSW *et al*. The night eating syndrome in the general population and among post-operative obesity surgery patients. *Int J Eat Disord* 1997; 22: 65–69.
35. Cerù-Bjork C *et al*. Night eating and nocturnal eating: two different or similar syndrome among obese patients? *Int J Obes* 2001; 25: 365–372.
36. Adami GF *et al*. Night eating and binge eating disorder in obese patients. *Int J Eat Disord* 1999; 25: 335–338.
37. Marshall HM *et al*. The night eating syndrome among nonobese persons. *Int J Eat Disord* 2004; 35: 217–222.
38. Morse SA *et al*. Isn't this just bedtime snacking? The potential adverse effects of night-eating symptoms on treatment adherence and outcomes in patients with diabetes. *Diabetes Care* 2006; 29: 1800–1804.

39. Grilo CM, Masheb RM. Night-time eating in men and women with binge eating disorder. *Behav Res Ther* 2004; 42: 397–407.
40. Lundgren JD *et al*. The prevalence of night eating syndrome and binge eating disorder among overweight and obese individuals with serious mental illness. *Psychiatry Res* 2010; 175: 233–236.
41. Lundgren JD *et al*. Prevalence of the night eating syndrome in a psychiatric population. *Am J Psychiatry* 2006; 163: 156–158.
42. Napolitano MA *et al*. Binge eating disorder and night eating syndrome in young adult women: prevalence and correlates. *Int J Eat Disord* 2001; 30: 193–203.
43. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*, 2nd edn. Westchester, IL: American Academy of Sleep Medicine, 2005.
44. Winkelman JW *et al*. The prevalence of sleep-related eating disorder in psychiatric and non-psychiatric population. *Psychol Med* 1999; 29: 1461–1466.
45. Howell MJ, Schenck CH. Treatment of nocturnal eating disorders. *Curr Treat Options Neurol* 2009; 11: 333–339.
46. Howell MJ *et al*. A review of nighttime eating disorder. *Sleep Med Rev* 2009; 13: 23–34.
47. Eiber R, Friedman S. Correlation between eating disorders and sleep disturbances. *Encephale* 2001; 27: 429–434.
48. Provini F *et al*. A pilot double-blind placebo-controlled trial of low-dose pramipexole in sleep-related eating disorder. *Eur J Neurol* 2005; 12: 432–436.
49. Winkelman JW. Efficacy and tolerability of open-label topiramate in the treatment of sleep-related eating disorder: a retrospective case series. *J Clin Psychiatry* 2006; 67: 1729–1734.
50. Winkelman JW. Treatment of nocturnal eating syndrome and sleep-related eating disorder with topiramate. *Sleep Med* 2003; 4: 243–246.
51. Miyaoka T *et al*. Successful treatment of nocturnal eating/drinking syndrome with selective serotonin reuptake inhibitors. *Int Clin Psychopharmacol* 2003; 18: 175–177.
52. O'Reardon PJ *et al*. Clinical trial of sertraline in the treatment of night eating syndrome. *Int J Eat Disord* 2004; 35: 16–26.
53. O'Reardon PJ *et al*. A randomized, placebo-controlled trial of sertraline in the treatment of night eating syndrome. *Am J Psychiatry* 2006; 163: 893–898.
54. Miller JD *et al*. New insights into the mammalian circadian clock. *Sleep* 1996; 19: 641–667.
55. Stunkard AJ, Lu XY. Rapid changes in night eating: considering mechanism. *Eat Weight Disord* 2010; 15: 2–8.
56. Stunkard AJ *et al*. A biobehavioural model of the night eating syndrome. *Obes Rev* 2009; 10(Suppl. 2): 69–77.
57. Friedman S *et al*. Light therapy, obesity, and night-eating syndrome. *Am J Psychiatry* 2002; 159: 875–876.
58. Allison KC *et al*. Cognitive behavior therapy for night eating syndrome: a pilot study. *Am J Psychother* 2010; 64: 91–106.