Behavioral and Neuroendocrine Characteristics of the Night-Eating Syndrome

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NIGHT-EATING SYNDROME (NES), characterized by morning anorexia, evening hyperphagia, and insomnia, was described in 1955 by Stunkard and colleagues.1 It occurred during periods of stress and was associated with a poor outcome of efforts at weight reduction. Since 1955, NES has not been subjected to careful clinical study, but its prevalence has been estimated at 1.5% in the general population,2 8.9% in an obesity clinic,3 12% of the obese patients in a nutrition clinic,4 and 27% and 26%, respectively, in 2 samples of patients in a nutrition and obesity clinic, 3,12% of the obese patients in a nutrition clinic,4 and 27% and 26%, respectively, in 2 samples of severely obese persons.5 Although it does occur among nonobese persons, NES appears to be more common among obese persons and to increase in prevalence with increasing adiposity.

This report describes 2 related studies designed to characterize NES. The behavioral study attempted to define the behavioral characteristics of the syndrome in terms of timing of energy consumption during eating episodes, level of mood throughout the waking hours, and frequency of nighttime awakenings. The neuroendocrine study attempted to characterize the syndrome in terms of circadian profiles of plasma melatonin, leptin, and cortisol levels.

For editorial comment see p 689.

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Context Investigators first described the night-eating syndrome (NES), which consists of morning anorexia, evening hyperphagia, and insomnia, in 1955, but, to our knowledge, this syndrome has never been subjected to careful clinical study.

Objective To characterize NES on the basis of behavioral characteristics and neuroendocrine data.

Design and Setting A behavioral observational study was conducted between January 1996 and June 1997 in a weight and eating disorders program at the University of Pennsylvania. A neuroendocrine study was conducted from May through August 1997 at the Clinical Research Center of the University Hospital, Tromsø, Norway.

Subjects The behavioral study included 10 obese subjects who met criteria for NES and 10 matched control subjects. The neuroendocrine study included 12 night eaters and 21 control subjects. Behavioral study subjects were observed for 1 week on an outpatient basis, and neuroendocrine study subjects were observed during a 24-hour period in the hospital.

Main Outcome Measures The behavioral study measured timing of energy intake, mood level, and sleep disturbances. The neuroendocrine study measured circadian levels of plasma melatonin, leptin, and cortisol.

Results In the behavioral study, compared with control subjects, night eaters had more eating episodes in the 24 hours (mean [SD], 9.3 [0.6] vs 4.2 [0.2]; P < .001) and consumed significantly more of their daily energy intake at night than did control subjects (56% vs 15%; P < .001). They averaged 3.6 (0.9) awakenings per night compared with 0.3 (0.3) by controls (P < .001). In night eaters, 52% of these awakenings were associated with food intake, with a mean intake per ingestion of 1134 (1197) kJ. None of the controls ate during their awakenings. In the neuroendocrine study, compared with control subjects, night eaters had attenuation of the nocturnal rise in plasma melatonin and leptin levels (P < .001 for both) and higher circadian levels of plasma cortisol (P = .001).

Conclusion A coherent pattern of behavioral and neuroendocrine characteristics was found in subjects with NES.

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BEHAVIORAL STUDY

The behavioral study was conducted from January 1996 to June 1997 on an outpatient basis in the Weight and Eating Disorders Program of the Department of Psychiatry of the University of Pennsylvania School of Medicine, with the approval of the institutional review board of the University of Pennsylvania.

Subjects Subjects were recruited by announcements in local newspapers that asked for volunteers with morning anorexia, evening overeating, and insomnia. Candidates for the study were interviewed by 1 of us (G.S.B.), who selected subjects who reported the above charac-

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teristics, including consumption of at least 50% of their daily food intake after 6 PM. Exclusion criteria were serious physical or emotional illness, including diabetes mellitus and other endocrine disorders; use of psychotropic medications, steroids, diuretics, or hypnotics; excessive consumption of alcohol; a concurrent eating disorder; participation in a weight reduction program; or an occupation that involved night shifts or other unusual time requirements that interfered with meals. The use of tobacco, caffeine, and illegal drugs was not assessed.

Subjects consisted of 8 women and 2 men, all of whom were overweight. A control group of 10 overweight subjects, matched for sex, age, and weight with the night eaters, was recruited from persons who applied to take part in the study but were found not to manifest signs of NES. To compare the size of the ingestions, particularly at night, with the binges reported by persons with bulimia nervosa, we enrolled 4 subjects with bulimia nervosa who followed the standard protocol.

Methods
At the beginning of the study, subjects were given motion sensors and instructed in their use. They were also given a diary in which to record each nighttime awakening, all food consumed at each ingestion, and mood on a 10-cm visual analog scale at the time of each ingestion. After the completion of 1 week of data collection, the motion sensors were collected and analyzed for nighttime awakenings. Records of food intake were collected and analyzed for energy intake from 6 AM to 5:59 AM the complete data were analyzed graphically by examining the cumulative energy intake from 6 AM to 5:59 AM the next morning. Data were analyzed using generalized estimating equations, which accommodated the dependence between the multiple measurements for each subject and allowed separate line segments for the daytime and nighttime periods for night eaters and controls. The effect of status (night eaters or controls) on cumulative energy intake throughout the 24 hours was tested using this model. A piecewise regression using generalized estimating equations was also used to assess the significance of the difference between night eaters and controls in level of mood throughout the 24 hours, as well as the slope of the mood of the night eaters after 4 PM. A Poisson distribution, also fit using generalized estimating equations, assessed the significance of the difference between night eaters and controls in the number of nighttime awakenings. A Wilcoxon test was used to compare age differences between night eaters and controls.

The average number of eating episodes, amount of kilojoules consumed per episode, and nighttime awakenings of the 4 women with bulimia nervosa are reported, but, because of small sample size, data comparing them with the night eaters and controls are not. In both the behavioral and neuroendocrine studies, data are reported as mean (SD) if not otherwise stated, and all P values are 2-tailed.

Results
The body mass index (BMI) of the night eaters was 28.5 (3.9) kg/m², and that of the control subjects was 28.2 (4.9) kg/m². The ages of the night eaters (57.3 [12.2] years) were marginally greater than those of the control subjects (47.1 [10.7] years; P = .06).

The amount of food intake by night eaters and controls differed only moderately. The night eaters consumed 12 259 (8326) kJ/d, compared with 9765 (3853) kJ/d for the control subjects (P = .05). By contrast, the night eaters had 9.3 (0.6) eating episodes in the 24 hours, compared with 4.2 (0.2) for the control subjects (P < .001). Furthermore, the pattern of daytime and nighttime food intake of the 2 groups differed dramatically (P < .001) (Figure 1). During the daytime hours, the cumulative energy intake of the night eaters lagged behind that of the control subjects so that, in accordance with the selection criteria, at 6 PM they had consumed only 37% of their daily intake, compared with 74% consumed by the controls (P < .001). While the food intake of the controls slowed markedly by 8 PM, that of the night eaters continued at a rapid pace until after 12 AM. During the period from 8 PM to 6 AM, the night eaters consumed 56% of their energy intake, compared with 15% consumed by the control subjects (P < .001).

Figure 1 also shows that, during the 24 hours, the average mood of the night eaters (5.1 [1.5] out of a possible 10 units) was lower than that of the controls (7.8 [1.1]) (P < .001). Furthermore, after 4 PM, the mood of the night eaters fell at a rate of 0.25 units per hour (95% confidence interval, 0.13-0.37) while that of the controls remained unchanged (P < .001).

Nighttime awakenings were far more common among the night eaters (3.6 [0.9] per night) than among the controls (0.3 [0.3]) (P < .001). For the night eaters, 52% of the 178 awakenings were associated with food intake, which averaged 1134 (1197) kJ. The carbohydrate content of this food intake was 70.3% (12.5%) compared with 46.6% (13.6%) of kilojoules for the rest of the day (P < .001). The ratio of carbohydrate to protein in the snacks was 7:1. None of the 13 awakenings of the controls was associated with food intake.

Subjects with bulimia nervosa averaged 6.2 (5.0) eating episodes per day and consumed an average of 7987 (11 443) kJ per ingestion. None reported nighttime awakenings.

NEUROENDOCRINE STUDY
The neuroendocrine study, conducted in the Clinical Research Department and the Laboratory of Gastroenterology of the University Hospital, Tromso, Norway, from May through August 1997, investigated circadian neuroendocrine patterns of subjects with NES. The study was conducted with the approval of the Ethical Committee of Region V, Norway.
Subjects
Night eaters were recruited, as in the behavioral study, by announcements in local newspapers. Twelve night eaters and 21 control subjects, all women, were selected by 1 of us (G.S.B.) using the same criteria as in the behavioral study except that the criterion of consumption of more than 50% of the daily food intake after 6 PM was shifted to 8 PM to allow for the later Norwegian supper hour.

Methods
Subjects were admitted to the Clinical Research Center at 8 AM after an overnight fast. They remained for 24 hours, during which time they were free to move about until 11 PM, when they went to bed. Four meals of 1255 kJ each were served at 8 AM, 1 PM, 4 PM, and 8 PM. Shortly after admission, a blood sample from fasting subjects was drawn from an indwelling catheter, and blood was drawn every 2 hours thereafter. Blood was collected in precooled glass tubes containing 20 mmol of EDTA and 1000 kallikrein inhibitor units of aprotinin per milliliter of blood and kept on ice until centrifugation at 4°C and storage at −27°C. Melatonin was measured with a commercial kit, and lipid extraction of the samples was performed. Intra-assay and interassay precisions were 10.8% and 15.1%, respectively. Leptin was measured using a commercial kit, and intra-assay and interassay precisions were 2.7% and 3.9%, respectively. Cortisol was measured using a commercial immunoassay kit, and intra-assay and interassay precisions were 5.1% and 7.3%, respectively. Blood glucose was measured by a glucose analyzer. Insulin was measured by radioimmunoassay.

Every effort was made to control and equalize exposure to light. For this purpose, subjects were admitted to the Clinical Research Center in groups of 4. To further control exposure to light, the study was performed during 2-month periods, from May to June and July to August, when the length of daylight hours was the same and the ambient light energy was 70 W/m² and 1 W/m² at 12 PM and 12 AM, respectively. Subjects slept in a room designed to exclude any outdoor light. As an additional precaution, nighttime blood drawings were carried out with the aid of a small flashlight while the subjects’ eyes were covered.

Statistical Analysis
Statistical analysis of the differences between groups in plasma melatonin, plasma cortisol, plasma insulin, blood glucose, and incremental plasma leptin values (after subtracting the levels at baseline, 8 AM) during the 24-hour observation period were evaluated by repeated measures multivariate analysis of variance. A Wilcoxon rank sum test was used to compare age differences and the time of the highest and lowest plasma concentrations of melatonin, leptin, and cortisol.

Results
The 12 night eaters were divided into 7 nonobese (BMI, 23.1 [3.6] kg/m²) and 5 obese (BMI, 36.1 [4.4] kg/m²) subjects. The BMI of the 10 nonobese control subjects was 23.1 (1.5) kg/m², whereas that of the 11 obese control subjects was 30.4 (3.1) kg/m². The ages of the 12 night-eating subjects (53 [10] years) did not differ significantly from those of the overweight control subjects (55 [10] years; P = .39) or those of the normal-weight control subjects (46 [11] years; P = .06). No subject reported having been diagnosed as having sleep apnea and no episodes of sleep apnea were observed during the studies in the clinical research department. As in the behavioral study, the nighttime awakenings were far more common among the night eaters (3.0 [1.2]) than among the controls (0.1 [0.2]) (P<.001).

Figure 1. Twenty-four–Hour Food Intake and Mood

Twenty-four–hour pattern of mean cumulative energy intake and mood for a 5-day period. The intake of the night eaters lags behind that of control subjects until 11 PM and then greatly exceeds it (P<.001). Daytime mood of the night eaters is lower than that of the controls (P<.001) and falls even lower during the evening and night (P<.001). Error bars represent SEs in all figures. NES indicates night-eating syndrome.
Dysregulation of the circadian levels of melatonin, leptin, and cortisol was found among the night eaters and not among members of the 2 control groups.

**Plasma Melatonin**

Among the night eaters, both overweight and normal-weight, plasma melatonin levels at night were lower than those of their respective control groups from 10 PM to 6 AM (P < .001) (Figure 2). The nocturnal plasma melatonin concentrations were higher in the overweight control group than in the normal-weight control group from 2 AM to 4 AM (P < .001), but there was no difference between the overweight and normal-weight night eaters (P = .63). Similarly, no difference was found between the normal-weight groups (P = .11) and between the overweight groups (P = .73) in the time of the highest plasma melatonin concentration.

**Plasma Leptin**

Plasma leptin levels were higher among the overweight subjects than among the normal-weight subjects (both night eaters and controls) (P < .001) (Figure 3). When compared with their respective control groups, the rise in the nocturnal (12 AM to 6 AM) plasma leptin levels was lower in both normal-weight and overweight night eaters (P < .001). The time of the highest plasma leptin concentration did not differ between the normal-weight groups (P = .28) or between the overweight groups (P = .63).

**Plasma Cortisol**

There were no differences in plasma cortisol levels between overweight and normal-weight subjects, either among night eaters or controls. The weight groups were combined accordingly for comparison of night eaters with controls. Figure 4 shows that plasma cortisol levels of the night eaters were higher than those of the control subjects from 8 AM to 2 AM (P < .002). The times of the highest (P > .99) and lowest (P = .19) plasma cortisol concentrations did not differ among the groups.

**Blood Glucose and Plasma Insulin**

The preprandial and postprandial blood glucose and plasma insulin levels did not differ between night eaters and controls among either the overweight or normal-weight groups.

**COMMENT**

This study revealed a surprising coherence of the behavioral 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, quite unexpectedly, nighttime awakenings during half of which food was ingested. This distinctive circadian pattern of behavior 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. The circadian neuroendocrine findings included attenuation of the usual nighttime rise in melatonin and leptin as well as elevated levels of plasma cortisol.

Night-eating syndrome appears to represent a new eating disorder, different from the established disorders of anorexia nervosa, bulimia nervosa, and binge eating disorder. It differs from the latter 2 disorders in the frequency and size of ingestions, particularly at night. In contrast to the very frequent night eating of persons with NES, Greeno et al11 reported that only 6 of 40 patients with binge eating disorder ever ate at night and did so only once a week. The size of ingestions by the night eaters...
(1134 kJ) is far smaller than that of patients with bulimia nervosa (7987 kJ) whom we studied, than that reported by Rosen et al12 (6104 kJ), by Rossiter and Agras13 (4908 kJ), and by patients with binge eating disorder reported by Grilo and Schiffman (5263 kJ).14 Clearly they do not represent “objective binges”15 or “night binging.”

The carbohydrate-rich (70.3%) nighttime snacks, especially the high carbohydrate to protein ratio (7:1), suggests that night eating is designed to restore the disrupted sleep of the night eaters. It has been reported that this pattern of eating increases the availability of tryptophan for transport into the brain and conversion into serotonin,16,17 resulting in facilitation of sleep.

Night-eating syndrome appears to differ also from the “nocturnal sleep-related eating disorders” reported by sleep disorder clinics and characterized by eating upon awakening from sleep, often in association with sleepwalking and related sleep disturbances. The relation between these disorders and NES is unclear, in part because of uncertainty regarding the nature of the former disorders. Thus, they have been reported either mostly in infants18 or mostly in adults,19,20 primarily during sleep19,20 or primarily during wakefulness,20,22 and with19,21 or without20 polysomnographic evidence of parasomnias. These inconsistencies may contribute to the uncertainty regarding their prevalence. For example, Schenk and Mahowald19,22 reported only 38 (0.5%) cases out of approximately 8000 polysomnographic examinations, whereas Manni et al23 reported 18 (15%) cases out of 120.

As noted above, the criterion for the time of onset of night eating differed between the behavioral and neuroendocrine studies to accommodate the different supper times in Philadelphia and Tromsø, Norway. Supper occurs even later in the Mediterranean cultures but NES is still defined there as overeating following the evening meal. These considerations make it appropriate to establish the onset of night eating as that which occurs after the end of the evening meal rather than by hour of the day (TABLE).

The minimal criteria used to define NES identified not only persons with eating disorders but also those with sleeping and probably mood disorders. The criteria also identified persons with a distinctive neuroendocrine pattern: attenuation of the usual nocturnal rise in melatonin and leptin levels and an elevated level of cortisol throughout the day. There is an intriguing concurrence between the salient neuroendocrine findings—attenuation of the nocturnal elevation in melatonin and leptin—and the salient behavioral findings of nighttime awakenings, often linked with eating.

Melatonin appears to induce and maintain sleep.24 Diminished melatonin levels have been associated with impaired sleep25-28 and documented in those individuals with depression.29 It has been proposed that this hypomelatoninemia may be involved in the causal chain leading to impaired sleep.27,28 The attenuation of the nocturnal rise in melatonin that we observed in night eaters may well play a similar role in their nighttime awakenings.

Attenuation of the nocturnal rise in leptin may also contribute to the nighttime awakenings and the associated food intake. Leptin levels rise at night,30 and Sinha et al31 have proposed that this rise suppresses appetite and helps to maintain sleep, but Matkovic et al32 suggest that attenuation of this rise prevents adequate suppression of appetite. The latter sequence may have

**Figure 3. Circadian Leptin Levels**

![Circadian Leptin Levels](https://jama.jamanetwork.com/content/282/7/661.fgh)

Twenty-four–hour mean plasma leptin levels in night eaters (7 overweight, 5 normal-weight) and control subjects (10 overweight, 11 normal-weight). Asterisks and brackets indicate significant differences in levels of nocturnal concentrations (when compared with the baseline concentrations at 8 AM) between night eaters and control subjects, both overweight and normal-weight (P<.001). NES indicates night-eating syndrome.
occurred in night eaters in this study, with the breakthrough of urges to eat and the resultant disruption of sleep.

The attenuation of the nocturnal rise in leptin and melatonin may be related through the agency of corticotropin-releasing hormone (CRH), which suppresses the secretion of melatonin. We did not measure CRH, but 3 findings suggest that CRH levels are increased. First, the lack of a nocturnal increase in leptin removes the leptin-mediated inhibition of CRH, resulting in an increase in levels of CRH. Second, the elevated plasma levels of cortisol reflect increased activity of CRH. Third, stress influences CRH. Our relatively brief contact with the subjects of the 2 studies precludes assessment of their level of stress, although the lower mood and its deterioration during the course of the day is compatible with a stress response. In the 1955 study, however, intensive, long-term psychotherapy of 20 night eaters revealed that NES occurred during periods of life stress and, significantly, was alleviated with reduction of the stress.

The limitations of this report should be noted. The studies involved a small number of subjects and were conducted in different settings with different patients. The behavioral data were collected on an ambulatory basis during 1 week in which subjects had access to food at night. The neuroendocrine data were collected in a clinical research department during a 24-hour period in which the last meal was eaten at 8 PM. The distribution of ages and body weights of subjects in the 2 studies did not differ significantly, however, and, with 4 exceptions, all subjects were women. In the neuroendocrine study, it is possible that the restriction of nighttime food intake may have stressed the night eaters and affected the neuroendocrine results. However, in our experience, night eaters do not persist in their usual eating patterns in the hospital. It was thought that our design of 4 small meals was most likely to reveal circadian patterns. The concurrence between the behavioral and neuroendocrine findings suggests that NES is a sufficiently robust phenomenon to be identified despite the limitations noted in this report. Data from future behavioral and neuroendocrine studies should, however, be collected from the same population.

Delineation of a new syndrome raises the question of treatment, and features of NES suggest potentially fruitful approaches. Thus, the presence of a sleep disorder linked to attenuation of the nighttime rise in melatonin suggests administration of exogenous melatonin. The night eating related to attenuation of the nighttime rise in leptin might be corrected by the administration of exogenous leptin. Subjects’ ingestion of high-carbohydrate snacks suggests an attempt to improve sleep and mood by raising levels of serotonin; selective serotonin reuptake inhibitors might more readily achieve this goal. Measures to control stress may be useful in alleviating NES. More modern pharmacotherapy, such as the use of CRH receptor antagonists, may be added to the old prescription of psychotherapy.

**Table.** Provisional Criteria for Night-Eating Syndrome

| Morning anorexia, even if the subject eats breakfast |
| Evening hyperphagia, in which ≥50% of the daily energy intake is consumed after the last evening meal |
| Awakenings at least once a night |
| Consumption of snacks during the awakenings |
| Repetition of the provisional criteria for ≥3 mo |

Subjects do not meet criteria for bulimia nervosa or binge eating disorder.
CHARACTERISTICS OF THE NIGHT-EATING SYNDROME

REFERENCES