

Assessment of Sleep in Women With Night Eating Syndrome

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Study Objectives: Evaluation of sleep in subjects with night eating syndrome (NES).

Design: Polysomnographic and questionnaire comparisons between subjects with NES and controls.

Setting and Participants: Fifteen women with NES (mean \pm SD = 41 \pm 8 years) and 14 women (comparable age and weight) without NES (39 \pm 10 years) were studied in the laboratory for 3 days.

Interventions: N/A.

Measurements and Results: Subjects with NES did not differ from controls in timing of sleep onset or offset. They had less stage 2 sleep than controls (minutes, $p = .012$; percentage, $p = .016$) and less stage 3 sleep ($p = .023$), which contributed to their having a lower total sleep time ($p = .05$) and reduced sleep efficiency ($p = .03$). Subjects with NES did not have more awakenings than controls, but 93.3% of them ate on awakening during all 3 nights, while 92.9% of controls did not eat on any night. Logistic discriminant analyses identified a multiple sleep parameter model

associated with increased likelihood of NES that had sensitivity of 84.6% and specificity of 76.9%. Patients with NES were more depressed than controls ($p < .001$) and reported greater sleep disturbance that included lower sleep quality ($p \leq .001$), reduced sleep duration ($p \leq .001$), and increased number of awakenings ($p \leq .001$).

Conclusions: Patients with NES appear to have sleep maintenance insomnia rather than sleep-related eating disorder or a parasomnia. The maintenance of normal timing for sleep-wake behavior in the presence of a phase delay in the timing of caloric intake suggests this disorder reflects a state of internal circadian desynchrony associated with significant sleep complaints. It remains unknown whether the sleep disturbance precedes the abnormally timed eating.

Keywords: Night eating syndrome, polysomnography, subjective sleep assessments

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INTRODUCTION

THE NIGHT EATING SYNDROME (NES), FIRST DESCRIBED IN 1955,¹ CONSISTS OF MORNING ANOREXIA, EVENING HYPERPHAGIA WITH CONSUMPTION OF AN average of 35% of daily caloric intake after the evening meal, sleep-onset insomnia, and awakenings at least once a night on at least 3 nights per week with consumption of snacks on most of these awakenings.^{2,3} NES was first noted among obese patients,¹ but it also occurs among nonobese persons.⁴ Its prevalence has been estimated at 1.5% in the general population,⁵ 8.9% in an obesity clinic,⁶ 12.3% in two psychiatry clinics,⁷ and from 9%⁸ to 28%⁵ among

extremely obese persons seeking bariatric surgery.

It is important to distinguish NES from similar disorders associated with eating and sleeping, in particular, sleep-related eating disorder (SRED).⁹ Clinical characteristics of SRED consist of eating with partial or no awareness at the time and partial or full amnesia for the episode afterward. Large amounts of food and often bizarre items, such as buttered cigarettes, are consumed following awakenings from non-rapid eye movement (REM) sleep.⁹ SRED most often occurs in persons with past or current histories of sleepwalking but also in those with restless legs syndrome, periodic movements of sleep, obstructive sleep apnea, and at times in those with other sleep disorders. Its prevalence in a sleep disorder clinic has been reported as very low—only 38 out of 8066 patients (0.47%),¹⁰ although there is evidence that SRED is more common than is generally recognized, especially in those with a daytime eating disorder.¹¹

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While both SRED and NES appear to be more common in women than in men and share a number of overlapping features these two disorders are distinct from one another in a number of characteristics, in addition to their prevalence. Unlike SRED, NES is distinguished by overeating between the evening meal and nocturnal sleep onset, eating during complete awakenings from sleep with full subsequent recall, absence of bizarre food consumption, and absence of an associated primary sleep disorder.

Two studies have investigated sleep patterns in patients with NES using polysomnography (PSG), in a clinical setting.^{12,13} Patients were observed to have frequent awakenings, many of which were associated with food consumption. These studies did not include a control group, however.

The current investigation builds on our earlier study of sleep and eating by 46 subjects with NES and 43 control subjects in the home, over a period of 1 week, using actigraphy, questionnaires, and sleep and food diaries. Subjects with NES had

significantly more awakenings than control subjects (1.5 ± 1.0 /night vs 0.5 ± 0.5 /night).² This outpatient study found no difference in the timing of sleep onset, sleep offset, and sleep duration between the two groups.² The primary aim of the present study was to polysomnographically assess sleep in patients with NES and age-matched, healthy control subjects who had been studied in our earlier outpatient study. Secondary analyses compared the degree of subjective sleep disturbances reported by these two groups.

METHODS

Subjects

Fifteen patients with NES (mean age 41 ± 8 years) and 14 control subjects, (mean age 39 ± 10 years), all women, completed the protocol. Subjects were recruited directly from an outpatient study, in which we investigated at-home sleep patterns using actigraphy, questionnaires, and sleep and food diaries. Prior to entry into the initial study, patients reported the presence of NES on a Night Eating Questionnaire.⁴ Those who met criteria completed the 1-week outpatient study to confirm the presence or absence of NES, which included 7 days of keeping sleep and food diaries and wearing actigraphs (Actiwatch, Minimitter, Bend, OR) at home. Subjects then underwent a complete history and physical examination and assessment of blood chemistries, electrocardiogram, blood count, urinalysis, and urine pregnancy test.

Subjects were excluded from the study if they were diagnosed with diabetes mellitus, thyroid disease, or other endocrine or metabolic disorders; were currently participating in a weight loss program; were severely depressed, as determined by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria; had a lifetime diagnosis of bipolar disorder or any psychotic disorder; reported substance abuse or dependence within the last 6 months; were currently taking any psychotropic medications (including hypnotics); were working a night-shift or swing shift schedule; were diagnosed with another eating disorder; had an increased risk for sleep apnea, as determined by either the Multivariable Apnea Risk Index (MAP¹³) or clinical PSG assessment on the first night of the in-laboratory study; or if they lacked awareness of their night eating at the time and amnesia for it later, indicative of the presence of SRED. The University of Pennsylvania Institutional Review Board approved the study protocol and consent form, and subjects gave written voluntary informed consent. Subjects were compensated for their involvement in this study.

Procedures

Subjects entered the General Clinical Research Center of the Hospital of the University of Pennsylvania for a 3-night protocol that included 2 nights of PSG sleep assessment and 25 hours of blood sampling for neuroendocrine analysis (reported elsewhere).¹⁵ Subjects were allowed to eat ad libitum throughout the protocol and brought snacks that were placed next to their beds, readily available throughout the night.

Sleep Physiology

Nocturnal PSG recordings were collected on 2 consecutive nights. Night 1 was considered an adaptation night and included a clinical assessment to detect the presence of occult sleep dis-

orders, such as obstructive sleep apnea syndrome, periodic limb movements of sleep, or restless legs syndrome. No subjects were suffering from any occult sleep disorder. Sleep variables collected on night 2, using a standardized research PSG montage (electroencephalogram, electrooculogram, electromyogram), were used for analysis. Sleep stages were visually scored on a computer screen using standardized criteria.¹⁶

Awakenings

In addition to standard sleep scoring, the frequency and duration of awakenings from sleep were measured, as was the sleep stage from which the awakening occurred. An awakening was defined as three or more consecutive 30-second epochs of wakefulness. The two subject groups were compared for total awakenings and for awakenings that were 5 minutes or greater in duration.

Questionnaires

Subjects completed four questionnaires asking about their sleep quality, sleep disturbance, circadian preference, and daytime sleepiness levels. The Pittsburgh Sleep Quality Index (PSQI¹⁷) assessed sleep quality and sleep disturbance during the previous 1-month period. The MAP index¹⁴ was initially used to screen out subjects with increased sleep apnea risk and then to provide information regarding other sleep disturbances. In addition to sleep apnea risk, the MAP questionnaire included four sleep-related symptom-frequency indexes: Index 1: sleep-disordered breathing; Index 2: difficulty sleeping; Index 3: excessive daytime sleepiness; and Index 4: narcolepsy-like symptoms, each providing self-reports of recent symptom frequency in terms of days or nights per week. The Morningness-Eveningness Scale¹⁸ provided an indication of circadian preference. The Epworth Sleep Scale¹⁹ (ESS) assessed daytime sleepiness levels by asking about the likelihood of falling asleep while engaged in a number of passive and active waking activities, including watching television, driving a car, and sitting quietly. Epworth Sleepiness Scale values of 11 or greater are conventionally used to indicate elevated daytime sleepiness. The Beck Depression Inventory²⁰ was used to evaluate the possibility of differences in depression between subjects with NES and control subjects.

Statistical Analyses

Assessment of NES versus control-group differences in a set of 22 PSG sleep variables was considered the primary analysis of this study. Subjective ratings were assessed in secondary analyses. In primary analyses, Student t-tests were first used to assess the “strength of the signals” reflecting real differences in the 22 PSG sleep-architecture parameters between patients with NES and control subjects. The impact of multiple comparisons was addressed in two ways. The stepdown bootstrap technique of Westfall and Young was used to determine the likelihood that there would be at least one false-positive finding, assuming all null hypotheses of no group differences were true.²⁰ Because of the exploratory nature of this study, we also undertook an alternative approach to quantitatively evaluate the impact of multiple comparisons quantitatively using a method often applied to control the effects of multiple comparisons in gene discovery and in functional magnetic resonance imaging evaluations. Thus, we used the method of Benjamini and Hochberg²¹ to determine the expected percentage of rejected null hypotheses that were falsely

Table 1—Characteristics of the Patients With Night Eating Syndrome (NES) and Control Subjects of Comparable Age and Weight

Variable	Patients with NES	Control subjects
No.	15	14
Age, y	41 ± 8	39 ± 10
BMI, kg/m ²	36 ± 7	38 ± 7
Race		
Caucasian 8 (53.3)	6 (42.9)	
African American	7 (46.7)	8 (57.1)
Marital status		
Married	5 (33.3)	5 (35.7)
Single	7 (46.7)	7 (50.0)
Separated or divorced	3 (20.0)	2 (14.3)
Education Level		
High school	5 (33.3)	6 (42.9)
Two-year college	6 (40.0)	2 (14.3)
Four-year college	1 (6.7)	5 (35.7)
Graduate school	3 (20.0)	1 (7.1)
Employment Status		
Full time 7 (46.7)	8 (57.1)	
Part time 3 (20.0)	1 (7.1)	
Homekeeper	2 (13.3)	2 (14.3)
Looking for work	2 (13.3)	2 (14.3)
Unable to work	1 (6.7)	1 (7.1)

Age and body mass index (BMI) are presented as mean ± SD. All other variables show the number of subjects (%).

rejected and various statistical significance levels. This percentage—known as the realized false discovery rate—provides an alternative measure to control the impact of multiple comparisons when the goal is to characterize the likely overall pattern of group differences but allows for a known small number of false positives. Exploratory multivariate evaluations were implemented using a stepwise logistic discriminant analysis in order to evaluate whether group differences in sleep architecture could be reliably summarized based in a parsimonious fashion using a small number of PSG variables. Multiple comparison analyses were implemented using the SAS procedure MULTTEST and the logistic regression analyses implemented using the SAS procedure LOGISTIC (SAS Online Documentation Version 9.1, SAS Institute, Cary, NC, <http://support.sas.com/91doc/docMainpage.jsp>).

RESULTS

There were no significant differences between patients with NES and control subjects in mean age, height, weight, or body mass index. The two groups were comparable demographically. A summary of their demographics is presented in Table 1.

Sleep Hypnogram

Figure 1 illustrates a typical PSG of a subject with NES and a control subject. A summary of the sleep variables is contained in Table 2. Among 22 PSG parameters evaluated, five differed at $p < .05$ between patients with NES and control subjects (two differed at $p < .10$). Multiple comparison analyses indicated an expected false discovery rate of 21.8% for $p < .05$ (29.7% for $p < .10$) such that one of the PSG variables with $p < .05$ (two PSG variables for $p < .10$) were expected to be false positives. The observed p values and Benjamini and Hochberg²⁰ realized false discovery thresholds for $\alpha = .05$ (and $\alpha = .10$) are illustrated in Figure 2. The Westfall and Young stepdown bootstrap estimated probability of at least one false positive under the

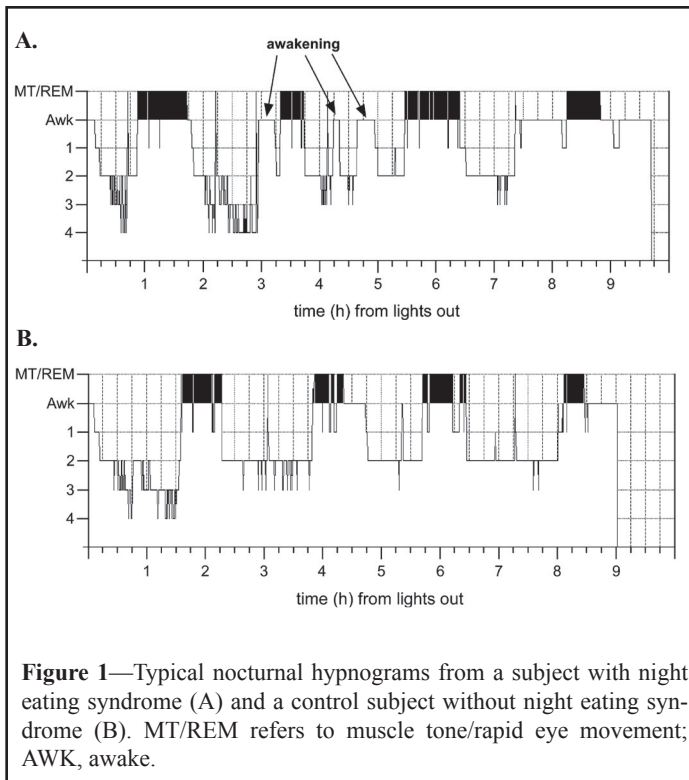


Figure 1—Typical nocturnal hypnograms from a subject with night eating syndrome (A) and a control subject without night eating syndrome (B). MT/REM refers to muscle tone/rapid eye movement; AWK, awake.

global null hypothesis of no group differences in PSG variables was determined to be 15%. The potential differences between those with and without NES included less stage 2 sleep in subjects with NES ($p = .012$), a lower percentage of stage 2 sleep ($p = .016$), less stage 3 sleep ($p = .023$), a reduced sleep efficiency ($p = .030$), reduced total sleep time in subjects with NES ($p = .049$), and a trend toward a greater frequency of awakenings ($p = .069$) and increased percentage of sleep in REM ($p = .094$). Logistic discriminant analyses identified a model containing number of awakenings, percentage of sleep in REM, and total minutes of stage 3 sleep as simultaneously associated with an increased likelihood of NES. All 3 variables were among the 7 with the smallest crude p values. All three 95% confidence intervals (CI) excluded 1.0. A 1-SD increase ($SD = 2.1$) in the number of awakenings was associated with a 5.2-fold (95% CI, 1.5 to 38.6) increase in the odds of NES. Similarly, a 1-SD increase ($SD = 5.9\%$) in the percentage of sleep spent in REM was associated with a 9.0-fold (95% CI, 1.5 to 302.4) increase in the odds of NES. In contrast, a 1-SD decrease ($SD = 10.2$) in total stage 3 minutes was associated with a 12.3-fold increase (95% CI, 2.1 to 285.2) in the odds of NES. The area under a receiver operating characteristic curve for the logistic predictive model was 0.923.²³

Awakenings

Subjects with NES had a total of 78 PSG awakenings of 1.5 minutes or longer (79% from non-REM sleep and 21% from REM sleep), whereas control subjects had a total of 47 PSG awakenings (81% from non-REM sleep and 19% from REM sleep.) Subjects with NES had a total of 54 awakenings that were 5 minutes or longer (76% from non-REM and 24% from REM sleep) compared with the control subjects, who had 29 awakenings that were 5 minutes or greater (69% from non-REM and 31% from REM sleep). None of these differences were statistically reliable.

Despite no differences in the frequency of awakenings, subjects with NES and controls differed in whether food was consumed during an awakening. On PSG clinical assessment night 2, 14 out of 15

Table 2—Differences in Sleep Polysomnography (PSG) Between Patients With Night Eating Syndrome (NES) and Control Subjects of Comparable Age and Weight

PSG variable	Patients with NES	Control subjects	p Value
Time of sleep onset ^a	23:38 ± 1:59	22:52 ± 1:04	
Time of sleep offset ^a	07:04 ± 0:48	07:06 ± 0:41	
Sleep efficiency, %	71.5 ± 17.2	83.3 ± 7.3	.030
Total sleep time, min	354.9 ± 96.7	421.2 ± 68.5	.049
Sleep-onset latency, min	25.6 ± 29.3	16.2 ± 22.8	
REM-onset latency, min	71.6 ± 47.3	85.2 ± 60.7	
Sleep stage, min			
1	39.0 ± 21.5	37.1 ± 15.7	
2	164.6 ± 75.6	235.0 ± 60.6	.012
3	29.2 ± 8.2	38.0 ± 10.7	.023
4	24.4 ± 24.6	26.1 ± 22.9	
SWS	53.6 ± 29.6	64.1 ± 26.6	
REM	94.6 ± 31.3	85.5 ± 23.0	
Sleep stage, %			
1	8.2 ± 4.0	7.6 ± 3.3	
2	37.5 ± 11.9	47.8 ± 8.7	.016
3	6.8 ± 1.8	7.7 ± 2.0	
4	5.2 ± 4.7	5.5 ± 4.7	
SWS	11.7 ± 5.3	13.3 ± 5.5	
REM	21.3 ± 7.1	17.3 ± 4.3 ^b	
WASO, min	59.3 ± 48.6	39.0 ± 38.8	
Awakenings			
No.	4.5 ± 1.6	3.1 ± 2.1 ^c	
Latency to first, min	71.0 ± 47.9	50.0 ± 38.1	
Duration final, min	14.3 ± 18.7	6.8 ± 7.5	

Data are presented as mean ± SD. REM, rapid eye movement sleep; SWS, slow-wave sleep; WASO, wake after sleep onset.

^aTime of day: 00:01-24:00

^bDifference at $p = .069$

^cDifference at $p = .094$

subjects with NES awoke and ate at least once during the night, compared with none of the control subjects. Across all 3 inpatient nights, 14 of 15 subjects with NES (93.3%) ate on at least 2 of the 3 nights, whereas one control subject ate on 1 night. In comparison, 13 of 14 control subjects (92.9%) did not eat on any of the nights, whereas one NES subject did not eat on 1 night.

Napping

During the 3 inpatient days of the study, 60% of subjects with NES napped at least once, for a total of 12 naps (mean duration 47.5 min [SD = 14.7 min]), compared with 50% of control subjects, for a total of 14 naps (mean duration 61.9 min [SD = 35.2 min]). Neither the proportion of days with naps nor nap duration was significantly different between subjects with NES and control subjects.

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index showed a significantly

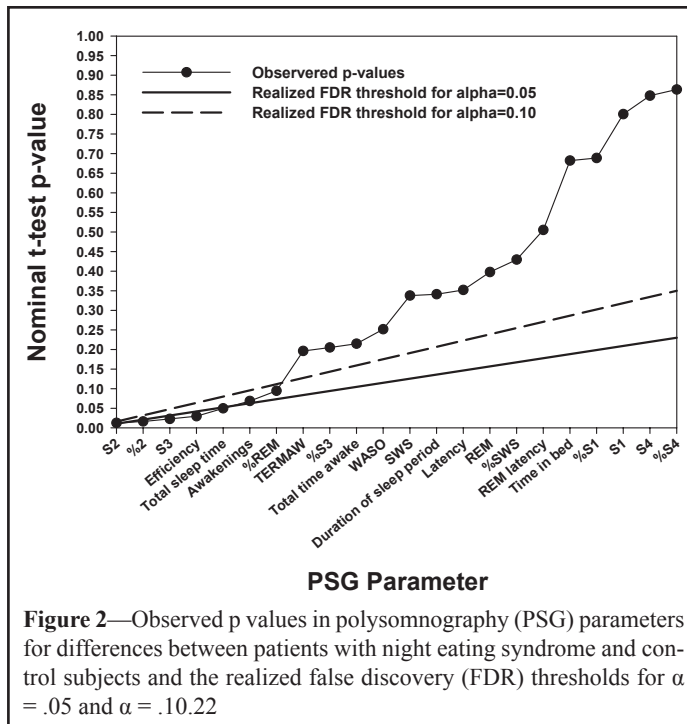


Figure 2—Observed p values in polysomnography (PSG) parameters for differences between patients with night eating syndrome and control subjects and the realized false discovery (FDR) thresholds for $\alpha = .05$ and $\alpha = .1022$

higher level of subjective sleep disturbances in the NES group compared with the control group. Relative to controls, NES subjects reported taking significantly longer to fall asleep ($p = .004$), a shorter sleep duration ($p \leq .001$), reduced sleep quality ($p \leq .001$), and increased consumption of sleep medications ($p = .035$). The subscales of the Pittsburgh Sleep Quality Index showed that subjects with NES also had significantly more trouble than control subjects in falling asleep ($p \leq .001$), more awakenings ($p \leq .001$), more episodes of being unable to breathe ($p = .044$) and coughing ($p = .039$), being too cold ($p = .001$), and having a greater frequency of having bad dreams ($p = .040$) and an increased incidence of leg twitching ($p = .020$).

Beck Depression Inventory

Although subjects were excluded from the study if they were severely depressed, as determined by the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Beck Depression Inventory scores were significantly higher in subjects with NES (mean ± SD; 19.7 ± 10.0) than in controls (3.9 ± 3.6, $p < .001$).

MAP Index

Subjects with NES reported via the MAP index a significantly higher frequency of symptoms of excessive daytime sleepiness, as compared with control subjects ($p = .003$), with no significant differences between the 2 subject groups on the remaining 3 indexes (sleep-disordered breathing, difficulty sleeping, and narcolepsy-like symptom frequency).

Morningness-Eveningness Scale

The Morningness-Eveningness Questionnaire showed no significant differences between subjects with NES and control subjects in their circadian preference, their usual time of going to bed or waking, the time of day at which they feel most tired, their preferred time for rising to go to work, and their alertness during the first 30 minutes following morning awakening. Subjects with

NES reported feeling significantly less refreshed during the first 30 minutes following awakening ($p = .020$), experiencing greater difficulty in rising if forced to wake at 6:00 AM ($p = .035$), and requiring more time to recover their senses upon awakening ($p = .011$), compared with control subjects.

Epworth Sleepiness Scale

There was no significant difference in mean Epworth Sleepiness Scale scores between the NES and control groups.

DISCUSSION

This study was the first systematic evaluation of sleep PSG in patients with NES relative to healthy control subjects of comparable age and weight. Subjects with NES displayed significant objective and subjective evidence of sleep disturbance. However, the timing of their physiologic sleep onset and offset were normal, which is consistent with our outpatient study of their sleep-onset and awakening times at home²; their average sleep onset at home was at 11:57 PM \pm 1:33, compared with 11:38 PM \pm 1:59 in the laboratory, and their average sleep offset at home was at 7:35 AM \pm 1:11, compared with 7:04 AM \pm 0:48 in the laboratory. From the standpoint of sleep timing, their laboratory sleep was representative of their sleep at home.

Despite sleep timing similar to that of controls, once asleep, subjects with NES had reduced non-REM stage 2 and stage 3 sleep time, which contributed to their reduced total sleep time and reduced sleep efficiency relative to controls. Although PSG showed no extended sleep latencies in subjects with NES, on the Pittsburgh Sleep Quality Index, they reported significantly more trouble falling asleep and taking longer to fall asleep than did control subjects. These complaints are consistent with subjects with NES having higher depression scores on the Beck Depression Inventory. The Pittsburgh Sleep Quality Index also revealed that NES patients were more likely to report an increased incidence of tossing and turning, leg twitches, coughing, and difficulty in breathing. While all the subjects were screened to be free of comorbid sleep disorders, such as periodic limb movements of sleep and obstructive sleep apnea syndrome, it is possible that some patients with NES may have milder forms or early stages of these disorders.

Logistic discriminant analyses identified a model containing number of awakenings, percentage of sleep in REM, and total minutes of stage 3 sleep as simultaneously associated with increased likelihood of NES, which suggests that the profile of sleep architecture group differences is multidimensional. The area under a receiver operating characteristic curve for the logistic predictive model was 0.923. That is, if one subject with NES and one control subject are selected at random and evaluated (blind to condition) relative to these three variables based on the logistic model, the subject with NES will have a larger predicted probability of having NES than the control subject 92% of the time. A cutoff of 0.5 had a sensitivity of 84.6% and specificity of 76.9%. Why these sleep parameters combined to provide such robust discrimination between NES and healthy controls is unclear, but the role of depression in NES cannot be ruled out.²⁴ The PSG findings require replication and perhaps concomitant study of peripheral physiologic signals to eat, to determine if such signals during sleep produce not only awakenings, but also decreased amounts of stage 3 sleep and increased REM sleep.

The 24-hour ingestions of subjects with NES at home show a strong circadian pattern, with the rate of eating increasing over the course of the day.^{2,15} In NES, the increased consumption of energy is not confined to the sleep period, but rather occurs across the evening and nighttime hours. This phenomenon makes it most unlikely that NES is a parasomnia and suggests instead that the sleep disturbance associated with this disorder is secondary to the shifted eating profile. On the other hand, the natural history of NES is not sufficiently understood to conclude whether or not the insomnia-like symptoms of these patients occurred prior to the emergence of eating at night, or vice versa. It is possible that sleep disruption following a traumatic event was a predisposing factor for NES, such that the sleep maintenance problem became conditioned to eating, ultimately resulting in a phase delay of the energy-intake profile relative to the sleep-wake cycle.^{2,15} This possibility is consistent with a preliminary report, in which the disorder began after a traumatic life event in 76% of patients²⁵, and it fits with evidence that there is substantial heterogeneity in the variability of night-to-night sleep among people with chronic insomnia.²⁶

Elsewhere, we have suggested that NES may be maintained by a circadian disorder,² which results from a desynchrony between the primary circadian oscillator, located in the suprachiasmatic nuclei of the anterior hypothalamus,²⁷ and peripheral oscillators in the liver that may be entrained by food timing.²⁸ Not only was the sleep-wake timing of NES patients comparable to controls in both our outpatient study² and this inpatient study, but it is noteworthy that there were also no significant differences between the two groups with regard to circadian preference, as measured by the Morningness-Eveningness Scale—both were in the normal range. In contrast, the timing of food intake by patients with NES was phase delayed,^{2,15} and there were alterations of glucose, insulin, and ghrelin levels, consistent with delayed energy intake.¹⁵ Thus, the findings from the present study are consistent with a normally entrained sleep-wake cycle and a phase-delayed profile of eating behavior in NES, which appears to disrupt sleep.

The PSG findings indicate that patients with NES do not show evidence of SRED. Subjects with NES ate after awakening at least once a night on virtually every night of the 3 nights in the hospital, whereas control subjects virtually never ate. During the eating episodes, not only did subjects with NES report that they were fully conscious, but PSG showed no evidence of slow-wave sleep during arousals, which is characteristic of SRED ingestions. NES and SRED appear to be different disorders in terms of sleep pathology.

Patients with NES did not show an increased tendency to fall asleep during the daytime on the Epworth Sleepiness Scale, but excessive daytime sleepiness and reduced daytime functioning were indicated by the excessive daytime sleepiness symptom frequency index on the MAP and the Morningness-Eveningness scale. This suggests that subjects with NES had greater difficulties with feeling refreshed and in their ability to rise easily in the mornings. This finding may be due to the reduced sleep efficiency and sleep duration of patients with NES, as well as reflecting an ability to recognize broad functional deficits without recognizing specific deficits in waking function. Both healthy and insomniac populations have decreased ability to self-rate their sleep and sleepiness levels with respect to objective measures.^{26,29}

In summary, we report sleep-wake patterns in patients with NES assessed using PSG in the laboratory that are consistent with our

studies of these patients at home using actigraphy, questionnaires, and sleep and food diaries. Their sleep is disturbed physiologically, as manifested by reduced sleep quantity and quality, making them more similar to insomniacs than to patients with SRED. The findings are consistent with our earlier hypothesis that NES is maintained by a circadian-based sleep disorder and possibly by depression, with patients demonstrating normal entrainment to the 24-hour day with regard to their sleep-wake behavior, whereas the circadian pattern of eating is delayed, resulting in sleep being disturbed by awakenings to eat. Further studies are required to determine what aspects of the circadian and sleep systems perpetuate the disorder and how it is most effectively treated.

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REFERENCES

1. Stunkard AJ, Grace WJ, Wolff HG. The night-eating syndrome: A pattern of food intake among certain obese patients. *Int. J. Med.* 1955;19:78-86.
2. O'Reardon JP, O'Reardon JO, Ringel BL, et al. Circadian eating and sleeping patterns in the night eating syndrome. *Obes Res.* 2004;12:1789-96.
3. Birketvedt GS, Florholmen J, Sundsfjord J, et al. Behavioral and neuroendocrine characteristics of the night-eating syndrome. *J Am Med Assoc* 1999;282:657-63.
4. Marshall HM, Allison KC, O'Reardon JP, Birketvedt GS, Stunkard AJ. Night eating syndrome among nonobese persons. *Int J Eating Dis* 2004;35:217-22.
5. Rand CS, Macgregor AM, Stunkard AJ. The night eating syndrome in the general population and among postoperative obesity surgery patients. *Int J Eating Dis* 1997;22:65-9.
6. Stunkard AJ, Berkowitz R, Wadden T, Tanrikut C, Reiss E, Young L. Binge eating disorder and the night eating syndrome. *Int J Obes Relat Metab Disord* 1996;20:1-6.
7. Lundgren JD, Allison KC, Crow S, et al. Prevalence of the night eating syndrome in a psychiatric population. *Am J Psychiatry*, 2006;163:156-8.
8. Allison KC, Wadden TA, Sarwer DB, et al. Night eating syndrome and binge eating disorder among persons seeking bariatric surgery: prevalence and related features. *Obes Res* 2006: In Press.
9. The International Classification of Sleep Disorders: Diagnostic and Coding Manual, 2nd ed. Westchester, Ill: American Academy of Sleep Medicine; 2005.
10. Schenk CH, Mahowald MW. Review of nocturnal sleep-related eating disorders. *Int J Eating Dis* 1994;15:343-56.
11. Winkelman JW, Herzog DB, Fava M. The prevalence of sleep-related eating disorder in psychiatric and non-psychiatric populations. *Psychol Med* 1999; 29:1461-6.
12. Spaggiari MC, Granella F, Parrino L, Marchesi C, Melli I, Terzano MG. Nocturnal eating syndrome in adults. *Sleep* 1994;17:339-44.
13. Manni R, Ratti MT, Tartara A. Nocturnal eating: Prevalence and features in 120 insomniac referrals. *Sleep* 1997;20:734-8.
14. Maislin G, Pack AI, Kribbs NB, et al. A survey screen for prediction of apnea. *Sleep* 1995;18:158-66.
15. Allison KC, Ahima RS, O'Reardon JP, et al. Neuroendocrine profiles associated with energy intake, sleep, and stress in the night eating syndrome. *J Clin Endocrinol Metabol* 2005;90:6214-7.
16. Rechtschaffen A, Kales A, eds. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Los Angeles: Brain Information Service/Brain Research Institute; 1968.
17. Buysse DJ, Reynolds CFd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Res* 1989;28:193-213.
18. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *Int J Chronobiol* 1976;4:97-110.
19. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* 1991;14:540-5.
20. Beck, A.T. The Beck Depression Inventory II. San Antonio: Harcourt Brace; 1996.
21. Westfall PH, Young SS, eds. Resampling-based multiple testing: Examples and methods for p-value adjustment. New York: John Wiley & Sons, Inc.; 1993.
22. Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J R Stat Soc* 1995;57:289-300.
23. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic curve (ROC). *Radiology* 1982;143:29-36.
24. Tsuno N, Besset A, Ritchie K. Sleep and depression. *J Clin Psychiatry* 2005;66:1254-69.
25. Stunkard AJ, Allison KC, O'Reardon JP. The night eating syndrome: New findings. *Obes Res* 2003;11:A23.
26. Vallieres A, Ivers H, Bastien CH, Beaulieu-Bonneau S, Morin CM. Variability and predictability in sleep patterns of chronic insomniacs. *J Sleep Res* 2005;14:447-53.
27. Moore RY. Organization and function of a central nervous system circadian oscillator: The suprachiasmatic hypothalamic nucleus. *Fed Proc* 1983;42:2783-9.
28. Stokkan K, Yamazaki S, Tei H, Sakaki Y, Menaker M. Entrainment of the circadian clock in the liver by feeding. *Science* 2001;291:490-3.
29. Dorrian J, Lamond N, Dawson D. The ability to self-monitor performance when fatigued. *J Sleep Res* 2000;9:137-44.