Sleep and Sleepiness in Children with Nocturnal Enuresis

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Study Objectives: To assess if sleep patterns and sleepiness are compromised in children with nocturnal enuresis (NE), in comparison with normal control subjects, and to evaluate the role of enuresis-related events during sleep.
Design: Assessment of natural sleep patterns at home in a sample of children referred to enuresis clinics and controls.
Setting: Children's homes.
Participants: Thirty-two children (19 boys and 13 girls aged 5.1 to 9.1 years) who suffer from primary NE and 94 healthy control subjects (49 boys and 45 girls aged 5 to 8.58 years).
Interventions: N/A.
Measurements and Results: Sleep measures were derived from 3 to 5 nights of actigraphy and daily logs. Additional information on events related to enuresis and daytime sleepiness was collected using daily reports. Children with NE slept significantly worse than did the control subjects. Their compromised sleep patterns were reflected in a higher number of actigraphic nighttime awakenings, the reduced percentages of motionless sleep, the higher number of reported nighttime awakening, and the increased sleep latency. Children with NE also reported higher levels of sleepiness in the morning and in the evening.
Conclusions: Compared with the sleep of control subjects, the natural sleep of children with NE is significantly more fragmented, and the children with NE experience higher levels of daytime sleepiness. This phenomenology is associated with bedwetting episodes and attempts to keep the child dry during the night. These findings may suggest that children with NE suffer from sleep fragmentation, which may explain their higher arousal threshold. These findings have clinical implications for enuresis management.
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NOCTURNAL ENURESIS (NE) IS ONE OF THE MOST COMMON PROBLEMS IN PEDIATRICS.[1-4] PREVALENCE RATES OF NE RANGE BETWEEN APPROXIMATELY 3% and 15%, depending on its definition.[2,5-8] The etiology of NE is complex, and different models and explanatory factors have been proposed.[4,9,10] Butler[4,9] proposed the 3-systems model, which postulates that the following underlying factors are involved in NE: (1) excessive nocturnal urine production, (2) nocturnal bladder overactivity, and (3) failure to awaken in response to bladder sensations. This third component is related to sleep, which is the focus of the present study.

Sleep-related factors have often been implicated in the etiology and maintenance of NE.[10-13] Parents of children with NE often complain that the children's sleep is too deep, and, therefore, they fail to wake up in response to signals from their full bladder.[1-3,5,14,15] However, research focused on this question provided no clear support to the notion that NE is related to deep sleep. Polysomnographic studies have shown that NE episodes occur in all sleep stages.[16-19] Furthermore, polysomnographic studies have revealed no major differences in the sleep architecture of children with or without NE[11,16,17,19] and no major differences in the sleep of children with NE during wet versus dry nights.[20]

The fact that sleep architecture is quite similar in children with or without NE does not imply that the perceived difficulty of children with NE to arouse is unfounded. When arousal threshold during sleep has been evaluated using auditory stimuli, while controlling for sleep stages, the difficulty of children with NE to respond to auditory stimuli has been corroborated.[21,22] Because auditory arousal threshold has a clear developmental trajectory manifested in reduced threshold with age, this fact that children with NE have higher thresholds has been interpreted as a manifestation of a neurodevelopmental delay.[9,21,23,24]

Clinical experience and a review of the literature suggest that, in an attempt to cope with or manage the NE, many parents adopt methods associated with waking the child during the night or "maneuvering" the child to the toilet during sleep.[9] Because of these coping strategies, our main hypothesis was that sleep of children with NE would be significantly more disrupted than sleep in normal control subjects and that fragmented sleep in children with NE would be associated with higher reported daytime sleepiness.

In light of the growing interest in sleep and arousal in children with NE, our aim was to evaluate a relatively neglected but important issue, which is the naturalistic sleep and enuresis-related events during sleep in children with NE. Previous studies on sleep in children with NE have been based on either subjective reports, which have serious limitations, or on polysomnographic studies that significantly alter the natural sleep environment of the child. To the best of our knowledge, our study is the first actigraphy study comparing naturalistic sleep patterns in children with NE and controls.

METHODS

Participants

The study included 32 children (19 boys) referred to an enuresis clinic because of primary nocturnal enuresis (age

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Table 1—Sample characteristics

Demographic	Children with NE	Control children
Mother's age, y	36.8 ± 5.8	37.3 ± 4.3
Father's age, y	40.3 ± 6.0	40.0 ± 5.5
Mother's education, y	14.1 ± 2.3	14.7 ± 2.5
Father's education, y	15.4 ± 3.6	14.2 ± 2.3
Number of residents at home	4.3 ± 1.2	4.6 ± 0.8
Number of rooms at home	4.5 ± 0.9	4.8 ± 1.3
Number of children in family[a]	2.3 ± 0.8	2.7 ± 0.8
First or only child	44.8	30.9
Two-parent family	86.2	94.6

Data are displayed as mean ± SD or %. NE refers to nocturnal enuresis.
[a]Significant group difference, $P < 0.05$

range = 5.1-9.1 years, mean = 6.5, SD = 1.1) and 94 healthy control children (49 boys; age range = 5- 8.6 years; mean = 6.8, SD = 1.2).

Exclusion criteria included (1) reported active medical problems, (2) use of medication, and (3) underlying known urologic or other medical causes for enuresis. The control group was based on children participating in an earlier study on sleep patterns of normal children.[25]

The majority of children from both groups came from 2-parent families, both of whose education was at the higher end (see Table 1). The only significant difference between the groups was that families of the control sample had more children than did families in the clinical sample, $P < 0.05$.

Measures

Actigraphy

Actigraphy is based on a wristwatch-like device that can be worn by the child for an extended period and can monitor sleep-wake patterns in the child's natural sleep environment.[26-28] The children were instructed to attach the miniature actigraphs (Mini-Motionlogger, Ambulatory Monitoring, Inc., Ardsley, NY) to their nondominant wrist. Sleep assessment was performed for 5 continuous nights during school days. The actigraph collected data in 1-minute epochs. Sleep measures were derived from the raw data using the Actigraphic Scoring Analysis program (ASA) for an IBM-compatible PC. These sleep measures have been validated against polysomnography, with agreement rates for minute-by-minute sleep-wake identification higher than 90% in children and adults.[27,29,30]

Actigraphic measures included (1) true sleep time—sleep time excluding all periods of wakefulness, (2) the number of nighttime awakenings (lasting at least 5 min), (3) motionless sleep—the percentage of sleep without any detected motion (motionless sleep), and (4) the longest sleep period—the longest period of continuous sleep without any arousal. Sleep measures were averaged over all of the nights during the assessment period.

Sleep diary

The diary included items to be completed by the child and the parents. The evening items assessed sleep latency and the level of sleepiness prior to bedtime. The morning items assessed the level of morning sleepiness, the number of nighttime awakenings, and the specific reasons for waking up.[31]

Family background information questionnaire

This questionnaire included 25 questions covering demographic and developmental data.

Procedures

All parents signed informed consent. School-aged children also signed the forms, expressing their willingness to participate. Children completed 3 to 5 monitoring days. During the monitoring period, the children and their parents were asked to complete the questionnaires and to follow the sleep-assessment instructions, including actigraph attachment and diary completion.

Data Analysis

Multivariate analysis of covariance was used to compare the clinical and control groups on both actigraphic and sleep-diary measures. The independent variables were group (children with NE vs controls) and sex. Age was entered as a covariate to control for potential age effects. Because of the unevenness in sample sizes of the clinical and control groups, we tested the variance of the measures to assess for potential statistical errors due to different sample sizes and variances. There were no significant group differences in variances. Nonparametric Wilcoxon rank-sum test was used to assess group differences on the sleep-diary measures: sleep latency, morning sleepiness, and evening sleepiness. Because the children with NE had significantly more monitored nights than did the control children (average of 4.4 vs 4.0, respectively), we used the number of nights as a covariate in the multivariate analysis of covariance for group differences. No significant impact on the results has been documented.

RESULTS

Significant group differences were found on several actigraphic and sleep-diary measures (see Table 2). Specifically, actigraphic sleep measures indicated that, in comparison with control subjects, children with NE had shorter periods of continuous sleep, lower proportions of motionless sleep, and a higher number of nighttime awakenings. In addition, sleep-diary measures indicated that, in comparison with control subjects, children with NE needed more time to fall asleep, woke up more often, felt more tired prior to bedtime, and were more tired in the morning.

To clarify the source of these group differences in sleep measures, we analyzed the reason given for each nighttime awakening in the clinical group. Of all nighttime awakening, 27.4% were initiated by a parent to prevent bedwetting, 2.4% were initiated by a parent following bedwetting, 20.4% were spontaneous awakening following bedwetting, and 49.9% were unrelated to bedwetting. There were no group differences in the number of nighttime awakening unrelated to bedwetting.

The only finding related to sex was that girls had higher percentages of motionless sleep (66.3% versus 60.4%, respectively, $F = 7.7$, $P < 0.01$). There were no significant group-by-sex interactions.

DISCUSSION

To our knowledge, this is the first study that has assessed sleep in children with NE using objective measures in their natural environment over multiple nights.

Our findings reflect significant group differences on both actigraphic and sleep-diary measures. In comparison with control children, children with NE had poorer sleep quality, as reflected by both actigraphic measures (more nighttime awakening, lower percentages of motionless sleep, and shorter periods of continuous sleep) and reported measures (more nighttime awakenings and longer sleep latencies). Furthermore, children with NE reported being more sleepy in the mornings and evenings. As documented in earlier studies, actigraphy detected more nighttime awakenings than were reported in sleep diaries in both groups.[32,33] This probably occurs because children and their parents are not fully aware of all nighttime awakenings. It is important to note that actigraphy cannot reliably document microarousals and other changes in sleep architecture (e.g., sleep stages) that may underlie these group differences in actigraphic and reported sleep patterns.

Parents of children with NE reported that they woke up twice as often at night, in comparison with parents of control subjects. To gain a better understanding of these differences in sleep quality, we examined the reasons for waking up in these children and found that 50% of all awakenings in children with NE were related to bedwetting. This distribution of nighttime awakenings related to bedwetting events or their prevention provides a solid explanation for the group differences in sleep quality. These findings coincide with those of other reports on compromised sleep quality in children with NE.[16,20,34]

In light of earlier research suggesting that a high arousal threshold is one of the causes for NE and that deep sleep prevents arousals when the bladder is full,[14,21,22,35-39] the results of our study may underscore additional components of the underlying mechanism: if the sleep of children with NE is more fragmented in their habitual sleep environment, they are likely to be more sleep deprived (as manifested by their higher sleepiness level) and they may have higher arousal thresholds because of their sleep-deprived condition.

We therefore suggest that a vicious cycle is contributing to the maintenance of NE: children who continue to wet at night are more likely to have more initiated nighttime awakenings because of their bedwetting and prevention attempts. This sleep fragmentation leads to an increased arousal threshold,[40,41] which, in turn, leads to failure to respond to full-bladder signals and additional bedwetting.

Recent research highlights additional sleep-related factors in children with NE. Dhondt et al.[42] found a higher incidence of periodic limb movements and increased cortical arousability in sleep at night (leading to awakening) in children with NE, compared with children without NE. Taken together, these findings suggest that poor sleep quality may play a role in the maintenance of NE.

CONCLUSIONS

The sleep of children with NE is more fragmented because of enuresis-related events. Parents and child-health professionals should be aware that children with NE may suffer from additional consequences associated with poor sleep and increased daytime sleepiness.[43] Enuresis-management programs employing parent-initiated nighttime awakenings as a treatment component should consider the potential adverse implications for sleep and daytime alertness and functioning.

Table 2—Comparison of actigraphic and reported sleep measures of children with nocturnal enuresis and the control subjects

	Children with NE	Control Children	F (Z)
Actigraphic Measures			
Nighttime awakenings, no.	3.2 ± 1.5	2.4 ± 1.3	7.1[a]
Longest sleep period, min	154.3 ± 53.8	186.4 ± 70.0	4.7[a]
Motionless sleep, %	58.6 ± 10.0	64.3 ± 9.3	6.6[a]
True sleep time, min	502.3 ± 51.3	516.2 ± 43.0	n.s
Sleep Diary Measures			
Nighttime awakenings, no.	1.0 ± 0.6	0.5 ± 0.5	19.9[c]
Sleep latency[d]	2.0 ± 0.6	1.5 ± 0.9	2.5[b]
Morning sleepiness[e]	1.5 ± 0.4	1.3 ± 0.5	1.8[a]
Evening sleepiness[e]	2.1 ± 0.4	1.5 ± 0.6	3.9[c]

Data are displayed as mean ± SD. F value is based on analysis of covariance for all measures expect for the measures marked by [a] and [b], which were analyzed using nonparametric Wilcoxon rank-sum test (Z). NE refers to nocturnal enuresis.
[a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.0001$
[d]0 refers to < 5 min; 1, 5-14 min; 2, 15-30 min; 3, > 30 min.
[e]0 refers to very alert; 1, somewhat sleepy; 2, very sleepy.

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DISCLOSURE STATEMENT

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