Nocturnal Sleep Measured by Actigraphy in Children with Prader-Willi Syndrome

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Objective To assess nocturnal sleep duration by actigraphy in children with Prader-Willi syndrome (PWS).
Study design Baseline measurements including height, weight, and body mass index (BMI) were collected on 8 children with PWS (6 boys) with each subject age- and sex-matched to 2 control children. From 7 consecutive nights of actigraphy data, values for total sleep time (TST), sleep efficiency, sleep latency (SL), number of awakenings after sleep onset, and duration of awakenings after sleep onset (WASO) were extracted. Parents also completed a sleep diary and questionnaire during this period.
Results Subjects with PWS ranged from 4.2 to 15.4 years, and they had a lower height *z* score and higher BMI *z* score compared with controls. The PWS group had a shorter SL ($P = .0007$), longer WASO ($P = .009$), and higher daytime sleepiness score. TST, sleep efficiency, and number of awakenings after sleep onset were not significantly different between the groups, and subjects with PWS did not wake earlier than controls. There was no correlation between WASO and BMI or between WASO and sleepiness score.
Conclusion Children with PWS appear to have a shorter SL but more time awake in the night than normal children and have similar TST and morning wake time compared with controls. *(J Pediatr 2013;162:765-9)*.

Prader-Willi syndrome (PWS), a genetic disorder with an estimated prevalence of 1:10 000 to 1:25 000 live births, is characterized by hypotonia, initial poor feeding, later childhood-onset obesity, short stature, global developmental disorder, hypogonadism, characteristic facial features, and behavioral problems.[1-5] Sleep disturbances are commonly described in the population with PWS and include excessive daytime sleepiness, abnormal organization of rapid eye movement sleep, abnormal arousal, and sleep disordered breathing.[6-8]

Short sleep duration is associated with cognitive deficits and mood disturbance in adults and children and has also been linked to obesity.[9-12] Limited and inconsistent literature is available for the adult population with PWS regarding total sleep time (TST), sleep latency (SL), and episodes of awakening after sleep onset (both number [Aw] and duration [WASO]) despite the documented incidence of sleep disordered breathing in this group.[13-15] Even fewer reports exist for the pediatric population with PWS, although they may have reduced sleep efficiency (SE) and increased Aw.[16] Clinically, parents of children with PWS often report that their child is awake during the night and rises early in the morning, suggesting that children with PWS may have reduced nocturnal sleep duration. Given the importance of adequate sleep duration in its relation to mood, cognition, and risk of obesity, sleep duration may be a potentially modifiable component to these problems in the pediatric population with PWS. This study aimed to assess total nocturnal sleep duration in children with PWS and to explore the relationship with body mass index (BMI) and daytime sleepiness. We hypothesized that children with PWS would have a shorter nocturnal TST and wake earlier in the morning in comparison to the control group.

Methods

Children with PWS were recruited consecutively from regional pediatric endocrinology and sleep medicine clinics at Wellington Hospital. Children aged 2-16 years were eligible, including those with a preexisting sleep disorder. Children under 2 years of age were excluded because they have regular daytime sleep and this study was assessing nocturnal sleep duration. Controls were recruited through staff members from the pediatric and neonatal service at Wellington Hospital. Two controls were matched to each case by age (±6 months), sex, and pubertal stage. Controls were excluded if they had a preexisting medical condition or a known sleep disorder or if the screening sleep questionnaire suggested a sleep disorder. The study was approved by the

AHI	Apnea-hypopnea index	PSG	Polysomnography
Aw	Number of awakenings after sleep onset	PWS	Prader-Willi syndrome
BMI	Body mass index	SE	Sleep efficiency
BT	Bedtime	SL	Sleep latency
CSHQ	Children's Sleep Habits Questionnaire	TST	Total sleep time
GH	Growth hormone	TTB	Total time in bed
OSA	Obstructive sleep apnea	WASO	Duration of awakenings after sleep onset

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The authors declare no conflicts of interest.

 http://dx.doi.org/10.1016/j.jpeds.2012.09.019

Central Ethics Committee (reference CEN/11/02/04), and written informed consent was obtained from the parents.

Subjects were enrolled at their routine clinic appointment or during a separate visit to one regional center. Controls were assessed in the outpatient department at the family's convenience. Baseline measurements were taken for subjects, and parents were provided information about the 7-night data collection period. Data were collected over a period typical of the child's normal routine. No data were collected during school holidays. Unless the normal sleep routine was disrupted significantly during the 7 nights (ie, by prolonged or significant illness or other events such as sleepovers), data were included. Parents also completed a sleep diary for the study period and a questionnaire regarding their child's sleep.

Subjective Sleep Measures

A modified version of the Children's Sleep Habits Questionnaire (CSHQ) and a sleep diary were used.[17] The CSHQ screens for common clinical presentations of prevalent sleep disorder diagnoses according to the International Classification of Sleep Disorders (1997). It is specific to the pediatric population and has been shown to be a comprehensive and valid screening tool.[18] The questionnaire was modified to separate weeknight data from weekend data.[19] The daytime sleepiness questions were adapted from a modified Epworth Sleepiness Scale to allow the degree of daytime somnolence to be quantified.[20] Parents recorded in the sleep diary their child's bedtime (BT), known Aw, and morning wake time. Total time in bed (TTB) was calculated from the sleep diary as the difference between BT and rise time and averaged over the number of nights of data collection. If the child was documented to be awake for periods overnight, this time was subtracted from the TTB for that night.

Objective Sleep Measures

Parents were instructed that their child was to wear the Actiwatch (Respironics Actiwatch 2, Bend, Oregon) for 7 consecutive nights and to attach the Actiwatch 1 hour before going to bed and to remove it 1 hour after getting up. This allowed a period of activity to be demarcated on the Actigraph to help differentiate periods of activity from periods of sleep. The parent, or child if old enough, was instructed to press the button (event-marker) on the watch when the lights went off at night and on waking. Data were collected by the Actiwatch in 1-minute intervals with the movement sensitivity set at medium. On Actiwatch return, data were downloaded and analyzed by the Actiwatch software. The Actigraph was visually inspected and compared with the sleep diary and event marker to establish the TTB. If the event marker and diary did not correlate, then the event marker and activity levels were used. If there was no event marker or there were multiple event markers, then the sleep diary and activity level were used. The Actigraphy software program automated algorithm established sleep onset and offset based on movement patterns and TST, SE (the time spent asleep as a ratio of the TTB), SL (the time from lights out to sleep onset), Aw, and WASO were calculated.

Anthropometric Measures

Weight was measured on digital scales (Wedderburn, New South Wales, Australia), with the child in light clothing and shoes removed, to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm with a calibrated wall-mounted Harpenden stadiometer (Holtain Ltd, Crymych, Great Britain). BMI was calculated as weight divided by height squared (kg/m^2). BMI *z* scores specific for sex and age were calculated from Centers for Disease Control and Prevention 2000 data.[21] Hip circumference was measured at the level of the greater trochanter, waist circumference at the midpoint between the lowest rib, and the iliac crest and neck circumference at the level of the hyoid prominence with the same plastic tape measure used for all participants. Blood pressure was measured seated at rest using an automated device (Dinamap; Critikon, Johnson and Johnson, Sydney, Australia) with an appropriate sized cuff and the average of 2 readings recorded.

Statistical Analyses

The sample size calculations were developed using an unpaired *t* test model. Sample size calculations were performed in Stata 12 (StataCorp LP, College Station, Texas) with an α of 0.05 and 80% power. The SD of SE in children with PWS has previously been estimated as 8.6 percentage points, and 13.3 in control children.[8] To detect a difference of 15 percentage points between children with PWS and controls, a sample size of 9 was required in each group. Data were analyzed using the Stata 12.0 statistical program. Data for individual subjects were averaged over the 7 days of data collection and then compared for group differences. Data were non-normally distributed; therefore, median and IQRs are reported. The Mann-Whitney U test was used to compare the PWS and control groups. A 2-sample test of proportions was used to compare groups for the variables of bedroom sharing and sleeping in different houses. Comparison of the diary TTB to actigraphy TTB was made with the 2-sample *t* test with equal variance. The Kendall tau test was performed to assess correlations between WASO and BMI and between WASO and sleepiness score. A value of $P < .05$ was considered statistically significant.

Results

Ten of 11 eligible children with PWS were enrolled. One family declined to enter the study for personal reasons. For 2 cases, Actiwatch data were incomplete: one due to Actiwatch malfunction during data collection and the other due to incomplete data collection. These cases were excluded from analysis, leaving 8 cases of PWS (6 boys and 2 girls) with 16 age- and sex-matched controls. All except 1 male subject, and the 2 associated control subjects, were prepubertal. One of the 8 patients had data collected for 6 nights and did not fully complete the CSHQ but was included in the analysis. The diagnosis of PWS had been previously confirmed by genetic analysis. Six patients had the 15q11-q13 microdeletion and 2 patients had maternal uniparental disomy. Seven of the