First Night Effect Analysis in a Cohort of Young Children with Autism Spectrum Disorder

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Study Objectives: To evaluate for the first night effect (FNE) in a group of young children with autism.

Design: Analysis of polysomnographic data from a 2-night sleep laboratory study.

Setting: Clinical Center of the National Institutes of Health.

Patients or Participants: 15 children (aged 2-10 years) with a diagnosis of an ASD.

Interventions: None.

Measurements and Results: Polysomnographic analysis showed the presence of a FNE for wake after sleep onset minutes, stage 2, and sleep efficiency, but not for REM sleep parameters or TST.

Conclusions: In this 2-night polysomnographic analysis of sleep stages in young children with autism, we did not find the expected second night increase in total sleep time or REM sleep percentage or a decrease in REM sleep latency. This lack of an FNE for TST and REM parameters suggests that a single-night polysomnogram may be sufficient to evaluate children with an ASD for TST or REM parameters.

Keywords: Autism, first night effect

Citation: Buckley A; Wingert K; Swedo S; Thurm A; Sato S; Appel S; Rodriguez AJ. First night effect analysis in a cohort of young children with autism spectrum disorder. *J Clin Sleep Med* 2013;9(1):67-70.

The first night effect (FNE) refers to the well-accepted phenomenon of a poorer quality of sleep on the first night when subjects undergo two or more consecutive nights in the sleep lab. Typically, FNE effects include lower sleep efficiency, less total sleep time, less REM sleep, longer latency to REM sleep, and more intermittent awake time on night one.^{1,2} While this phenomenon is well recognized among adult populations, there are few exclusively pediatric studies that have examined FNE, and fewer still that have included young children with disorders affecting development.

The largest pediatric study examining the FNE was performed in 1984. It was a laboratory-based evaluation of 87 healthy children between the ages of 6 and 15 years. This experiment reported an increase in TST and a decrease in sleep latency for night two. It also revealed similar second night findings as had been seen in adult cohorts, namely, better sleep efficiency, fewer wake after sleep onset (WASO) minutes, decreased REM latency, and increased REM percentage.³ Palm et al. conducted a 2-night *at home* study in 1989 on 18 healthy children between 8 and 12 years and did not find such an effect.⁴ Instead, there was an increase in sleep latency, an increase in percentage of stage 1 sleep, and an increase in REM latency, all on the second night.

The majority of FNE data in children have come from studies using patient populations that frequently undergo overnight polysomnography (PSG) as part of a routine diagnostic assessment. Several studies have examined the FNE among children with suspected sleep disordered breathing (SDB) and obese children who are at risk for developing SDB. Scholle et al. evaluated 131 children between the ages of 2 and 17 years with suspected SDB for 2 nights in the laboratory.⁵ The work concluded that

BRIEF SUMMARY

Current Knowledge/Study Rationale: This study was done to ascertain whether young children with an ASD acclimate the same way to the sleep lab as non-patient populations. In particular, we wanted to evaluate whether REM parameters would be affected between nights.

Study Impact: Although, polysomnograms are expensive and time consuming exams, they can yield invaluable information regarding sleep physiology in special populations. This study suggests that only a single night in laboratory may be needed to inform on the TST and REM parameters in children with an ASD.

while there was a FNE effect for WASO and REM percentage, a second night was not needed for pertinent respiratory parameters. Similarly, Verhulst et al. examined 70 children between the ages of 2 and 17 years, also referred for SDB, and found a FNE for REM sleep parameters but not for respiratory measures.⁶ Li et al. compared 46 obese children to 44 normal weight children between the ages of 7 and 15 years.⁷ The groups were later further broken down for the presence or absence of SDB, and sleep architecture was examined using a 2-night, laboratory-based study. Children with and without SDB had increased TST and greater sleep efficiency on the second night. Children without SDB were found to have more REM, decreased REM latency, and decreased stage 2 on the second night.⁷

Several studies have used the FNE principle to compare children with mood disorders or ADHD with typical controls as a way to interrogate sleep as a proxy for optimal mental health. For instance, Bertocci et al. examined 51 children between the ages of 8 and 17 years with a diagnosis of major depressive disorder (MDD) for three consecutive nights in the lab.⁸ This study explored sub-

Table 1—Sample demographics

	N = 15
Male/Female	13/2
Diagnosis Autism/PDD-NOS	13/2
Age, mean $\pm$ SD	5.24 (1.69)
Nonverbal DQ, mean $\pm$ SD	59.49 (18.84)
Vineland ABC, mean $\pm$ SD	66.93 (7.28)

DQ, developmental quotient.

jective reports of sleep and waking in both MDD subjects and controls compared to the objective EEG correlates of sleep and waking. They did not analyze for sleep staging, but found that sleep latency was decreased and TST was increased on night two for both groups.⁸ The third night was not analyzed due to blood draws performed during the night, which precluded the ability to measure normal sleep stages. Likewise, both Dahl et al. and Emslie et al. evaluated children with MDD on consecutive nights and found REM latency decreased on the second night.^{9,10} In addition, Dahl found an increase in REM minutes on the second night in both MDD subjects and controls. Prihodova et al. examined 31 children between the ages of 6 and 12 years with a diagnosis of ADHD and compared them to 26 age-matched typically developing controls.¹² This consecutive, 2-night sleep laboratory-based study is unique in that it reports that there was no first night effect on any variable in the control group of children. The ADHD group is reported to have an increase in sleep efficiency, a decrease in wakefulness, and shortened sleep latency on the second night.¹²

Sleep problems are widely reported in children with autism spectrum disorders (ASD), and understanding the nature of the problems may provide insight into pathophysiology and potential treatments. Conducting laboratory-based sleep studies on children with ASD is not only expensive but often difficult, due to the neurodevelopmental deficits and behavioral challenges common in autism. Therefore, it is important to know whether data collected on the first night in the sleep laboratory are representative of typical sleep in children with autism or whether multiple nights will give a more accurate picture of the child's typical sleep patterns. The specific parameters affected by the FNE are also of interest.

Very few studies have examined night-to-night variation of sleep parameters among children with autism or other developmental disorders. Malow et al. brought 21 high-functioning children and adolescents with ASD into the sleep laboratory for 2 consecutive nights of PSG, divided the cohort into good and poor sleepers, and compared them to typically developing controls.¹¹ This study reported on the differences between groups but did not report an analysis of the presence of FNE within groups.¹¹ The goal of the current analysis is to examine night-to-night variation in sleep quality between two consecutive nights of PSG in 15 young, well-characterized children with ASD.

MATERIALS AND METHODS

Subjects

The National Institutes of Health's (NIH) Combined Neurosciences Institutional Review Board approved the protocol.

Sixteen children between the ages of 2 and 10 years, including 2 females, were enrolled in the study after their parents/guardians consented to participation. One subject's data could not be used, as loss of leads during night 2 prevented the acquisition of a readable study. No children were taking any medications during data collection period. Subjects were evaluated via a 2-step process that included testing both behavior and sleep.

Behavioral evaluations at the NIH assessed cognitive function and symptoms of ASD. The ASD diagnosis was based on clinical observations and information obtained from the Autism Diagnostic Observation Schedule¹³ and the Autism Diagnostic Interview-Revised.¹⁴ Development and overall functioning were assessed with the Vineland Adaptive Behavior Scales, Second Edition¹⁵ and cognitive/developmental testing using either the Mullen Scales of Early Learning¹⁶ or the Differential Ability Scales, Second Edition.¹⁷ Nonverbal developmental quotients were obtained for each child. The ratio score was calculated as the mean of the age equivalents of the nonverbal sections of the test divided by the chronological age and multiplied by 100 (**Table 1**).

Polysomnogram

Eligible participants completed a 2-night polysomnographic observation in the NIH clinical center sleep laboratory. The overnight recordings included a referential, 21-lead electroencephalogram montage, electro-oculogram, electrocardiogram, and surface electromyogram (chin, anterior tibialis). Lights out approximated child's usual bedtime. All recordings were videotaped. The data were then analyzed for sleep architecture using Grass telefactor software (Grass Technologies, West Warwick, RI) by AJR, a neurologist with board certification in neurology, neurophysiology, and sleep medicine; he was blind to diagnosis and night order. Scoring was done according to the guidelines published in the AASM (American Academy of Sleep Medicine) Manual for the Scoring of Sleep and Associated Events.¹⁸ The following variables were calculated: total sleep time (the total time in bed minus the sleep latency and time spent in wakefulness after sleep onset), sleep efficiency index (total sleep time divided by time in bed $\times$ 100), minutes spent in each sleep stage (N1, N2, N3, and REM sleep), percentage of each stage relative to total sleep time, latency to sleep onset (measured from lights out to the first epoch of sleep), and latency to REM sleep (measured from the first epoch of sleep to the first epoch of REM sleep).

RESULTS

Summary data are presented for the 15 subjects studied for 2 nights. Descriptive statistics for the first and second night as well as statistical comparison of differences are presented in **Table 2**.

There were no significant differences between night one and night two for the following parameters: TST, stage 1%, SWS%, REM%, sleep latency, or REM latency. Stage 2 showed a significant difference, with 53.22% of the night spent in this stage on the first night versus 57.52% of the night on the second. The WASO decreased on night two from a mean of 26.05% to 7.33% of the night, and the sleep efficiency increased from 78.03% to 88.71%. Both WASO and sleep efficiency also showed significantly different standard deviations between nights, as the variance decreased appreciably for both these parameters on the second night (**Figure 1**).

Table 2—Mean differences in sleep variables by night

	Night 1 Mean (SD)	Night 2 Mean (SD)	Difference (SE)	p-value
Total sleep time, min	460.32 (105.94)	501.99 (72.20)	-41.67 (38.37)	0.30
Stage 1, %	4.97 (2.15)	4.33 (2.60)	0.65 (0.90)	0.48
Stage 2, %	53.22 (5.94)	57.52 (5.28)	-4.31 (1.98)	0.047
SWS, %	24.16 (7.10)	21.83 (5.74)	2.33 (2.27)	0.32
REM, %	17.67 (5.57)	16.30 (5.70)	1.37 (1.99)	0.50
WASO, %	26.05 (26.37)	7.33 (5.65)	18.72 (7.36)	0.023
Sleep latency, min	28.33 (31.46)	28.17 (27.29)	0.17 (10.78)	0.99
REM latency, min	109.80 (53.08)	131.93 (67.36)	-22.13 (17.57)	0.23
Sleep efficiency, %	78.03 (13.82)	88.71 (6.03)	-10.67 (4.15)	0.022

Standard errors and p-value are based on paired t-tests. All p-values are two tailed. Number of observations = 15.

Figure 1—Plot of subjects, n = 15, for common sleep variables affected by FNE: TST, SE, WASO, and REM %

Gray boxes denote the means.

DISCUSSION AND LIMITATIONS

Growing interest in the interaction between sleep and overall health, including obesity and mood disorders, has led to several studies examining the FNE in children and adolescents. Evidence from a variety of patient populations and studies of healthy children suggest that children, much like adults, show

improvements in sleep quality from the first to second night in the sleep laboratory,^{3,5-10,19} with some measures of sleep quality continuing to improve when data from subsequent nights are collected.³ The most consistently reported changes are in TST, SE, WASO, and REM parameters. Prior to this report, no study has explicitly examined the first night effect in a group of young children with autism.

The examinations included herein represent modified sleep studies, as respiratory measures were not recorded. The children were primarily very low functioning and non-verbal, and initial attempts to include the respiratory belts and thermistor were not successful. We acknowledge that it is a limitation that renders it impossible to know the potential contribution of obstructive sleep apnea (OSA) to sleep architecture in this particular study. However, the lack of respiratory parameters may not have had a direct impact on the interpretation of the results, as sleep architecture is preserved in children with OSA without the associated EEG arousal and measurable sleep fragmentation that often follows obstructive events in adults.²⁰

In this cohort of young children with autism, we found a significant first night effect for WASO minutes, sleep efficiency, and N2 percentage. We did not find a first night effect for either REM percentage or REM latency. We acknowledge that the sample size was small. A post hoc power analysis (conducted using G*Power 3.1.2) suggests a minimum detectable effect size of $d = 0.78$ for our sample size, assuming $\alpha = 0.05$ (2-tailed) and a power of 0.80. This effect size is larger than those estimated from the data reported in the largest healthy pediatric sample to date³ for first to second night differences in healthy children for REM latency (-0.36), REM percentage (0.63), sleep efficiency (0.71), wake after sleep onset minutes (-0.46), and N2% (-0.17); therefore, we would not have expected to find differences in any of the sleep parameters had the population we were studying been drawn from a similarly healthy cohort.

The lack of REM parameter change in this population stands in marked contrast to cumulative existing data on sleep acclimation from other populations and opens up interesting questions regarding underlying neuropathologic differences. While it is possible that the WASO and sleep efficiency changes in the expected direction were found by chance, we feel it is more likely that this population of children acclimates to the sleep lab differently. This information is valuable, given both the expense and expertise needed to evaluate the sleeping brain in individuals with autism. Although our small sample size limits generalizability of these results, they suggest that it may not be necessary to submit young children with autism to two consecutive nights in the sleep lab to mitigate the FNE on either TST or REM measurements.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication April, 2012

Submitted in final revised form July, 2012

Accepted for publication July, 2012

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DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.