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S.I. : AUTISM INPATIENT COLLECTION - STUDYING THE SEVERELY AFFECTED

Sleep Problems and Their Relationship to Maladaptive Behavior Severity in Psychiatrically Hospitalized Children with Autism Spectrum Disorder (ASD)

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Abstract We examined the relationship between sleep duration and awakenings to Aberrant Behavior Checklist-Community (ABC-C) and Autism Diagnostic Observation Schedule (ADOS-2) scores in hospitalized youth with ASD and behavioral disturbance. Participants included 106 patients with a stay of at least 10 nights. Sleep in the hospital was recorded by staff observation. Higher scores on the ABC-C (irritability, stereotypy, and hyperactivity subscales) at admission were significantly associated with fewer minutes slept during the last five nights of hospitalization. There was no association between total awakenings and ABC-C scores or ADOS-2 comparison scores. Improved understanding of the relationship between sleep quality and maladaptive behavior in this challenging cohort of patients with ASD is vital to the definition and design of future effective interventions.

Keywords Autism spectrum disorder · Sleep · Behavior problems · Children and adolescents

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Introduction

Autism spectrum disorder (ASD) is a costly public health problem affecting people of all racial, ethnic, and socioeconomic groups. The Center for Disease Control's Autism and Developmental Disabilities Monitoring Network reports that ASD occurs in approximately 1 in 68 individuals, based on data collected between 2002 and 2012 (Christensen et al. 2016). Sleep problems are common in individuals with ASD, having been described in up to 50–80% of children and adolescents with ASD, compared to 9–50% of those without a neurodevelopmental disorder (Veatch et al. 2015; Souders et al. 2009). A variety of sleep issues including decreased sleep efficiency, reduced total sleep time, increased nighttime awakenings, bedtime resistance, and daytime sleepiness are present in this population (Cohen et al. 2014), but the predominant problem is insomnia (Malow et al. 2006; Reynolds and Malow 2011). The International Classification of Sleep Disorders-3 defines insomnia as adequate sleep opportunity with a persistent sleep difficulty and associated daytime dysfunction (Sateia 2014). Insomnia includes difficulty falling asleep (initial insomnia), difficulty staying asleep (middle insomnia) and early morning awakening (late insomnia). Differences in sleep quality between youth with and without ASD have been described in multiple prior studies. These differences have been reported both subjectively through parent report and objectively through actigraphy and polysomnography. In 2006, Malow et al. demonstrated that a single caregiver response indicating poor sleep on the Children's Sleep Habit Questionnaire (CSHQ) correlated with prolonged sleep latency and decreased sleep efficiency on polysomnography (Malow et al. 2006). In a 2015 meta-analysis, Elrod and Hood (2015) showed that children with ASD have objective differences in sleep quality as measured by polysomnography and actigraphy when compared to their neurotypical peers. There

is no research consensus of the definition of sleep quality, but descriptors typically include sleep latency, number of awakenings, sleep efficiency, and total sleep time (Richdale and Schreck 2009).

Sleep is a crucial mechanism for overall adaptive functioning. Sleep restriction has negative impacts on behavior and attention in typical populations (Baum et al. 2014; Fallone et al. 2001). Similarly, poor sleep is correlated with greater behavioral issues in individuals with ASD. There is ample evidence that individuals with poor sleep have increased hyperactivity and inattention, more stereotypic behaviors, and higher autism severity scores (Cohen et al. 2014; Fadini et al. 2015; Goldman et al. 2012; Liu et al. 2006). Negative influences on cognition and adaptive behavior are also observed (Taylor et al. 2012). There is a strong correlation between shorter sleep duration and hyperactivity in neurotypical youth (Touchette et al. 2007, 2009). In individuals with ASD, the number of nighttime awakenings also has a strong association with behavior problems, and may be a better predictor of poor sleep than total sleep time (Mazurek and Sohl 2016). Multiple studies have demonstrated a relationship between sleep issues and problem behavior in ASD, but questions regarding causation and the directionality of the relationship remain. There is some evidence that the presence of problem behaviors may impact sleep quality. Patients with psychiatric symptoms including impulsivity and anxiety have high levels of arousal, making it more difficult to for them to fall asleep. In turn, their poor sleep can further exacerbate behavioral symptoms (Cohen et al. 2014).

Although sleep disturbance in individuals with ASD has been well described, little is known about sleep differences within the cohort of those needing hospitalization for acute behavioral disturbance. This unique population is complex and often very challenging to treat. High quality research specifically addressing this population is needed to inform treatment targets and decisions.

In this study, we aimed to better characterize the relationship between sleep quality, as defined by total sleep time and number of awakenings, and behavioral problems. We hypothesized that total sleep time and number of awakenings would correlate with maladaptive behavior [as measured by the Aberrant Behavior Checklist-Community (ABC-C)] and autism severity [as measured by the Autism Diagnostic Observation Schedule (ADOS-2)] in hospitalized youth with ASD.

Methods

Participants

Data was collected through the Autism Inpatient Collection (AIC). Children and adolescents aged 4–20 admitted to 1 of 20 specialized inpatient psychiatry units were eligible for participation in the AIC if they had a score of greater than or equal to 12 on the Social Communication Questionnaire (SCQ) (Rutter et al. 2003) or if there was a high clinical suspicion of ASD from the inpatient clinical team. The study protocol was approved by the Institutional Review Board at each of the six investigating sites: the Cincinnati Children's Hospital Medical Center Human Research Program, the Lifespan—Rhode Island Hospital Research Protection Office, the Maine Medical Center Office of Research Compliance, the Sheppard Pratt Institutional Review Board, the University of Pittsburgh Research Conduct and Compliance Office, and the University of Colorado Denver Office of Regulatory Compliance. Only children with a confirmed ASD diagnosis were included in this study's dataset. Children first needed to meet the clinically derived cutoffs for autism or ASD on the ADOS-2, administered by a research reliable examiner. The examiner then utilized DSM-5 criteria, chart review, and behavioral observation to make a final diagnosis of ASD. If the additional information led the examiner to believe the child did not in fact met criteria for ASD, this could override a positive ADOS-2 result. At the time of the current study, 350 patients were enrolled in the AIC across the 6 specialized psychiatry sites. 106 children and adolescents with a confirmed diagnosis of ASD, a hospital length of stay of at least 10 nights and a complete data set (no missing questionnaire or sleep data) were included in the current study. Patients without a confirmed ASD diagnosis, a stay of less than ten nights, missing questionnaire data, and/or missing sleep data were not included in the study. There were no statistically significant differences in gender, age, or parental income levels between patients included in and excluded from the study. For details regarding the overall methods of the AIC and description of the full inpatient sample, please see Siegel et al. (2015).

Measures

Aberrant Behavior Checklist-Community (ABC-C)

Within the first 10 days of admission, parents and caregivers completed the ABC-C, a 58-item caregiver questionnaire used to assess maladaptive behavior in individuals with developmental disabilities (Aman et al. 1985). Its use has been validated in children and adolescents with co-morbid psychiatric illness and developmental disability (Rojahn and Helsel 1991). Questions are answered on a 4-point rating scale (0 = not a problem at all, 1 = the behavior is a problem but slight in degree, 2 = the problem is moderately serious, and 3 = the problem is severe in degree). Caregivers are asked to report on the patient's behavior over the previous 4 weeks. Scores are reflected by empirically derived subscale domains—rritability, lethargy, stereotypy, hyperactivity, and

inappropriate speech. The admission ABC-C was used in analysis and reflected the severity of the patient's symptoms before treatment. A discharge ABC-C was not used, as the patient had been out of the direct care of their parent or caregiver for at least ten days (or longer depending on length of stay).

Autism Diagnostic Observation Schedule (ADOS-2)

The ADOS-2 is a semi-structured standardized observation based assessment used to diagnose ASD (Lord et al. 2000). Participants were assessed with the ADOS-2 by a research reliable examiner. The ADOS-2 was completed when the patient was clinically stable enough to cooperate with the assessment and when a research reliable clinician was available. Results from Modules 1, 2, and 3 included a comparison score, ranging from 0 to 10, representing the severity of symptoms. Module 1 is for patients who are minimally verbal and Module 2 is for those with phrase speech. Modules 3 and 4 are used in individuals with fluent speech. Only recently has there been an algorithm available to calculate comparison scores for individuals assessed using Module 4 of the ADOS-2. Comparison scores were not available for individuals assessed for ASD with Module 4 in this study (n = 14).

Procedure

Sleep habits of the patients were collected through direct observation by unit staff, and later recoded by research assistants. As required by regulation of The Joint Commission, psychiatric hospital staff are mandated to record every patient's location and activity, including when the patient was awake or asleep. Individuals were recorded as asleep if they had their eyes closed and appeared to be resting or sleeping and awake if their eyes were open and/or if they were out of bed. All recordings were placed into the child's medical chart. Research assistants then abstracted this information from the patient's chart to calculate the total number of minutes asleep (total 15-min increments marked as "asleep") and number of awakenings (each 15-min increment marked as "awake") for each night the patient was in the hospital. Sleep during the daytime period was not counted towards the patient's total number of minutes asleep. Data from the first five nights of hospitalization (pre-stabilization) and the last five nights of hospitalization (post-stabilization) were used in data analysis. Total minutes asleep and number of awakenings served as indices of sleep quality.

Tabulation and Statistical Analysis

Analyses were completed using epidata and STATA version 12 (StataCorp 2011). Demographic data was analyzed using T-tests for continuous variables and Chi square tests for categorical variables. Total ABC-C subscale scores and ADOS-2 comparison scores were calculated and linear regression analysis was used to compare sleep variables and behavioral variables.

Results

The sample consisted of 106 patients with ASD who spent at least 10 nights in the hospital for behavioral stabilization (Table 1). The table is divided between male and female, as ASD is known to be about four times more common in males as in females (Lai et al. 2015). Although there were no a priori hypotheses about gender, dividing the sample between male and female ensured that there were no differences in results that could possibly be attributed to gender. The sample was 76% male and 25% female with an average age of 12.9 ± 3.4 years old. The majority of patients were Caucasian (78%). The average nonverbal intelligence quotient (IQ) as measured by the Leiter-3 International Performance Scale was 69.9 ± 28.4. 60 patients (62%) were assessed with Modules 1 and 2 of the ADOS-2 (for those with minimal or phrase speech) and 36 patients (38%) were assessed with Modules 3 and 4 of the ADOS-2 (for patients with fluent speech). Length of stay for the patients in the study ranged from 10 to 120 days, with an average of 25.5 days.

ABC-C subscale total scores were 28.6 ± 8.3 (maximum score 45) for irritability, 8.8 ± 5.4 (maximum score 21) for stereotypy, and 29.9 ± 10.2 (maximum score 48) for hyperactivity. (Table 2). Total duration of sleep during the last five nights of hospitalization was significantly negatively associated with higher irritability ($p = 0.03$), stereotypy ($p = 0.02$), and hyperactivity scores ($p = 0.01$) as measured by the ABC-C at admission (Table 3). The estimated change in the average number of minutes slept over five nights was calculated for each of the behavior subscales through linear regression. For example, on the irritability subscale, for each point increase on the total subscale ABC-C score (0–45), the patient slept a total of approximately 9 min less per night. (Table 3). This translates as an individual with an irritability subscale score of 30 sleeping approximately 132 min less than an individual with a score of 45 over a period of 5 nights. For the stereotypy subscale, patients slept 14.3 min less for every point increase and for the hyperactivity subscale they slept 8.9 min less. There was no significant correlation on the lethargy ($p = 0.13$) or inappropriate speech ($p = 0.11$) subscales. There was no significant correlation between the number of minutes slept and any of the ABC-C subscales during the first five nights of hospitalization (irritability $p = 0.69$, lethargy $p = 0.34$, stereotypy $p = 0.37$, hyperactivity $p = 1.0$, and inappropriate speech $p = 0.38$). There was no significant correlation between total number

Table 1 Demographics of 106 hospitalized patients with ASD and behavioral dysregulation

Demographic variables	Male (n = 81)	Female (n = 25)	Total (n = 106)	Statistic
Age (years)	13.0 ± 3.5	12.6 ± 11.3	12.9 ± 3.4	T(104) = 0.49 p = 0.62
Ethnicity				
Hispanic/Latino	5 (6%)	0 (0%)	5 (5%)	$X^2 = 1.62$ p = 0.20
Not Hispanic/Latino	73 (94%)	24 (100%)	97 (95%)	
Race				
White	64 (79%)	19 (76%)	83 (78%)	$X^2 = 8.16$ p = 0.086
African American	8 (10%)	3 (12%)	11 (10%)	
Asian	0 (0%)	2 (8%)	2 (2%)	
American Indian/Alaskan Native	5 (6%)	0 (0%)	5 (5%)	
Other	4 (5%)	1 (4%)	5 (5%)	
Leiter-3 non-verbal IQ	70.9 ± 28.4	66.9 ± 28.7	69.9 ± 28.4	T(91) = 0.61 p = 0.54
ADOS-2 modules				
Module 1 and 2	44 (59%)	16 (73%)	60 (62%)	$X^2 = 1.43$ p = 0.23
Module 3 and 4	31 (41%)	6 (27%)	37 (38%)	

Table 2 Aberrant Behavior Checklist-Community (ABC-C) average subscale scores of 106 hospitalized patients with ASD and behavioral dysregulation

	Mean ± SD	Range
ABC-C irritability	28.6 ± 8.3	(7, 45)
ABC-C lethargy	16.1 ± 8.1	(1, 39)
ABC-C stereotypy	8.8 ± 5.4	(0, 20)
ABC-C hyperactivity	29.9 ± 10.2	(1, 47)
ABC-C inappropriate speech	5.8 ± 3.7	(0, 12)

of awakenings and ABC-C scores for either the first five nights (irritability p = 0.67, lethargy p = 1.0, stereotypy p = 0.86, hyperactivity p = 0.11, and inappropriate speech p = 0.12) or the last five nights of hospitalization (irritability p = 0.78, lethargy p = 0.89, stereotypy p = 0.59, hyperactivity p = 0.87, and inappropriate speech p = 0.38). ADOS-2 comparison scores were also not significantly correlated with sleep duration during either the first five nights (p = 0.38) or the last five nights of hospitalization (p = 0.10).

Table 3 Relationship between minutes of sleep during the first and last five days of hospitalization and Aberrant Behavior Checklist-Community (ABC-C) subscale and ADOS-2 comparison scores in 106 hospitalized patients with ASD and behavioral dysregulation

	Minutes of sleep	p-value	Adjusted R^2
First five days of hospitalization (N = 106)			
ABC-C irritability	−26.93 (−160.16, 106.29)	0.69	−0.008
ABC-C lethargy	70.04 (−74.72, 214.95)	0.34	−0.001
ABC-C stereotypy	43.05 (−52.01, 138.10)	0.37	−0.002
ABC-C hyperactivity	−0.29 (−116.36, 115.78)	1.0	−0.010
ABC-C speech	−34.93 (−114.13, 44.27)	0.38	−0.002
ADOS-2 composite	−22.06 (−71.88, 27.77)	0.38	−0.003
Last five days of hospitalization (N = 106)			
ABC-C irritability[a]	−132.40 (−247.96, −16.84)	**0.03**	0.038
ABC-C lethargy	−99.60 (−227.32, 28.12)	0.13	0.013
ABC-C stereotypy[b]	−100.53 (−182.97, −18.08)	**0.02**	0.044
ABC-C hyperactivity[c]	−139.07 (−238.52, −39.61)	**0.01**	0.060
ABC-C speech	−56.47 (−126.20, 13.26)	0.11	−0.015
ADOS-2 composite	−35.21 (−76.82, 6.41)	0.10	0.020

Bold values indicate statistically significant $p < 0.05$

[a]A 1 unit increase on the ABC-C irritability subscale score equaled 132 less minutes of sleep over the last five nights of hospitalization

[b]A 1 unit increase on the ABC-C stereotypy subscale score equaled 101 less minutes of sleep over the last five nights of hospitalization

[c]A 1 unit increase on the ABC-C hyperactivity subscale score equaled 139 less minutes of sleep over the last five nights of hospitalization

Discussion

This study examined the relationship between sleep duration and total awakenings (as indices for sleep quality) and maladaptive behavior severity in hospitalized youth with ASD. Most sleep research is conducted with higher functioning community samples of patients with ASD. Much less is known about the complex relationship between sleep and behavior in the hospitalized population. These patients are often lower functioning and have multiple psychiatric and medical co-morbidities. The current study offers insight into this challenging and costly to treat cohort.

Consistent with our hypothesis, sleep duration was negatively correlated with irritability (mood disturbance, self-injury, and aggression), stereotypy (repetitive movements and behavior), and hyperactivity (motoric over-activity), as measured by the admission ABC-C, during the last five nights of hospitalization. The results suggest that patients who have more maladaptive behaviors, as reported by their caregivers at admission (pre-treatment) have a shorter sleep duration when they are nearing discharge (post-stabilization). These results are concordant with reports associating sleep duration and difficult behaviors in both typically developing children (Touchette et al. 2007) and in patients with ASD (Mazurek and Sohl 2016).

A significant correlation between sleep duration and behavioral symptoms was not apparent during the first five nights of hospitalization. Many factors may have influenced this result. When first admitted, patients are often in severe behavioral crisis with frequent aggression and self-injury. They are adjusting to their new environment and many are exhausted from prolonged behavioral dysregulation. Many of the patients will have received medication for agitation or insomnia in the emergency department. All of these factors can impact sleep quality and override the effect of sleep on specific maladaptive behaviors near admission. Whereas, by the time the patient is almost ready for discharge (during the last five nights of hospitalization), they have adjusted to the unit and the association between select maladaptive behaviors and sleep duration may more readily emerge.

The lack of significant correlation between ABC-C scores and the total number of awakenings during both the first five and last five nights of hospitalization was surprising. The number of awakenings is often noted as an important index of sleep quality (Mazurek and Sohl 2016). It may be that our method of detecting awakenings (direct observation at 15-min intervals) is insufficiently sensitive. Some patients may wake for only a few moments and not get out of bed. Such subtler awakenings may not be appreciated through visual observation only. A more objective recording of sleep and wake time through actigraphy would allow for a better characterization of sleep quality. Many individuals with ASD have sensory integration issues and may struggle with wearing a sleep monitor. However, literature supports that with appropriate training patients with ASD can comply with actigraphy (Johnson et al. 2013). Although not providing direct physiological data, another method of observation is video monitoring. This method would allow for continuous observation and would create an opportunity for an assessment of inter rater reliability both within and across sites.

We found no significant correlation between autism severity scores (ADOS-2 comparison score) and sleep duration. This differs from previous studies (Tudor et al. 2012; Adams et al. 2014). Our hospitalized patients have multiple co-morbidities, including medical diagnoses and intellectual disability, compared to community ASD populations. For example, in their study of the relationship between autism severity and sleep duration, Tudor et al. (2012) used a sample of patients with ASD and no co-morbidities. Another explanation for our findings could be the choice of autism assessment instrument. Adams et al. (2014) used the *ASD-child version (ASD-C)* scale, a parent report measure, to describe autism severity, versus our use of the ADOS-2.

The relationship between sleep duration (our index for sleep quality) and maladaptive behavior symptoms in this study is one of correlation, rather than causality. The study design does not allow for a conclusion as to whether sleep problems cause maladaptive behavior symptoms or whether maladaptive behaviors cause sleep problems. Likely, the relationship between sleep quality and behavior in individuals with ASD is bidirectional. In keeping with this relationship, an important question is whether there is an etiology common to both sleep and behavioral problems in individuals with ASD. The neurochemical changes that underlie a diagnosis of ASD may impact both sleep and behavior. GABA, serotonin, and melatonin are all involved in sleep physiology. The modulation of these neurobiological factors is impacted in ASD and behavioral problems (Reynolds and Malow 2011). Medical factors, frequent in individuals with ASD, such as constipation and seizures, can impact both sleep quality and behavior. Psychiatric and medical co-morbidities are common in individuals with ASD (Cohen et al. 2014) and medication side effects and paradoxical responses can have a significant impact on the sleep wake cycle, as well as on behavior.

Future studies may focus on the subgroup of patients in the Autism Inpatient Collection with the shortest sleep duration and highest scores on the ABC-C. Additional information about the most challenging patients within this hospitalized cohort would be useful in developing treatment guidelines. If the relationship between sleep and behavior in ASD is truly bidirectional, improvements in sleep should lead to improvements in behavior and vice versa, making both appropriate treatment targets. Exploring the relationship between use of sleep medications and

behavioral change could provide additional evidence of bidirectionality. However, many medications chosen to improve sleep can also impact behavior, making interpretation in such a study challenging. Comparing sleep problems in patients with different psychiatric co-morbidities (those with high levels of arousal such as Attention Deficit Hyperactivity Disorder and Anxiety Disorder vs. lower arousal diagnoses such as Depressive Disorders) would also be instructive in understanding correlations of sleep and behavior.

In summary, this study examines a large sample of hospitalized patients with ASD and severe behavioral disturbances. It lays the groundwork for future investigations of the relationship between sleep and behavior in this unique group.

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Author Contributions ES conceived of the study, participated in its design, and drafted the manuscript; TP participated in the design and interpretation of the data; CB conceived of the study and participated in its design and interpretation of the data, CP participated in the design, coordination of the study and interpretation of the data; DK participated in the design and interpretation of the data; MV participated in the design, coordination of the study and interpretation of the data; MS conceived of the study and participated in its design, SK performed the statistical analysis; MG participated in the design and performed the statistical analysis. All authors read and approved the final manuscript.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants when they enrolled in the AIC. As the current study involved retrospective review, formal consent was not required.

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