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Dev Neuropsychol. Author manuscript; available in PMC 2010 September 27.

Published in final edited form as:
Dev Neuropsychol. 2009 September ; 34(5): 560–573. doi:10.1080/87565640903133509.

Defining the Sleep Phenotype in Children with Autism

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Abstract

Sleep concerns are common in children with autism spectrum disorders (ASD). We identified objective sleep measures that differentiated ASD children with and without parental sleep concerns, and related parental concerns and objective measures to aspects of daytime behavior. ASD poor sleepers differed from ASD good sleepers on actigraphic (sleep latency, sleep efficiency, fragmentation) and polysomnographic (sleep latency) measures, and were reported to have more inattention, hyperactivity, and restricted/repetitive behaviors. Fragmentation was correlated with more restricted/repetitive behaviors. This work provides the foundation for focused studies of pathophysiology and targeted interventions to improve sleep in this population.

Keywords

Actigraphy; Polysomnography; Insomnia; Children's Sleep Habits Questionnaire; Child Behavior Checklist; Repetitive Behavior Scale

Autism spectrum disorders (ASD) are disorders of neurodevelopment characterized by impaired social interaction and communication (American Psychiatric Association, 2000). The prevalence of these disorders is estimated at approximately 1 in 150 children (CDC, 2007). Sleep disorders are common associated conditions(Ming et al., 2008), with a prevalence estimated to range from 44–83% (Richdale, 1999; Couturier et al., 2005; Krakowiak et al., 2008). Sleep-onset insomnia and nocturnal awakenings are the most frequent and consistent findings (Richdale, 1999; Honomichl et al., 2002; Wiggs and Stores, 2004; Williams et al., 2004). A recent consensus statement identified the treatment of insomnia in ASD to be a high priority area (Mindell et al., 2006). Treating disordered sleep in ASD also represents a potential avenue to improve daytime behavior and family functioning in this population (Malow and McGrew, 2008).

An essential component in planning interventional trials to improve sleep in children with ASD is to define objective measures of sleep that can be measured to document improvement with the intervention, and related to parent concerns. Objective measures used to define sleep concerns include polysomnography (PSG) and actigraphy. In our prior work, PSG differentiated children with ASD who had significant parental sleep concerns from those who did not(Malow et al., 2006). However, some children with ASD may not be able to tolerate

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PSG, given the anxiety of "sleeping with wires" in a non-home environment, intolerance due to a given child's tactile sensitivities, or both. Furthermore, PSG is a costly methodology and the limited amount of information provided by a pediatric PSG study may not justify its large expense. Actigraphy, a modality that measures sleep and wake patterns based on limb movement, is less-intrusive and costly than PSG, and can be performed in a child's home setting. It is recognized as a useful adjunct in the evaluation of patients with sleep disorders by the American Academy of Sleep Medicine, and is widely used in studies of childhood sleep (Mindell et al., 2006). However, studies have shown mixed results in using actigraphy to define parental sleep concerns in ASD, with most (but not all) investigators documenting a mismatch between parent report and actigraphic measures (Hering et al., 1999; Wiggs and Stores, 2004; Allik et al., 2006; Goodlin-Jones et al., 2008; Sitnick et al., 2008). This mismatch has been attributed to parent overreporting/overconcern in highly stressed caregivers (Hering et al., 1999; Wiggs et al., 2005), but may also reflect methodological limitations of actigraphy. These limitations may be due to either the technical performance of the actigraph (e.g., ability to measure sleep/wake patterns based on rest/activity) or to use of the actigraph in the home setting (e.g, ability of parents to record "lights out" accurately so that sleep latency can be calculated appropriately).

In this study, our goal was to determine whether parental sleep concerns are reflected in objective measures of sleep, so that these measures could be used to track improvement in interventional studies of sleep in ASD. This current study expands on our previous work relating parental sleep concerns to PSG and daytime behavior. We include a larger sample size and additional testing, including actigraphy, performed in a sleep laboratory simultaneously with PSG. Our rationale for performing actigraphy simultaneously with PSG was to identify its strengths in measuring sleep relative to PSG independent of the limitations of the home setting; follow-up studies of actigraphy in the home setting will be critical as well. Based on our earlier findings, we hypothesized that (1) There exist distinct subgroups (phenotypes) of children with ASD with and without parental sleep concerns, who can be distinguished by using PSG and actigraphy, as well as sleep questionnaires and (2) Sleep phenotype in ASD, as defined by both parent report and objective measures, is associated with daytime behavior.

METHODS

Participants

Fifty-eight children, ages 4 to 10 years, participated in this study. Participants were recruited from Vanderbilt University Medical Center subspecialty clinics as well as from the surrounding community. All had received a clinical diagnosis of ASD((American Psychiatric Association, 2000) confirmed by the Autism Diagnostic Observation Schedule(Lord et al., 2000). Children were excluded from the study if review of their medical history showed a history of epilepsy or intellectual disability, or if they were taking psychotropic medications. This protocol was approved by the Vanderbilt University Institutional Review Board with parents providing consent and children providing assent.

After informed consent was obtained, parents completed a series of questionnaires providing information on the child's demographic, social, and medical background. Included in the questionnaires was the collection of information about parental occupation and education, which was used to calculate socioeconomic status according to Hollingshead's Four Factor Index of Social Status (Hollingshead, 1975). Other questionnaires included the Parental Concerns Questionnaire (PCQ) (McGrew et al., 2007), the Children's Sleep Habits Questionnaire (CSHQ) (Owens et al., 2000), the Repetitive Behavior Scales-Revised (RBS-R)(Bodfish et al., 1999), and the Child Behavior Checklist (CBCL)(Achenbach TM and Rescorla LA, 2001).The Peabody Picture Vocabulary Test-III (PPVT-III) was given as a

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measure of receptive language understanding (Dunn, 1997). A sleep and medical history was performed on each child by a sleep specialist (BAM).

Sleep Measures

Children's Sleep Habits Questionnaire (CSHQ)—The CSHQ is a validated parentally-completed questionnaire used to examine sleep behavior in toddlers, preschool and school-aged children with a variety of conditions, including ASD (Malow et al., 2006; Goodlin-Jones et al., 2008). Subscales measure insomnia-related dimensions such as bedtime resistance, sleep anxiety, sleep onset delay, sleep duration, and night wakings, as well as other dimensions such as daytime sleepiness, sleep disordered breathing, and parasomnias. A total score can be calculated from all of the dimensions.

Parental Concerns Questionnaire (PCQ)—The Parental Concerns Questionnaire (PCQ) is a validated rating scale where parents describe the extent to which each of 13 behaviors have been a problem for the past month (McGrew et al., 2007). On this questionnaire, parents were asked one item to ascertain their perception of their child's sleep. The question was "Please describe the extent to which sleep disturbance (does not fall asleep easily, wakes often, etc.) has been a problem for you in the past month on a scale from 1 to 4 (1=no concerns; 2=mild concerns; 3=moderate concerns; 4=severe concerns)." Children whose parent's indicated no or mild concerns were classified as "good sleepers" and those with moderate or severe concerns were classified as "poor sleepers". Parental response on the PCQ was used to dichotomize groups based on our prior work, in which the PCQ response was more predictive of the child's objective sleep testing and behavioral findings than CSHQ data (Malow et al., 2006a).

Behavioral Measures

Child Behavior Checklist (CBCL)—The Child Behavior Checklist (CBCL) is a validated parentally completed questionnaire used to examine daytime behaviors in children (Achenbach TM and Rescorla LA, 2001; Achenbach and Rescorla, 2001; Achenbach and Rescorla, 2001). As the CBCL consists of two separate forms spanning the age range of our participants (ages 1 ½ to 5 years and 6 – 18 years), we collapsed our data across the age groups, including the scales common to both age groups. The CBCL defines T-scores ≥70 (≥98th percentile) within the clinical range, <65 (<93rd percentile) within the normal range, and between 65 and 70 (93rd – 98th percentile) within the borderline clinical range.

The Repetitive Behavior Scale-Revised (RBS-R)—The Repetitive Behavior Scale-Revised (RBS-R) is a validated scale used in autism to capture the breadth of repetitive behaviors (Bodfish et al., 1999). It consists of 6 subscales; stereotyped, self-injurious, compulsive, ritualistic, need for sameness, and restricted behaviors.

PSG–Actigraphy

Children were admitted to the Vanderbilt Sleep Research Core, located within the Vanderbilt Clinical Research Center (CRC) to undergo two consecutive nights of PSG and actigraphy monitoring. Video was recorded simultaneously, and a 21-channel EEG was also applied as part of the PSG recording. Children were accompanied by a parent. After being admitted to the CRC, the actigraph was placed on the child's dominant wrist in a standardized fashion. Children had previously been given the opportunity to wear the actigraph in their home environment, and were also desensitized to the PSG experience using story books describing the procedure. Participants were allowed to fall asleep according to their usual bedtime routine. "Lights out" was notated on both PSG and actigraphy recordings by the polysomnographic technologist (PSGT) performing the study, and start times for the PSG and actigraphy recordings were synchronized on the same computer.

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The following morning, children were allowed to awaken spontaneously. “Lights on” was notated by the PSG technologist at the conclusion of the study. Following disconnection from all PSG equipment, the participant was discharged from the CRC “on pass” for the remainder of the day. The actigraph was maintained on the child’s wrist, as tolerated. Later that evening, the same process was repeated, and the same actigraph was used for the second night of sleep.

Instrumentation—Actigraphy measurements were obtained with the use of AW-64 Actiwatch® monitors (Philips Respironics, Bend OR). The actiwatch is a small computerized wristwatch- like device that is used to detect movement (Sadeh A and Acebo C, 2002). It was worn on the dominant wrist over seven consecutive 24-hour periods. Actigraphy, widely used in sleep research and clinical practice, has been validated as a highly reliable method to differentiate sleep from wake(Sadeh and Acebo, 2002; Ancoli-Israel et al., 2003) based on the detection of movement and rest. Each actigraphy watch contains an accelerometer, which is able to detect motion greater than 0.01 g-force in all directions, and translate it into an electrical signal. This information is subsequently stored in memory within the watch as activity counts, a unit that expresses the largest of all measured accelerations over a predefined measurement epoch.

Data from the actigraphs were downloaded to a personal computer where all sleep intervals were manually placed on an actogram, or visual representation of the actigraphy data. The total nighttime sleep duration (TST) was the sum of all sleep epochs within the interval between the time set on the actogram for nighttime sleep and morning wake time. Sleep efficiency (SE) was calculated as the ratio of total nighttime sleep duration to the total time in bed. Sleep latency (SL) was calculated as the time required for sleep onset after lights out (first attempt to go to sleep). Wake after sleep onset (WASO) was measured as the sum of all wake epochs during the sleep period and reflects the number of minutes scored as wake that exceeded the sensitivity threshold. The fragmentation index (FI), captures all movement regardless of the intensity of the movement. All sleep variables were calculated using Actiware V5 software (Philips Respironics, Bend OR).

PSG data were obtained using the Nihon-Kohden 9200 sleep acquisition system. Monitoring included 21-channel electroencephalography (to evaluate for epileptic seizures), electrooculography, chin and bilateral leg (tibialis anterior) electromyography, nasal thermistor, nasal pressure transducer, electrocardiography, thoracic and abdominal effort, and pulse oximetry. Proper equipment functioning, which included replacement of electrodes as needed, was continuously monitored during each study by the sleep technologist.

Following acquisition, PSG data were manually scored by the sleep technologist, using standard criteria (Iber C et al., 2007). The scorer was blinded to participant group (ASD-GS, ASD-PS, TD). Sleep parameters were calculated for each PSG study by the sleep software package (Polysmith Acquisition and Review software, version 4.0.17.0, Neurotronics, Inc.). The definitions of PSG parameters resembled that of actigraphy parameters. Total sleep time (TST) was the total time comprised of epochs of sleep, with sleep efficiency (SE) calculated as the ratio of TST to total time in bed. Sleep latency (SL) was calculated as the time to the first epoch of sleep after lights out, and wake time after sleep onset (WASO) as the total time comprised of epochs of wake after sleep onset. Arousal index (AI) was calculated based on the American Academy of Sleep Medicine definition of an EEG arousal (Iber C et al., 2007).

Statistical Analysis

PSG and actigraphy parameters were averaged across nights for each participant. Descriptive statistics were conducted on all major variables. Kruskal-Wallis tests were used to determine overall difference among the three groups, and for those parameters that showed overall significance, Mann-Whitney U tests were used for pair-wise between-group comparisons.

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Spearman rank correlations (r_s) were used to evaluate associations between PSG and actigraphic sleep variables, subjective sleep measures, and behavioral scales. Results are presented as mean (standard deviation) and given the pilot nature of the study, we did not pursue formal multiple comparison adjustment. A p-value of less than 0.05 was considered statistically significant. Analyses were performed using SPSS V 15 (Chicago, IL) and SAS V 9 software (Cary, NC).

RESULTS

Participant Characteristics

Fifty-eight children met the study criteria and participated in the study between April 2004 and December 2007. Forty-two children (90% male) had ASD and 16 (75% male) were age-comparable typically developing (TD) children. Of the 42 children with ASD, 15 were classified by their parents as good sleepers (ASD-GS) and 27 were classified as poor sleepers (ASD-PS) based upon the PCQ. All TD children were classified as good sleepers based on the PCQ. Age, gender, socioeconomic score and PPVT did not differ significantly among groups. Two nights of overnight PSG were obtained for 55 children and one night only was obtained in three children due to technical difficulties (two children) or electrode intolerance (one child). Simultaneous wrist actigraphy was obtained in 28 children (two nights on 26 children and for one night only in two children (watch malfunction in one and not wearing of actigraph during the second night in one), 12 in the ASD-PS group, 7 in the ASD-GS group, and 9 in the TD group.

Sleep Histories

Sleep histories were reviewed in all participants. In the ASD poor sleepers, all described as having moderate to severe sleep problems. The major concern expressed by parents was difficulty falling asleep, which was reported in 19 of 27 children. Children were described as taking a long time to "wind down," with frequent vocalizations. Night wakings were of concern in 14 of 27 children, although only 4 parents considered night wakings to be the predominant sleep concern. Children were described to wander outside of their rooms and were found to be asleep outside of their bedrooms. In only one child, brief multiple night wakings associated with thrashing, inability to be consoled, and lack of recollection for the wakings in the morning were described. This child showed multiple wakings out of stage N3 sleep on PSG consistent with sleep terrors; actigraphy recordings were consistent with PSG showing multiple brief increases in activity coinciding with the PSG awakenings. Two children were reported to snore loudly; one showed evidence of obstructive sleep apnea and has been reported previously (Malow et al., 2006b). The other did not have evidence of sleep apnea on PSG. Other concerns voiced by parents were that their children did not get enough sleep or had restless sleep.

In the ASD good sleepers, nine parents rated their children as having no sleep problems and six as having mild sleep problems, which included mild bedtime resistance, mild sleep onset delay, presence of a parent to fall asleep, occasional night wakings with rapid return to sleep, or getting too little sleep. Several of the ASD good sleepers requested to go to bed at a scheduled time each night.

Comparison of Subjective and Objective Sleep Parameters Across Groups

Childhood Sleep Habits Questionnaire—Significant differences among all three groups were found on the CSHQ dimensions of sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, daytime sleepiness, modified total score, and total score (Table 2). The ASD-GS differed from the ASD-PS with the ASD-PS having higher scores on the dimensions of sleep onset delay, sleep duration, night wakings and total CSHQ score. The ASD-PS differed

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from the TD children with higher scores in all dimensions except sleep disordered breathing. There were no significant differences between the ASD-GS and the TD children.

Actigraphy—The three groups (ASD-GS, ASD-PS, TD) differed on objective measures of sleep (Table 3). With actigraphy, significant differences were found among all three groups for sleep latency, sleep efficiency, WASO, and FI. Compared to the ASD-GS group, the ASD-PS group took longer to fall asleep, had poorer sleep efficiency, had more WASO, and a higher FI. The ASD-GS also differed from the TD children in having less WASO and a lower FI.

Polysomnography—With PSG, significant differences were found among all three groups for sleep latency (Table 3). The ASD-PS took significantly longer to fall asleep than either the ASD-GS, or the TD children. In contrast to actigraphy, other sleep parameters (TST, SE, WASO, and AI) did not differ among the three groups. Because some children with PSG data lacked actigraphy data, it was possible that inherent differences in these children's sleep profile may have contributed to differences observed between PSG and actigraphy parameters for the three groups. To consider this possibility, a separate analysis comparing PSG parameters in the three groups was performed, limited to the 28 children who had simultaneous PSG and actigraphy. Results were comparable in this subset of children to those found in the 58 children who had PSG with or without actigraphy.

Apart from the child with sleep terrors, night wakings (lasting 15 minutes or more) were recorded in only two of the ASD-PS children, both of whom had parent concerns of night wakings. One awakened at 3 am and did not return to sleep. These night wakings were detected by both actigraphy and PSG. No epileptic seizures were recorded on PSG. No evidence of rapid eye movement behavior disorder was found, with tonic and phasic muscle tone during REM sleep normal in all children.

Relation of Parental Sleep Concerns to Daytime Behavior and Objective Sleep Measures

Parental Concerns Questionnaire—Differences were found between all three groups on the PCQ items. The ASD-PS group showed more inattention and hyperactivity than the ASD-GS group (Table 4). Additionally, in the ASD children, WASO measured by actigraphy was associated with the PCQ hyperactivity scale (r_s =0.48, p=0.04) The TD children scored lower than both the ASD-GS and ASD-PS groups on all items on the PCQ, with the exception of the sleep item, which was comparable for the ASD-GS and TD children

Repetitive Behavior Scale-Revised (RBS-R)—Differences were found between all three groups on the RBS-R subscales The ASD-PS group showed higher scores on the compulsive and ritualistic scales, as compared to the ASD-GS group (Table 5). The TD children scored lower than both the ASD-GS group and the ASD-PS group on all subscales. In the ASD children, nighttime fragmentation was significantly associated with the RBS-R subscales ritualistic (r_s=0.69, p <0.001), compulsive behavior (r_s=0.57, p =0.01), need for sameness (r_s=0.54, p =0.02), restricted (r_s=0.51, p =0.03), and total (r_s=0.505, p =0.04).

Child Behavior Checklist—No differences were found between the ASD-PS and ASD-GS groups. All CBCL scales differed significantly among the three groups (Table 6), with the TD children scoring lower than both the ASD-GS and the ASD-PS groups.

DISCUSSION

Our findings support the hypothesis that parental reports of sleep concerns in children with ASD can be confirmed not only by comprehensive questionnaires but by objective measures that include both PSG and actigraphy. Children classified as poor sleepers (as compared to

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good sleepers) had a longer sleep latency on both PSG and actigraphy, and more sleep fragmentation and WASO on actigraphy. Children with ASD who were classified as good sleepers showed comparable (or, in some cases, better sleep) compared to TD children on objective and subjective sleep parameters. Furthermore, we identified associations between the sleep phenotype and daytime behavior, with poor sleepers with ASD showing more hyperactivity and compulsive and ritualistic behavior than good sleepers with ASD. Objective actigraphic measures also related the sleep phenotype to daytime behavior, with WASO correlated with hyperactivity and sleep fragmentation correlated with restricted/repetitive behaviors. These associations will require confirmation in larger studies.

Our work is the first to simultaneously assess the ability of PSG and actigraphy to distinguish sleep patterns in children with ASD based on parental concern. We had expected to find that actigraphy and PSG were comparable in distinguishing sleep patterns. Our results show that actigraphy not only is comparable to PSG, but it also provides additional information in the areas of nighttime activity (e.g., FI and WASO). While PSG has traditionally measured arousals and awakenings as indicators of fragmentation and restlessness, it appears that movement itself, regardless of whether it results in an arousal or awakening, may impact adversely on sleep and daytime behavior. Further research is warranted into the nature and impact of these movements on the sleep and behavior of these children. The reason for the increased WASO depicted by actigraphy relative to PSG is unclear. WASO, measured with actigraphy, represents the sum of all wake epochs during the sleep period and reflects the number of minutes that exceed the sensitivity threshold and are scored as wake As PSG and actigraphy use different algorithms to detect wake epochs, it is possible that the differences in WASO reflect methodological differences in PSG and actigraphy Further analysis of fragmentation and WASO in larger samples, with attention to the number and durations of awakenings may help delineate these differences.

In prior studies, the ability of actigraphy to differentiate sleep patterns in children with ASD has been mixed. Allik et al (2006), collecting one week of actigraphy in 32 high functioning children with ASD ages 8–12 years, and age and gender matched typically developing children, demonstrated prolonged sleep latencies in the children with ASD. The 19 children with sleep problems also demonstrated prolonged sleep onset delay compared to those without sleep problems. Night wakings did not differ in either the total group of ASD compared to controls, or the ASD subgroups compared to each other. In a large group of preschoolers (n = 194) that included children with ASD, developmental delay (DD), and those who were TD, parental reports of sleep problems were higher in the children with ASD and DD compared to the TD group (Goodlin-Jones et al., 2008). However, while one week of actigraphy and sleep diaries were significantly positively correlated, mean values differed, with diaries underreporting sleep latency and WASO compared with actigraphy. A subsequent paper by the same group combining video with actigraphy examined night wakings in a subset of that group (n=58) (Sitnick et al., 2008). They concluded that actigraphy had poor agreement in detecting nocturnal awakenings compared to video recordings. Two other studies that included older children with ASD also found discrepancies between parent report and actigraphy, although in contrast to Goodlin-Jones et al., reported that parents appeared to *over report* sleep problems in their children.(Hering et al., 1999; Wiggs and Stores, 2004) With the exception of an early morning arousal time, Hering et al (1999) found that 72 hours of actigraphy did not differ in children with ASD and parental sleep concerns (n = 8; ages 3–12 years) as compared to age and gender-matched controls. Wiggs and Stores (2004) compared 38 ASD children with parentally-reported “sleeplessness” and 24 ASD children without a parentally-reported sleep problem, ages 5–16 years. Five nights of actigraphy were recorded. The two groups did not differ on actigraphic parameters, although sleeplessness was defined broadly and included reluctance to go to bed, insistence on sleeping with someone else, and excessive daytime sleepiness, in addition to sleep onset delay and night wakings.

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The differences between these studies and ours may be attributable to several factors. First, in our study, actigraphy data were collected in a controlled environment, rather than in the child's natural setting. Second, we used a restricted age range, with a sample limited to higher functioning children without intellectual disability, epilepsy, or psychiatric conditions requiring psychotropic medications. Both of these factors may have contributed to the integrity of our data and decreased variability in actigraphic measurements. In one study of actigraphy reliability, preschoolers and adolescents showed poorer reliability than 4 and 5 year olds. (Acebo et al., 1999). Third, our groups of children with and without parentally reported sleep problems showed significant differences on the CHSQ, with comprehensive sleep histories confirming parentally reported sleep concerns. Fourth, PSG was performed in all children to evaluate for co-existing sleep disorders. Finally, differences in actigraph equipment and scoring algorithms among studies may have affected our results.

Polysomnography remains the gold standard for detecting sleep disorders such as obstructive sleep apnea, and, when combined with video and EEG, parasomnias and seizures. Therefore, we recommend PSG be performed in any child in whom the clinical suspicion of one of these disorders is high. It is notable that we found a relatively low prevalence of sleep disorders other than insomnia in our cohort, with only one child having obstructive sleep apnea and another having sleep terrors. Both were suspected to have these disorders based on their sleep histories. None had REM behavior disorder or sleep-related epileptic seizures. REM behavior disorder has been reported previously in a case series of children with ASD, although this series differed from ours in containing children with coexisting intellectual disability (Thirumalai et al., 2002). REM behavior disorder can also be caused by some of the antidepressants used in this population to treat coexisting psychiatric disorders. Epilepsy has also been associated with intellectual disability in autism (Tuchman and Rapin, 2002), and in a cohort of children taking psychotropic medications with coexisting intellectual disability, parasomnias were more prevalent (Ming et al., 2008). Future studies examining sleep in a more heterogenous group of children with coexisting intellectual disability or taking psychotropic medications will be necessary to determine the true prevalence of sleep disorders other than insomnia in this population.

Our study had several strengths. Our participants were a well-defined group of children with ASD, whose clinical diagnosis was confirmed with the ADOS. Parental sleep concerns were confirmed by sleep histories, and all had video-EEG-PSG to exclude sleep disorders such obstructive sleep apnea, parasomnias, and sleep-related seizures. They were free of psychotropic medications and did not have intellectual disability or epilepsy. This has allowed us to establish a baseline sleep phenotype, free of confounders, in this population. Our staff were successful in obtaining recordings in all children, although the higher functioning nature of our cohort may have contributed to this success. The characteristics of our cohort may also be viewed as a limitation, in that results may not be generalizable to all children with ASD. Another important strength of our study, but also a limitation, is that actigraphy data were collected in a controlled setting, where precise measurements of "lights off" could be recorded and the integrity of the recordings could be ensured. In the home setting, with competing stressors, parents may not remember to activate event markers or even to place the watch on the child. Future studies will be necessary to confirm our findings in the home setting. Of note, we have documented a significant decrease in actigraphic sleep latency in a cohort of children whose parents received behavioral sleep education (Reed et al., in press). Another limitation of our study is that night wakings were relatively in common, both by history and by objective findings. In one large study surveying 210 children with ASD, night wakings were more frequent in children with ASD and coexisting intellectual disability (Williams et al., 2004). Had our sample contained children with mixed cognitive levels, it is possible we may have detected more night wakings. Finally, we used subjective parentally-reported measures of daytime behavior to differentiate the ASD-PS and ASD-GS groups. However, it is noteworthy

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that parents did not globally report problems in daytime behavior—inattention and hyperactivity were associated with sleep concerns. Inattention and hyperactivity have also been reported in association with sleep disorders in typically developing children (Chervin et al., 2002; Gottlieb et al., 2003).

In summary, our results suggest that parentally based sleep concerns in children with ASD are substantiated by objective parameters, and selectively influence measures of daytime behavior. Actigraphy and PSG are complementary objective measures for defining sleep that substantiate parental report. Defining the phenotype of sleep in ASD, its relation to daytime behavior, and appropriate measurement modalities provides the foundation for focused studies of sleep pathophysiology and targeted interventions in this population.

Acknowledgments

We acknowledge Peter Howard, RPSGT and Pagan Howard for assistance with polysomnography and Hannah Reed, BA for assistance with actigraphy. Megan Rothney, MS provided technical assistance and Ivy Andersen, MD assisted with admitting the children to the Clinical Research Center.

This research was supported by a Vanderbilt University Interdisciplinary Discovery Grant, Vanderbilt CTSA Grant 1 UL1 RR024975 from the National Center for Research Resources, National Institutes of Health, the Vanderbilt Kennedy Center for Research in Human Development, and the National Alliance for Autism Research.

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Table 1

Participant Characteristics

	Mean (SD)		
	ASD-Poor Sleep n=27	**ASD-Good Sleep n=15**	**Typically Developing Good Sleep n=16**
Age (Years)	5.8 (1.8)	5.9 (2.2)	6.9 (1.9)
Gender (Male)	88.9%	93.3%	75.0%
Socioeconomic Status	49 (8.8)	55 (10.0)	49.4 (9.2)
PPVT-Standard Score	99.6 (12.4)	102.6 (15.0)	104 (15.0)

PPVT = Peabody picture vocabulary test

ASD = autism spectrum disorder

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Table 2

Comparison of Children's Sleep Habits Questionnaire Subscales Among ASD Poor Sleepers, ASD Good Sleepers, and Typically Developing Children

	Mean (SD)			
	ASD-PS	**ASD-GS**	**TD**	**Overall Significance[1]**
Subscale	**n=27**	**n =15**	**n=15**	
Bedtime Resistance	8.5 (2.9)	7.5 (2.3)	8.3 (2.7)	0.60
Sleep Onset Delay	2.1 (0.9) *a, b*	1.5 (0.6)*a*	1.2 (0.5) *b*	<0.01
Sleep Duration	5.7 (1.7) *a, b*	4.1 (1.4)*a*	3.8 (1.1)*b*	<0.01
Sleep Anxiety	6.5 (2.3)*b*	5.4 (1.8)	5.2 (2.0)*b*	0.07
Night Wakings	5.5 (2.1) *a, b*	4.1 (1.8)*a*	4.0 (1.2)*b*	0.05
Parasomnias	10.5 (2.1)*b*	9.2 (2.0)	8.6 (1.5)*b*	0.02
Sleep Disordered Breathing	3.8 (1.2)	3.5 (0.7)	3.2 (0.4)	0.20
Daytime Sleepiness	15.4 (3.4)*b*	13.3 (3.7)	12.3 (3.0)*b*	.02
Total	53.8 (6.7) *a, b*	45.8 (8.2)*a*	43.8 (6.6)*b*	<0.01

Kruskal Wallis Test Statistic

a Significant at < 0.05 between ASD_GS and ASD_PS groups with Mann-Whitney U

b Significant at < 0.05 between ASD_PS and TD groups with Mann-Whitney U

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Table 3

Comparison of Actigraphy and Polysomnography Parameters Among ASD Poor Sleepers, ASD Good Sleepers, and Typically Developing Children

	Mean (SD)			
	ASD-PS n=27	**ASD-GS n=15**	**TD n=16**	**Overall Significance[1]**
Actigraphy Measured Sleep[1]	**n=12**	**n=7**	**n=8**	
Sleep Latency (minutes)	53.4 (25.6)[b]	23.0 (19.0)[b]	33.7 (32.2)	**0.01**
Sleep Efficiency (minutes)	80.9 (6.6)[b]	88.3 (5.1)[b]	84.7 (4.6)	**0.05**
Wake After Sleep Onset (minutes)	39.5 (12.6)[b]	19.5 (6.1)[a, b]	31.7 (12.4)[a]	**<0.01**
Total Sleep Time (minutes)	481.5 (56.8)	482.7 (58.9)	475.9 (38.8)	0.99
Movement & Fragmentation Index	13.5 (3.4)[b]	9.4 (3.1)[a, b]	14.0 (3.3)[a]	**0.04**
Polysomnography Measured Sleep[2]	**n=27**	**n=15**	**n=16**	
Total Sleep Time (minutes)	495.9 (65.8)	489.3 (52.4)	488.4 (44.7)	0.89
Sleep Latency (minutes)	54.0 (41.7)[b, c]	31.1 (28.9)[b]	34.9 (34.3)[c]	**0.02**
Sleep Efficiency (minutes)	84.7 (7.0)	88.3 (6.2)	87.8 (6.1)	0.19
Wake After Sleep Onset (minutes)	25.7 (14.9)	26.2 (23.1)	29.1 (18.6)	0.72
Arousal Index	8.5 (3.3)	7.7 (2.9)	7.8 (3.0)	0.72

Kruskal Wallis Test statistic.

[1] Average of two nights sleep.

[a] Significant at < 0.05 between ASD_GS and TD groups with Mann-Whitney U test.

[b] Significant at < 0.05 between AS_GS and ASD_PS groups with Mann-Whitney U test.

[c] Significant at < 0.05 between ASD_PS and TD with Mann-Whitney U test.

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Table 4

Parental Concerns Questionnaire: by ASD Good Sleeper, ASD Poor Sleeper, and Typically Developing Child

	Mean (SD)			
	ASD-PS	**ASD-GS**	**TD**	**Overall Significance[1]**
Scale	**n=27**	**n =15**	**n=16**	
Language use and understanding	2.3 (1.0)[b]	2.3 (2.3)[a]	1.1 (0.3)[a, b]	<0.01
Compulsive behavior	2.2 (0.8)[b]	1.7 (0.7)[a]	1.1 (0.3)[a, b]	<0.01
Anxiety	2.6 (0.7)[b]	2.3 (0.5)[a]	1.1 (0.3)[a, b]	<0.01
Sensory issues	2.3 (0.9)[b]	2.1 (0.7)[a]	1.1 (0.3)[a, b]	<0.01
Sleep disturbance	2.9 (0.9)[b,c]	1.4 (0.5)[c]	1.2 (0.4)[b]	<0.01
Aggression	1.7 (0.9)[b]	1.7 (0.5)[a]	1.2 (0.4)[a, b]	0.03
Hyperactivity	2.4 (0.9)[b, c]	1.9 (0.9)[a, c]	1.1 (0.3)[a, b]	<0.01
Attention span	2.7 (0.8)[b, c]	2.3 (0.7)[a, c]	1.3 (0.4)[a, b]	<0.01
Mood swings	2.1 (1.0)[b]	2.1 (0.8)[a]	1.2 (0.5)[a, b]	<0.01
Eating habits	2.3 (1.2)[b]	2.3 (1.1)[a]	1.3 (0.4)[a, b]	<0.01
Social interactions	2.7 (0.9)[b]	2.5 (0.8)[a]	1.1 (0.3)[a, b]	<0.01
Self-stimulatory and repetitive behaviors	2.3 (1.0)[b]	2.2 (0.9)[a]	1.1 (0.0)[a, b]	<0.01
Self-injurious behaviors	1.4 (0.6)[b]	1.3 (0.6)	1.0 (0.0)[b]	0.02

Kruskal Wallis Test Statistic.

[a] Significant at < 0.05 between ASD_GS and TD groups with Mann-Whitney U test.

[b] Significant at < 0.05 between ASD_PS and TD with Mann-Whitney U test.

[c] Significant at < 0.05 between AS_GS and ASD_PS groups with Mann-Whitney U test.

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Table 5

Repetitive Behavior Scale: by ASD Good Sleeper, ASD Poor Sleeper, and Typically Developing Child

	Mean (SD)			
	ASD-PS[c]	**ASD-GS[a]**	**TD[a, c]**	**Overall Significance[1]**
Subscale	**n=25**	**n =13**	**n=6**	
Stereotyped Behavior	5.8 (2.9)	4.3 (3.4)	0.2 (0.4)	<0.01
Self-Injurious Behavior	2.8 (3.5)	1.9 (2.7)	0 (0)	0.04
Compulsive Behavior	5.7 (3.9)[b]	2.8 (2.3)[b]	0.7 (1.6)	<0.01
Ritualistic Behavior	6.4 (3.9)[b]	3.8 (3.2)[b]	0.2 (0.4)	<0.01
Sameness Behavior	9.4 (6.4)	5.6 (3.9)	0.5 (1.2)	<0.01
Restricted Behavior	4.9 (3.1)	3.6 (2.6)	0.2 (0.4)	<0.01
All Total	35.0 (18.9)	22.2 (13.4)	1.7 (4.1)	<0.01

Kruskal Wallis Test Statistic.

[a] All subscales were significant at p< 0.05 between ASD-GS and TD groups with Mann-Whitney U test statistic.

[b] All subscales were significant at p< 0.05 between AS-GS and ASD-PS groups with Mann-Whitney U test statistic.

[c] All subscales were significant at p< 0.05 between ASD-PS and TD with Mann-Whitney U test statistic.

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Table 6

Sleep Classifications and Associations With the Child Behavior Checklist Scales

	Mean (SD)			
	ASD-PS	**ASD-GS**	**TD**	**Overall Significance[1]**
Scale	**n=27**	**n =15**	**n=15**	
Anxious/depressed	61.5 (13.2)[b]	57.4 (8.9)[a]	51.6 (3.2)[a, b]	<0.01
Somatic complaints	61.1 (8.8)[b]	59.9 (7.8)[a]	51.3 (2.1)[a, b]	<0.01
Attention problems	67.7 (10.9)[b]	63.7 (9.2)[a]	51.7 (1.7)[a, b]	<0.01
Aggressive behavior	60.6 (7.7)[b]	58.9 (9.0)[a]	51.1 (1.5)[a, b]	<0.01
Internalizing	66.9 (7.7)[b]	62.6 (9.3)[a]	42.4 (8.1)[a, b]	<0.01
Externalizing	60.4(7.8)[b]	54.6 (10.2)[a]	45.1 (6.4)[a, b]	<0.01
Total Score	67.4(8.0)[b]	61.6 (11.9)[a]	43.5 (6.6)[a, b]	<0.01
Affective problems	69.6 (10.2)[b]	62.7 (10.3)[a]	51.9(3.0)[a, b]	<0.01
Anxiety problems	63.1(10.4)[b]	59.6 (10.8)[a]	51.3 (3.5)[a, b]	<0.01
ADD problems	62.5 (9.0)[b]	59.7 (10.8)[a]	51.2(2.0)[a, b]	<0.01
Oppositional defiant problems	59.1 (8.4)[b]	57.9 (7.6)[a]	52.1(3.3)[a, b]	0.01

Kruskal Wallis Test statistic.

[a] Significant at < 0.05 between ASD_GS and TD groups with Mann-Whitney U statistic.

[b] Significant at < 0.05 between ASD_PS and TD groups with Mann-Whitney U statistic.