LONGITUDINAL ANALYSIS OF SLEEP DISRUPTION IN PEDIATRIC SUBJECTS
WITH DOWN SYNDROME:
EFFECTS ON LANGUAGE AND EXECUTIVE FUNCTION

By

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Abstract

Sleep plays an important role in healthy development, and previous research has shown adverse effects of sleep disruption on executive function, memory, and learning. Individuals with Down syndrome experience an overwhelmingly high degree of sleep disturbance, and studies have found that even young children with Down syndrome experience greater sleep disruption than typically developing children. Thus, in this study we used an objective measure of sleep, actigraphy, to investigate the longitudinal progression of sleep disruption in a group of toddlers with Down syndrome (n=9), and examined the relations between poor sleep, language development, and executive function over two years. Results indicate that the effects of disrupted sleep manifest early in development: the development of syntactic complexity is significantly affected, with children who demonstrate more fragmented sleep at the first testing, which occurred between 2-5 years of age, experiencing smaller increases in grammatical complexity over the two-year period. More fragmented sleep at the first testing also correlates with greater impairment of executive function at both time points. These findings provide evidence that sleep disruption at a young age influences later executive functioning and language development, and underscore the importance of early screening and treatment for children with Down syndrome.

Keywords: sleep, Down syndrome, executive function, language, actigraphy
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Sleep is an essential component of healthy physical and cognitive development, and has been widely investigated in typically developing children and adults. Individuals with Down syndrome are one population highlighting the need for greater examination of sleep disruption in the context of atypical development as well; they have an overwhelmingly high prevalence of sleep problems, and thus may experience greater effects of sleep disruption than found in the typical population. Short-term language development has been shown to be affected by sleep in typically developing infants (Gomez, Bootzin, & Nadel, 2006), but effects over a longer time period have yet to be investigated with objective measures of sleep, as they are often difficult to implement with younger age groups. Thus, assessing the longitudinal extent of the interplay between sleep and language over two years in preschoolers with Down syndrome will allow for a greater understanding of the links between language development, behavioral function, and sleep disruption in this population.

Down syndrome (DS) is the most common genetic developmental disorder, occurring in approximately 1 of every 1000 live births (Weijerman & de Winter, 2010), and is most often characterized by a triplication of the twenty-first chromosome (trisomy 21). DS is one of the most prevalent causes of intellectual disability, and individuals with DS often experience delayed motor and cognitive development, with mental age lagging behind chronological age. More specifically, studies have shown deficits in neuropsychological measures tapping hippocampal, prefrontal, and cerebellar functioning (Pennington, Moon, Edgin, Stedron, & Nadel, 2003; Edgin, Pennington, & Mervis, 2010). DS is also associated with physical growth delays, as well as a particular set of facial characteristics that may contribute to the prevalence of sleep disruption in DS (Allanson, O’Hara, Farkas, & Nair, 1993). For newborns, the incidence of congenital heart
disease may be as high as 50% (Urbano, 2010), an important factor to consider in the investigation of early childhood sleep in children with DS.

Patients with Down syndrome have an overwhelmingly high degree of sleep problems, with between 70 and 80% of those diagnosed with DS experiencing obstructive sleep apnea syndrome (OSAS), a disorder characterized by cessation of breathing during sleep due to blockage of the upper airway (Churchill, Kieckhefer, Landis, & Ward, 2012). This is likely attributable to the physiological differences in individuals with Down syndrome that predispose the airway to collapse during sleep: craniofacial and upper airway abnormalities, a high incidence of obesity, and generalized hypotonia. OSAS causes both a decrease in blood oxygenation levels and an increase in arousals during sleep, and is ideally diagnosed using polysomnography (PSG), which provides a detailed assessment of sleep architecture and high specificity in detecting sleep disruption. However, the high level of intrusiveness makes PSG difficult to implement in studies including children of young ages or those with developmental disorders who may become distressed in a strange new environment. Movement monitoring (actigraphy) has previously been validated for the prediction of sleep and wake in typically developing groups (Sadeh, Hauri, Kripke, & Lavie, 1995), and has recently been shown to correlate highly with PSG reports in children with sleep disordered breathing (SDB), with an agreement of over 80% on measures of sleep time and sleep efficiency when compared epoch-by-epoch with PSG monitoring (Hyde et al., 2007). This suggests that actigraphy may provide an alternative method of monitoring sleep disruption in young children with DS: it is inexpensive, non-invasive, and suitable for use in-home. Actigraphy conducted over a period of 5 nights in school-aged children with DS found greater sleep disruption in the DS group as compared with typically developing children and those diagnosed with Williams syndrome; DS children had
lower sleep efficiency, higher fragmentation, and increased night wakings (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2013), all symptoms indicative of disrupted sleep and suggestive of OSAS.

Children with DS exhibit a unique pattern of deficit in language functions, and due to these deficits it is often difficult to accurately assess language development in DS, as assessments designed for TD children may display substantial floor effects. A large percentage of children with DS exhibit asynchronies in their development of language, with productive language skills lagging behind comprehension skills (Chapman, 1995; Miller, 1988), and particular difficulty emerging in the production of grammar and syntactic complexity (Chapman, 1997). Due to these asynchronies in expression of language, care must be taken to use instruments previously validated for use in DS populations: one such instrument is the MacArthur-Bates Communicative Development Inventory: Words and Sentences (CDI), which has been shown to correlate significantly with direct report of vocabulary in children of mental age 12-28 months with DS (Miller, Sedey, & Miolo, 1995). Use of the CDI confirmed a marked difference in the pattern of language acquisition, despite equivalent early language delay, between children diagnosed with DS and children diagnosed with Williams syndrome; cross-sectional data revealed that later in development, children with DS begin to exhibit deficits in grammatical development more severe than those predicted by their early performance (Singer Harris, Bellugi, Bates, Jones, & Rossen, 1997). Longitudinal studies are necessary in order to uncover the developmental trajectory of this language deficit, and the influence that the differing sleep patterns of these populations may have on their language acquisition abilities is as yet still unclear. As an alternative to parent report of vocabulary, naturalistic recording of the language environment using the LENA digital language processor (Language Environment Analysis,
LENA Foundation, Bend, OR) provides an unobtrusive method of assessing the level of child
and adult speech (Ford, Baer, Xu, Yapanel, & Gray, 2009), and the accuracy of LENA software
analysis of vocalizations has previous been established for TD children (Xu, Yapanel, & Gray,
2009). Oller et al. (2010) examined the use of LENA software analysis in children with autism
and language delay, finding that the automated analysis of natural language recordings also
provided accurate monitoring of developmental patterns in vocalization in these populations.
Preliminary work in the Down Syndrome Research Group indicates that the automated vocal
analysis of naturalistic recordings may provide a reliable and effective method of evaluating
speech production in DS populations as well (Casanova, 2012). Although there is a dearth of
research on the language environments of children diagnosed with DS, particularly
longitudinally, previous work with the LENA in TD populations has found that children who
hear more child-directed speech at 19 months exhibit larger expressive vocabularies at 24
months, even when controlling for their initial expressive language skill at 19 months (Weisleder
and Fernald, 2013). This suggests that the longitudinal analysis of naturalistic recordings may
provide invaluable insight into outside sources of influence on children’s language development,
over and above differences in their initial language abilities.

A large body of previous work has established the effects of sleep disruption on executive
function, memory, and performance on various neurocognitive tasks in typically developing
adults and children. However, studies involving both sleep and language measures are rare, and
work with DS populations is usually limited to correlational studies of children of school age or
older. Sleep-disordered breathing in adults with DS is associated with cognitive deficits, with
higher levels of apnea correlating with increased difficulty completing neuropsychological tasks
involving right hemisphere functioning (Andreou, Galanopoulou, Gourgoulianis, Karapetsas, &
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Molyvdas, 2002), and a recent study with individuals with DS ages 7-18 years demonstrated that children comorbid for OSAS had lower verbal IQ scores and lower performance on a test of cognitive flexibility (Breslin, Spanò, Bootzin, Anand, Nadel, & Edgin, 2014). Still, the extent to which this affects the early development of young children with DS is as yet uncertain. Cross-sectional work using actigraphy with school-aged TD children indicates that the correlation between sleep and performance was stronger for younger children-those who experience fragmented sleep are characterized by lower performance on neurobehavioral tasks of sustained attention and behavioral inhibition, and higher rates of parent-reported behavior problems—but this may be due to confounding effects of unidentified medical factors that have a stronger influence at a young age rather than the increased vulnerability of young children to sleep disruption (Sadeh, Gruber, & Raviv, 2002). As this study collected data at only one time-point, that question remains unanswered. That being said, it has been shown that treating school-aged children with OSAS results in modest improvements in executive functioning and motor skills as well as decreases in behavioral problems (Owens, Spirito, Marcotte, McGuinn, & Berkelhammer, 2000), permitting hope that, given an early diagnosis, alleviation of the detrimental effects of sleep disturbance on cognition and development is possible. In a rare longitudinal design, investigation of preschoolers at 1 year of age and 4 years of age established that a higher ratio of nighttime sleep in infancy-evidence of a more mature sleep state-led to higher performance on later measures of executive function and abstract reasoning, though not measures of general cognition (Bernier, Beauchamp, Bouvette-Turcot, Carlson, & Carrier, 2013). Results held when controlling for family socioeconomic status and prior executive functioning, suggesting that the importance of sleep for higher order cognition may appear very early in development. However, this study did not use objective measures of sleep disruption, relying instead on parent report,
which is highly susceptible to inaccuracy as parents may not always be aware of the characteristics of their children’s sleep (Schott et al., 2006).

Whereas the literature on the effects of SDB on cognition and behavior in DS is relatively consistent, studies involving effects of SDB on language impairments are less conclusive, and few investigations have examined infants or preschoolers through their developmental period. Sadeh (2007) hypothesized that good sleep favors optimal functioning in children through both its role in maturation and memory consolidation and by allowing alertness during the day, thus facilitating learning. As has been found in previous adult research, naps in school-aged children improve acquisition and integration of novel vocabulary (Henderson, Weighall, Brown, & Gaskell, 2012), and naps in infants appear to support more flexible learning, facilitating language abstraction (Gomez, Bootzin, & Nadel, 2006). A matched pairs study of preschoolers and school-aged children indicated that there may be a longitudinal adverse effect of sleep-disordered breathing on verbal skills, with preschoolers exhibiting difficulty processing linguistic complexity and older children demonstrating reduced ability of verbal concepts; this effect was particularly prominent in those children who met criteria for diagnosis of OSAS (Honaker, Gozal, Bennett, Capdevila, & Spruyt, 2009). Thus, it is suggested that these early verbal deficits may underlie the later negative effects of SDB on socioemotional behavior that have been previously observed in both DS and TD school-aged children.

There are clear adverse effects of sleep disruption on cognition and behavior in older children with DS, as well as younger TD children, however, the extent to which the influence of sleep disruption modulates language development in younger DS children and thus any potential for earlier intervention has yet to be addressed. Preliminary work with a group of DS toddlers (n=27) demonstrated a correlation between increased sleep fragmentation and parent-reported
total vocabulary of the child on the MacArthur-Bates CDI (r = -0.60, p = 0.001). However, the persistence of this effect is uncertain, as it could have long-lasting repercussions as was seen in Bernier et al., or be simply a state-dependent transient effect: longitudinal evaluation of language development in this population is needed to clarify this result. Thus, we propose to use an objective measure of sleep to investigate the links between language development, behavioral function, and sleep disruption in pediatric subjects with Down syndrome over time, in hopes of assessing the longitudinal extent of the interplay between sleep and language use.

**Methods and Materials**

*Participants*

Ten children between the ages of 2-7 (7 male, 3 female, mean age at first testing 3.7±1.0) and their parents participated in this study. The University of Arizona Institutional Review Board approved all procedures, and informed consent was obtained from the parents. Subjects’ first testing occurred in 2012-2012. A second testing was performed 2 years subsequent to the first testing, within 1 month of the first test date. Procedures were identical for tests at time 1 and time 2. Study equipment was mailed or hand-delivered to the participant’s homes, which were recruited from the surrounding Arizona area. All participants were diagnosed with Down syndrome. Exclusion criteria included diagnosis with types of Down syndrome other than Trisomy 21, a non-English speaking parent, or primary household language other than English. Additionally, data were excluded when less than 5 consecutive nights of actigraphy were obtained. Medical history was taken, and parents were asked to complete a developmental questionnaire, a child-language assessment (MacArthur-Bates CDI), and measures of executive
function and behavior. All participants were in good health. In cases of a temporary health problem (e.g. a cold), participants were reassessed following their recovery.

**Sleep Assessment**

Sleep was evaluated using actigraphy (Actiwatch 2, Phillips Respironics Mini-Mitter, Bend, OH, USA), a non-intrusive method of evaluating sleep-wake patterns in children and adults. The Actiwatch-2 has previously been validated against polysomnographic scoring, and has been shown to provide good sensitivity and accuracy in measuring sleep (Meltzer et al., 2012), as well as higher correlations with PSG in measuring sleep efficiency than other devices currently marketed (Weiss et al., 2010). All subjects wore the actigraph on the non-dominant wrist for 7 consecutive days. Parents completed a sleep log for the 7 day period, a widely used measure in sleep research with infants and toddlers (Sadeh, 2011), which was used as supplemental data to evaluate discrepancies between parental report and actigraphic data (for example, due to not wearing the device). One subject was unable to tolerate the actigraph and thus excluded from further analysis.

The Actiwatch 2 weighs 16 g and samples at 32 Hz. Data was collected in 30-s epochs, and analyzed using commercially available software (Respironics Actiware 5.71.0, Bend, OR). Actigraph data was scored at the medium sensitivity (activity counts=40/min), with sleep onset and sleep end marked by a period of 3 and 5 min of immobility or more, respectively (Meltzer et al., 2011). Each epoch of data from the Actiwatch was assessed as sleep or wake, based on whether the activity score exceeded the medium threshold. Variables of interest included sleep efficiency (percentage of time spent in bed scored as sleeping; scored total sleep time divided by duration of the given rest interval), fragmentation index (an index of the amount of movement over the sleep period; sum of percent mobile and percent one minute immobile bouts divided by
the number of immobile bouts for the given interval), and wake after sleep onset (total time scored as wake after onset of sleep).

*Language Assessment*

Child language development was assessed with the LENA digital language processor (Language Environment Analysis, LENA Foundation, Boulder, CO), a digital recorder that stores 16-h of sound environment for later analysis by LENA software speech-identification algorithms. The recorder weighs approximately 2.5 ounces, and fits into a pocket on the front of children’s clothing specifically designed for the device. Parents were instructed to begin recording when their child awoke on the morning of the first full day following receipt of study equipment, and completed a diary of sound and language interactions for that day (ex. television viewing, attending daycare). Software analysis of the sound file separates speech-related sounds from environmental sounds, and generates estimates of total child vocalizations, adult word counts, and conversational turns (number of times the child engaged in vocal interaction with an adult). For each 16-h period, the three 5-min segments with the highest child vocalization count as analyzed by LENA software were hand-coded by 2 independent transcribers for validity as well as for length of the longest meaningful utterance in the total 15-min segment. Utterances were counted based on previously established strategies for coding infant vocalizations (Nathani and Ollers, 2001). Data from the two transcribers was compared to produce a numeric variable for the longest utterance during each 16-h recording period.

*MacArthur-Bates CDI*

The MacArthur-Bates Communicative Development Inventory: Words and Sentences form is a vocabulary checklist for use with typically developing children ages 16-30 mo. It has
been shown to possess high concurrent and predictive validity with laboratory measures of vocabulary for children with Down syndrome with mental ages 12-27 mo (Miller, Sedey, & Miolo, 1995). The MacArthur-Bates CDI provides a measure of expressive vocabulary and of the level of productive grammatical complexity, as well as an indication of the parents’ best memory of their child’s longest utterances. Scores on the standard measures of the CDI were analyzed according to the test manual, and the three longest multiword utterances recorded by the parent were hand scored for length of utterance according to SALT transcription conventions (Miller & Chapman, 1993). Scores for the three sentences were then averaged to provide a measure of the parent-reported mean length of utterance. Variables of interest include total vocabulary addressed by the production checklist, the grammatical complexity measure, and parental report of the mean length of utterance.

*Behavior Rating Inventory of Executive Function-Preschool*

The BRIEF-P is a 63-item checklist completed by the parent that assess executive function behaviors in children ages 2-5 yrs. Parents are asked to rate each item as to whether it occurs sometimes, often, or never for the child. Items on the BRIEF-P comprise five executive domains: Inhibit, Shift, Emotional Control, Working Memory, and Plan/Organize. Scoring of the BRIEF-P yields three overlapping indexes that summarize these scales-the Inhibitory Self Control Index, the Emergent Metacognition Index, and the Flexibility Index- as well as global composite score. Higher scores are indicative of higher levels of dysfunction in a particular domain.
Results

All statistical analyses were generated using IBM SPSS 20. Comparisons between time 1 and time 2 variables were conducted with paired samples t-tests. We used correlation to examine the extent to which time 1 sleep quality relates to outcome variables at both time 1 and time 2. To account for non-normal distributions, non-parametric tests (Spearman’s rho) were used. As one subject was unable to complete the actigraphy portion of the study, final analyses were conducted with n=9.

Change over Time

The demographic and sleep characteristics of participants at both time 1 and time 2, as well as any significant differences between time points, are described in Table 1. At the first testing, toddlers slept between 9 and 10.7 hours per night (M=9.8, SD=0.6), and average sleep efficiency over 7 nights ranged from 71 to 80% (M=76.6, SD=4.1). Developmental age as measured by the LENA Snapshot ranged from 8 to 29 months (M=18.1, SD=8.3). At second test, two years following first test, sleep duration ranged from 8.8 to 10.3 hours per night (M=600.3, SD=32.1). Average sleep efficiency ranged from 68 to 86% (M=79.2, SD=6), and developmental ages fell between 5 and 36 months (M=22.3, SD=9.3).

Sleep efficiency measured at time 1 correlates with sleep efficiency at time 2 (rho=0.83, p<0.01), however, the correlation between fragmentation index at time 1 and time 2 was non-significant (rho=0.31, p=0.41), suggesting that the level of sleep fragmentation may be changing across the developmental trajectory. Sleep and executive function variables did not differ statistically between time points.
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Sleep in Relation to Executive Function

Longitudinal measurement of executive functioning provides an opportunity to investigate the rate and possible impairment of executive function development, as well as its relation to sleep quality. Table 2 presents correlations between the average fragmentation index at time 1 and scores on the BRIEF-P on the five clinical scales as well as three indexes and composite score. T1 score, T2 score, and the change in score from T1 to T2 are examined.

In this study, increased sleep fragmentation at time 1 positively correlates with dysfunction at time 1 in the several of the domains measured by the BRIEF. Higher levels of fragmentation correlate with increased impairment in the Inhibit and Working Memory domains ($\rho=0.78$, $p<0.05$; $\rho=0.87$, $p<0.01$), as well as higher scores on the Inhibitory Self Control and Emergent Metacognition indices ($\rho=0.78$, $p<0.05$; $\rho=0.76$, $p<0.05$). Overall executive functioning, as assessed by the Global Executive Composite score, correlates significantly with the amount of fragmentation at time 1 ($\rho=0.76$, $p<0.05$).

Increased sleep fragmentation at time 1 also demonstrates a relationship with increased executive dysfunction two years later, in several of the domains that were affected at time 1. Higher levels of fragmentation correlate with impairment in the Emotional Control, Working Memory, and Planning/Organization domains ($\rho=0.73$, $p<0.05$; $\rho=0.79$, $p<0.05$; $\rho=0.68$, $p<0.05$) at time 2. As was seen in the first testing of the Emergent Metacognition Index, higher fragmentation index at time 1 correlates with higher scores on the Emergent Metacognition Index at time 2 ($\rho=0.72$, $p<0.05$). The relationship between fragmentation and dysfunction in Working Memory remains strong even two years later, as did the relationship between fragmentation and the Emergent Metacognition Index. No significant relationships were found
between the rate of change in impairment of EF domains and the amount of sleep fragmentation at the first measurement (T1).

Correlations between average sleep efficiency at time 1 and scores on the BRIEF-P on the five clinical scales as well as three indexes and composite score were also calculated (see Table 3). Again, T1 score, T2 score, and the change in score from T1 to T2 are examined.

Higher sleep efficiency at time is negatively correlated with executive dysfunction at both time 1 and time 2, though not as strongly as the fragmentation index. Higher sleep efficiency at time 1 correlates with lower scores in the Inhibit domain at time 1 \((\rho=-0.67, p<0.05)\). No other significant correlations are found, however, a strong relationship with the Working Memory domain is again visible.

**Sleep in Relation to Language**

Accounting for the extent of language development at an early age allows for the examination of variables that may be affecting the rate of language development over time, such as sleep. Table 4 describes the strength of correlations between sleep fragmentation at time 1 and language outcomes at both time 1 and time 2, as well as the change between time points.

Trends in language outcome variables indicate that higher levels of sleep fragmentation are associated with decreased language skills, as measured by total productive vocabulary and the mean length of utterance. Fragmentation index at time 1 is negatively correlated with Grammatical Complexity two years later \((\rho=-0.68, p<0.05)\), as well as with the change in Grammatical Complexity from time 1, indicating that subjects who experienced more fragmentation had smaller increases in grammatical development over time \((\rho=-0.89, p<0.05)\).
In keeping with the results seen with sleep fragmentation, higher levels of sleep efficiency at time 1 are related to greater increases in grammatical complexity over a two-year span ($\rho=0.69$, $p=0.04$, see Table 5). Trends in outcome variables seem indicate that sleep efficiency is positively correlated with language outcomes; however, no significant relationships between utterance length or total vocabulary and sleep efficiency are found.

**Discussion**

In this study, we sought to elucidate the links between early sleep disruption, language development, and behavior in toddlers with Down syndrome using a longitudinal paradigm. In keeping with previous findings, the results suggest a high incidence of sleep problems in these young individuals with Down syndrome, above and beyond that of the general population and individuals with other developmental disorders (Ng, Hui, & Chan, 2006; Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2013). 56% (n=5) of our sample demonstrated average sleep efficiencies below an 80% cutoff, which might actually underestimate the occurrence of sleep disruption, as many studies use a more stringent 85% cutoff. However, this study is one of the first to use an objective measure of sleep, actigraphy, to examine sleep quality in children with DS early in development and subsequently across the developmental trajectory. Over the two-year span of the study, we found no significant change in the severity of a participants’ sleep disruption as measured by either sleep efficiency or sleep fragmentation (FI), indicating that early sleep problems are persisting beyond the toddler years. Our results suggest that these difficulties with sleep are not resolving themselves as children age, though larger samples are needed to confirm the extent of this longitudinal effect. This supports the hypothesis that the prevalence of OSAS in individuals with Down syndrome and its’ effects on cognition (Breslin, Spanò, Bootzin, Anand, Nadel, & Edgin, 2014) has origins earlier in development than has
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previously been detected, and emphasizes the importance of preventative screening and treatment.

However, our findings suggest that sleep fragmentation, as opposed to sleep efficiency, has a larger influence on later executive functioning and language development than previously considered. Stronger relationships with behavior and language outcomes were found with a measure of sleep fragmentation at the first testing than with a measure of sleep efficiency. Sleep efficiency calculates the percentage of the total time in bed that was spent asleep, while the fragmentation index measures the occurrence of short arousals over the duration of the time spent asleep. It seems that cognitive development may more detrimentally affected by these repetitive short interruptions of sleep than by latency of sleep onset or overall sleep efficiency, at least at in these young participants.

Results from this study reiterate and extend upon previous work with typically developing toddlers that demonstrated links between more consolidated sleep in infancy and increased complex executive functioning (EF) at preschool age (Bernier, Beauchamp, Bovette-Turcot, Carlson, & Carrier, 2013): we found an inverse relationship between the amount of sleep fragmentation at preschool age and the level of EF function in several domains at both preschool age and two years later. Higher levels of sleep fragmentation at the first measurement related to longitudinal impairment of both working memory and metacognition ability over two years, suggesting that sleep disruption may interfere with the development of these higher order cognitive functions at periods early in the developmental trajectory of these children. More fragmented sleep at preschool age also related to later dysfunction in children’s ability to regulate emotional responses and plan future events, which serves to emphasize the interrelated nature of executive function development, and the extensive influence of sleep on the maturation
of these domains. These findings are increasing evidence for a localized function of sleep, in the
development of brain areas involved in complex cognition, specifically executive functioning,
that begins to emerge very early in life. The manifestation of these early effects of sleep
disruption on EF in children diagnosed with DS suggests that the high incidence of sleep
problems in this population may underlie the some of the difficulties with day-to-day functioning,
learning, and performance in conventional academic settings that are often attributed to
intellectual disability, and underscores the importance of high quality sleep in healthy
development.

It appears that sleep also impacts language development in this population of young
children with Down syndrome. The development of syntactic complexity was clearly affected by
sleep disruption at an early age: children with more fragmented sleep at the first testing
experienced smaller increases in grammatical complexity over two years, emphasizing the
importance of sleep to higher level language development over time. Previous studies (Singer
Harris, Bellugi, Bates, Jones, & Rossen, 1997) have found delays in the grammar development
of older children with Down syndrome as compared to other developmental disorders, even
going so far as to coin the word “agrammaticism” to characterize the language production
tendencies of these children with DS. Our results indicated adverse effects of sleep fragmentation
on other areas of language as well, such as vocabulary production, but more specific measures
and larger sample sizes are needed to discern specific domains of language that are affected, and
the relative importance of sleep to each over a child’s developmental trajectory. Our findings
support previous work done with typically developing children suggesting that sleep disruption
has adverse effects on language skills, both in preschool aged children and at older ages
(Honaker, Gozal, Bennett, Capdevila, & Spruyt, 2009) and adds in the additional component of
longitudinal rather than cross-sectional evaluation. The profile of sleep-dependent language learning that has previously been introduced, in which preschoolers present difficulties with linguistic complexity and older children demonstrate reduced verbal ability for concepts and reduced verbal IQ, warrants investigation in younger children with Down syndrome to determine the extent to which these effects are compounded from an early age, and thus could be treated with interventions.

Several methodological limitations must be noted when considering results from this study, chief among them the small sample size, which limits the generalizability of our findings. Fortunately, there was no attrition of participants over the two-year study period, eliminating the possibility of data loss between the two test points, and our use of a longitudinal design enabled a detailed examination of the developmental process. One limitation stems from the characteristics of our subject population: although the objective assessment of sleep using actigraphy is novel for this population, and previous findings have often been based upon parent report of sleep, actigraphy cannot detect the presence of overnight hypoxia that is indicative of obstructive sleep apnea syndrome. That being said, the gold standard for sleep assessment, polysomnography, is less feasible these toddlers with Down syndrome, and future studies will likely continue to use actigraphy to investigate sleep disruption at this young age. Finally, participants in this study self-selected for the first testing, introducing the potential confound of pre-existing sleep problems that predisposed certain parents to participate.

Findings relating to language are limited in this study due to several factors, primary among them the use of productive language measures to assess the language development of our participants. Children with DS exhibit significant delays in expressive language development,
though their gestural and receptive abilities are only marginally delayed compared to typically developing children (Caselli et al, 1998; Miller, 1992) and thus confining our assessment of language to productive measures of language development may not have yielded the full picture of language acquisition. Although outcome data was collected both by parental report and by objective experimental measures, averting the possibility of parental bias, we were unable to clearly discern differences in the development of various domains of language. More specific measures of language comprehension, production, and gesturing, such as the Word & Gestures scale of the MacArthur Bates CDI, as well as the assessment of semantic and syntactic complexity, are needed in order to pinpoint the domains on which sleep disruption has the largest effect.

In ongoing research, we are attempting to account for the interplay of underlying factors that may explain the effects of sleep disruption in these young toddlers with Down syndrome. Our results may stem from an underlying level of neural maturation that is reflected both in sleep quality at an early stage and in later language and executive functioning, rather than from a causal link between the two. Continued follow-up assessments of these participants may provide additional clues as to the latent influences on and the progression of their development over time. Also, the incorporation of a control group of typically developing toddlers of the same age, as well as the expansion of the study to a larger community-based sample of children with Down syndrome from which demographic data is collected, will allow for the examination of confounds such as child BMI, family background, SES, or other comorbid disorders. Future work with this larger sample, controlling for baseline performance on language and EF measures, will further clarify the impact of disrupted sleep on the behavior and language development of these toddlers. In order to establish causative effects, studies should also examine the potential
for sleep interventions to alter the profile of delayed development in children with Down syndrome, as previous work with small samples of typically developing children has shown that treating OSAS results in improvements in executive functioning, attention, and behavior (Owens, Spirito, Marcotte, McGuinn, & Berkelhammer, 2000).

More broadly, given the influence of sleep disruption on executive functioning and language even in this young population of toddlers, these results serve to further emphasize the importance of early screening and treatment approaches for sleep disorders such as OSAS. Though current practice recommends children with Down syndrome undergo a baseline polysomnographic sleep study by the age of four, it seems likely that sleep problems may begin to manifest themselves earlier, and parent report of sleep problems has been shown to be unrelated to objective measures of sleep disruption (Schott et al., 2006). Thus, this study provides a foundation from which to expand our investigation of the relationship between sleep quality, language, and executive functioning, as well as to pinpoint the critical periods at which sleep disruption has the greatest detrimental effect and when early treatment could be most effective.
References


### Table 1

*Demographic and Sleep Characteristics of Participants*

<table>
<thead>
<tr>
<th></th>
<th>Time 1</th>
<th>Time 2</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological Age (yrs)</td>
<td>3.7 ± 1.0</td>
<td>5.2 ± 1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developmental Age (LENA Snapshot, mo)</td>
<td>18.1 ± 8.3</td>
<td>22.3 ± 9.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Efficiency (%)</td>
<td>76.6 ± 4.1</td>
<td>79.2 ± 6.0</td>
<td>-1.96</td>
<td>0.08</td>
</tr>
<tr>
<td>Fragmentation Index</td>
<td>32.6 ± 3.8</td>
<td>30.1 ± 5.5</td>
<td>1.35</td>
<td>0.21</td>
</tr>
<tr>
<td>WASO (avg min)</td>
<td>107.9 ± 22.2</td>
<td>100.7 ± 26.8</td>
<td>0.84</td>
<td>0.43</td>
</tr>
<tr>
<td>Sleep Interval Duration (min)</td>
<td>589 ± 38.1</td>
<td>600.3 ± 32.1</td>
<td>-0.63</td>
<td>0.55</td>
</tr>
<tr>
<td>Global Executive Composite Score (BRIEF)</td>
<td>110.6 ± 17.1</td>
<td>113.9 ± 18.3</td>
<td>-0.53</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Table 2

<table>
<thead>
<tr>
<th>Measures (BRIEF)</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Δ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit</td>
<td>0.78*</td>
<td>0.6</td>
<td>-0.23</td>
</tr>
<tr>
<td>Shift</td>
<td>0.24</td>
<td>0.16</td>
<td>0.03</td>
</tr>
<tr>
<td>Emotional Control</td>
<td>0.42</td>
<td>0.73*</td>
<td>0.21</td>
</tr>
<tr>
<td>Working Memory</td>
<td>0.87**</td>
<td>0.79*</td>
<td>-0.49</td>
</tr>
<tr>
<td>Planning/Organization</td>
<td>0.57</td>
<td>0.68*</td>
<td>0.19</td>
</tr>
<tr>
<td>Inhibitory Self Control Index</td>
<td>0.78*</td>
<td>0.66</td>
<td>-0.08</td>
</tr>
<tr>
<td>Flexibility</td>
<td>0.49</td>
<td>0.49</td>
<td>0.03</td>
</tr>
<tr>
<td>Emergent Metacognition Index</td>
<td>0.83*</td>
<td>0.72*</td>
<td>-0.33</td>
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<tr>
<td>Global Executive Composite</td>
<td>0.76*</td>
<td>0.55</td>
<td>0.1</td>
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</table>

Note: *p<0.05; **p<0.01
### Correlations between T1 Sleep Efficiency and Executive Functioning at T1, T2, and Δ

<table>
<thead>
<tr>
<th>Measures (BRIEF)</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Δ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit</td>
<td>-0.67*</td>
<td>-0.39</td>
<td>0.34</td>
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<tr>
<td>Shift</td>
<td>-0.14</td>
<td>-0.07</td>
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<tr>
<td>Emotional Control</td>
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<tr>
<td>Working Memory</td>
<td>-0.59</td>
<td>-0.49</td>
<td>0.34</td>
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<tr>
<td>Planning/Organization</td>
<td>-0.36</td>
<td>-0.26</td>
<td>0.19</td>
</tr>
<tr>
<td>Inhibitory Self Control Index</td>
<td>-0.59</td>
<td>-0.44</td>
<td>0.27</td>
</tr>
<tr>
<td>Flexibility</td>
<td>-0.28</td>
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<tr>
<td>Global Executive Composite</td>
<td>-0.57</td>
<td>-0.26</td>
<td>0.24</td>
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*Note:* *p<0.05; **p<0.01*
Table 4

**Correlations (ρ) between T1 Fragmentation Index and Language at T1, T2, and Δ**

<table>
<thead>
<tr>
<th></th>
<th>Time 1</th>
<th>Time 2</th>
<th>Δ Score</th>
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<tbody>
<tr>
<td>Grammatical Complexity</td>
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<td>MacArthur-Bates CDI</td>
<td>-0.47</td>
<td>-0.68*</td>
<td>-0.89*</td>
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<tr>
<td>Total Vocabulary</td>
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<tr>
<td>MacArthur-Bates CDI</td>
<td>-0.35</td>
<td>-0.59</td>
<td>-0.28</td>
</tr>
<tr>
<td>Longest Utterance</td>
<td></td>
<td></td>
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<tr>
<td>MacArthur-Bates CDI</td>
<td>-0.12</td>
<td>-0.44</td>
<td>-0.35</td>
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<tr>
<td>Longest Utterance</td>
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<td></td>
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<tr>
<td>LENA Recorder</td>
<td>-0.26</td>
<td>-0.19</td>
<td>0.3</td>
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</table>

*Note:* *p<0.05
Table 5

**Correlations (ρ) between T1 Sleep Efficiency and Language at T1, T2, and Δ**

<table>
<thead>
<tr>
<th></th>
<th>Time 1</th>
<th>Time 2</th>
<th>Δ Score</th>
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<tbody>
<tr>
<td>Grammatical Complexity</td>
<td>0.04</td>
<td>0.24</td>
<td>0.69*</td>
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<td>MacArthur-Bates CDI</td>
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<tr>
<td>Total Vocabulary</td>
<td>-0.17</td>
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<td>MacArthur-Bates CDI</td>
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<td>Longest Utterance</td>
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<td>Longest Utterance LENA Recorder</td>
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*Note: *p<0.05