

Sleep Disturbance and Expressive Language Development in Preschool-Age Children With Down Syndrome

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Recent evidence has suggested that sleep may facilitate language learning. This study examined variation in language ability in 29 toddlers with Down syndrome (DS) in relation to levels of sleep disruption. Toddlers with DS and poor sleep (66%, $n = 19$) showed greater deficits on parent-reported and objective measures of language, including vocabulary and syntax. Correlations between sleep and language were found in groups with equivalent medical and social backgrounds and after control for relevant behavioral comorbidities, including autism symptoms. These results emphasize the important role of quality sleep in all children's expressive language development, and may help increase our understanding of the etiology of language deficits in developmental disorders, potentially leading to new treatment approaches.

Recent evidence has highlighted the role of sleep in language learning in typical and atypical populations across development. In typical adults, Gaskell et al. (2014) experimentally demonstrated sleep's role in strengthening the production of newly learned phoneme combinations. Participants who napped 90 min after a brief exposure to syllable repetition exhibited patterns of speech showing they had integrated the syllables' patterns of phonotactic constraints. There were positive correlations between slow wave sleep (SWS) and these speech patterns, suggesting an active role of deep sleep in strengthening and integrating the new information to affect language production. In another study conducted with adults, participants recalled more novel words after a nighttime sleep period when compared to an equivalent period of wake. Signs of lexical integration correlated with sleep spindles, a marker of memory consolidation

in deep sleep (Tamminen, Payne, Stickgold, Wamsley, & Gaskell, 2010).

A growing corpus of work has also suggested the importance of sleep for children's learning. In typical infants, sleep facilitates the abstraction of artificial grammar rules and may be required soon after learning for long-term retention to occur (Gomez, Bootzin, & Nadel, 2006; Hupbach, Gomez, Bootzin, & Nadel, 2009). Naps and nighttime sleep have also been shown to improve the acquisition and integration of novel vocabulary in school-age children (Henderson, Weighall, Brown, & Gaskell, 2012; Williams & Horst, 2014). Relations between poor sleep and language impairment, including difficulties processing increasing levels of linguistic complexity, have been found in studies of children diagnosed with sleep disordered breathing (SDB), a condition in which there is sleep fragmentation caused by partial or complete cessation of breathing while asleep (Honaker, Gozal, Bennett, Capdevila, & Spruyt, 2009; Key, Molfese, O'Brien, & Gozal, 2009). In a population sample of typical children without SBD, Touchette et al. (2007) found that persistent shortened sleep duration (based on parent report) from 2.5 to 6 years resulted in a threefold increase in the risk of poor vocabulary scores. In Dionne et al. (2011), parent-reported sleep-wake consolidation (ratio of day to night sleep duration) was collected in 1,029 twins (45% late preterm) and

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examined in relation to vocabulary development on the MacArthur–Bates Communicative Development Inventory (CDI) and other measures (Fenson et al., 1993). Dionne's et al. analysis showed that sleep consolidation between 6 and 18 months had modest relations with the level of language development at 30 and 60 months, even after controlling for vocabulary scores at earlier time points. While these studies confirmed relations between sleep and language development in typical and sleep-disordered groups, they often relied on parent reports rather than objective measures. In addition, most studies have not taken into account the influence of behavioral difficulties often associated with sleep disruption when examining these associations.

Individuals with developmental disorders commonly show sleep abnormalities and language impairment—a confluence of symptoms highlighting the need for closer examination of sleep in the context of atypical development (Ashworth, Hill, Karmiloff-Smith, & Dimitriou, 2013; Churchill, Kieckhefer, Landis, & Ward, 2012). Children with Down syndrome (DS; trisomy 21) have an extremely high rate of sleep problems, including, but not limited to, obstructive sleep apnea (OSA), a variant of SDB. Estimates of the prevalence of OSA in children with DS range from 30% to as high as 80% (Dyken, Lin-Dyken, Poulton, Zimmerman, & Sedars, 2003; Ng et al., 2006). Children with DS demonstrate increased sleep fragmentation, including more shifts between deeper and lighter stages of sleep, as compared to controls with primary snoring (Levanon, Tarasiuk, & Tal, 1999). Disturbed sleep is also evident in mouse models of DS, which show increased waking at the expense of deep sleep (Colas et al., 2008; Heise et al., 2015). In our recent work, Breslin et al. (2014) found that children with DS with OSA showed reductions in SWS, the stage often shown to facilitate language learning and the integration of declarative knowledge. In addition to significant differences in SWS, rapid eye movement (REM) periods are significantly truncated in individuals with DS in comparison to the typical population with and without OSA (Miano et al., 2008; Nisbet, Phillips, Hoban, & O'Brien, 2014). Using actigraphy, a form of sleep monitoring based on movement patterns, Ashworth et al. (2013) found greater sleep disruption in children with DS than in typically developing (TD) children and children with Williams syndrome (WS), which was reflected in more night awakenings, greater wake after sleep onset (WASO), and increased sleep fragmentation. Given their frequent arousals and disruption of deep sleep, children with DS may

show deficits in memory consolidation resulting in impaired language learning. Individuals with DS do indeed show prominent language delays, an aspect of the phenotype that is often noted as their most striking deficit (Abbeduto, Warren, & Conners, 2007; Fidler, 2005; Gibson, 1978).

In particular, children with DS exhibit asynchronies in their language development, with productive language skills lagging behind comprehension (Abbeduto et al., 2007; Chapman, 1995; Miller, 1988) and difficulty in the development of grammatical and syntactic complexity (Chapman, 1997; Fidler, 2005). Use of the MacArthur–Bates CDI Words and Sentences has confirmed poorer grammar and vocabulary development in children with DS as compared to those with WS, another genetic syndrome resulting in intellectual disability. Specifically, Mervis and Robinson (2000) measured persistent deficits in expressive vocabulary across the toddler years in DS, showing that 92% of children had expressive vocabularies below the 5th percentile for their chronological age. Consistent with this work, recent studies from Yoder, Woynaroski, Fey, and Warren (2014) have employed longitudinal methods to document poor vocabulary growth in toddlers with DS. Singer Harris, Bellugi, Bates, Jones, and Rossen (1997) found that grammar deficits also increased in severity across the toddler years in relation to WS, a finding consistent with subsequent studies (Miller, 1999). Individuals with DS can also exhibit deficits in speech sound production and motivation to speak in socially demanding situations, factors that must be considered when determining the broader profile of their strengths and difficulties in language learning (Fidler, 2005).

Although the combination of disturbed sleep and language deficits is of concern, very few studies have examined correlations between sleep disruption and cognition in DS, with even fewer focusing on language development. To the best of our knowledge, only four studies have examined the relation between sleep disruption and cognition in children or young adults with DS. First, in Breslin et al. (2014) we describe the correlation between OSA and performance on the Arizona Cognitive Test Battery for DS (Edgin et al., 2010), showing that school-age children with DS with OSA had impaired executive functioning (EF) and a verbal IQ (including tests of word knowledge) 9 points lower than those without OSA. These results were unique because we were able to compare children of the same age, medical, and social background that differed only on OSA status, as defined by polysomnography (PSG).

Andreou, Galanopoulou, Gourgouljanis, Karapetsas, and Molyvdas (2002) used PSG to correlate OSA severity with cognitive outcomes in young adults with DS, finding that OSA related to performance on the baseline phases of the Raven's progressive matrices. Another investigation of school-age children did not detect a direct correlation with PSG-diagnosed OSA, but found that other measures of global sleep quality related to cognitive outcomes in DS (Brooks et al., 2014). Total sleep time correlated with measures of vocabulary and comprehension, and minutes spent in SWS related to a number of outcomes, including sentence memory, verbal and math achievement, and adaptive behavior. In a fourth study, Chen, Spanò, and Edgin (2013) examined the relation between parent reports of SDB and EF in young adults with DS, showing that these reports correlated with set shifting and verbal fluency, but not with response speed. These results suggest sleep might be an important correlate of cognitive development, with the most consistent evidence relating poor sleep to difficulties with language and EF. While these links have been examined in school-age children and adults with DS, no study has yet examined the relation between sleep and cognition in preschool children, a critical time period for intervention. Therefore, in this study we examine the relation between sleep quality, language development, and behavior in toddlers with DS.

The juxtaposition of cognitive and behavioral deficits in previous studies linking sleep disruption to poorer developmental outcomes presents a potential confound for interpreting these associations. Correlations between sleep and behavior could be explained by a direct effect of neural dysfunction (e.g., poor prefrontal cortex development) caused by poor sleep (Beebe & Gozal, 2002; Bernier, Beauchamp, Bouvette-Turcot, Carlson, & Carrier, 2013), or these correlations could result from the inclusion of a number of children with more severe behavioral and neurological issues, who also happen to exhibit poor sleep. In particular, children with autism spectrum disorders (ASDs) have higher rates of sleep disorders as well as co-occurring deficits in language development (Richdale, 1999). Taylor, Schreck, and Mulick (2012) found that children with autism had more parent-reported night wakings and that this difference correlated with poorer cognitive and adaptive scores. Given these links, and evidence suggesting that autism and ASDs may be present in 6.4%–18.2% of individuals with DS (DiGuseppi et al., 2010), it is essential to characterize (and control for) the extent of autism

symptoms or more general neurological dysfunction when relating sleep disturbance to cognitive outcomes, including language, in this population.

Thus, in this study we expand on previous work to examine the relations between sleep, language development, and behavior in DS in three ways. First, employing actigraphy as an objective measurement of sleep, as well as a parent-reported sleep log, we examine sleep quality in relation to the language development of toddlers with DS in groups equivalent for a number of medical and social background factors. Second, we compare their sleep, language, and behavior to a group of TD toddlers of the same age with no evidence of SDB (i.e., signs of OSA). Finally, we examine the level of difficulties in EF, autism symptoms, and speech sound production in relation to sleep quality, and we control for these factors when interpreting sleep-related differences in language. Because sleep disturbance may interrupt periods of memory consolidation in DS (i.e., SWS), we expect that sleep will relate to variation in language function in toddlers with DS, and that these correlations will be present after controlling for any behavioral differences.

Method

Participants

The sample was recruited between 2012 and 2015 and consisted of 32 children diagnosed with DS and 24 TD children ranging in age from 26 to 64 months. Four additional children from each group did not complete the required days of actigraphy and are not included in this report. The Biomedical Institutional Review Board at the University of Arizona approved all procedures, and informed consent was obtained from parents. Study equipment was mailed or hand-delivered to the participants' homes, which were located in the state of Arizona and throughout the United States. Parents were asked to complete a screening instrument for childhood sleep problems, a developmental questionnaire, a child-language assessment, medical history questionnaires, and parent-report measures of EF and symptoms of autism. Each child's medical records were reviewed for karyotype, cardiovascular health (including presence and type of heart defect), surgeries, and the most recent body mass index (BMI) measurement. Exclusion criteria included the following: (a) diagnosis of DS other than trisomy 21 (e.g., mosaicism or translocation, one case), (b) gestational age < 36 weeks (one case), (c) a history of cyanotic heart defects (one case),

and (d) a non-English-speaking parent, or a primary household language other than English.

Additionally, for the control sample of TD toddlers, exclusion criteria included any evidence of SDB, as assessed by the SDB subscale of the screening instrument for childhood sleep problems (Children's Sleep Habits Questionnaire [CSHQ]); four controls had at least one item endorsed and were removed from the analyses. Exclusions resulted in a final sample of 29 toddlers with DS, M (SD) age = 42 (10.3) months, range = 27–64 months, 21 males and 8 females, and 20 TD toddlers, M (SD) age = 44 (10.3) months, range = 26–58 months, 14 males and 6 females. All participants received the same test battery and set of questionnaires and were in good health condition at the time of the assessment. Demographic information for DS and TD sleep quality groups (based on clinically relevant actigraphy values) is shown in Table 2 later, showing that the samples were equivalent on a number of factors, including age, gender, BMI, ethnicity, and socioeconomic status.

Assessment of Sleep

Actigraphy

The Actiwatch-2 (Actiwatch 2, Phillips Respironics Mini-Mitter, Bend, OR) has been validated against polysomnographic recordings and shows higher correlations with PSG when measuring sleep efficiency (SE) than do other devices currently marketed (Meltzer, Walsh, Traylor, & Westin, 2011; Weiss, Johnson, Berger, & Redline, 2010). Previous studies have used actigraphy to measure sleep in DS, finding greater sleep fragmentation and poorer SE in DS as compared to same-age controls and other intellectual disability syndromes (e.g., WS; Ashworth et al., 2013). In previous examinations of children with SDB, actigraphy-derived sleep fragmentation estimates adequately correlated with the combined cortical and subcortical EEG arousal index from PSG ($r = .73$; O'Driscoll, Foster, Davey, Nixon, & Horne, 2010).

Based on the recommendations from previous reliability analyses in children, all subjects wore the actigraph on the nondominant wrist for a minimum of 5 consecutive days (Acebo et al., 1999), and the mean sleep scores were analyzed across this period. Parents completed a sleep log, which was used as supplemental data to evaluate the discrepancies between parental report and actigraphy data. Data were collected in 30-s epochs and analyzed using commercially available software (Respironics

Actiware 5.71.0, Bend, OR). Actigraphy data were scored at the medium sensitivity threshold (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, Montgomery-Downs, Insana, & Walsh, 2012). 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 SE (percentage of time spent in bed scored as sleeping, defined as clinically disrupted at < 80% based on past research), total sleep time, sleep onset latency, fragmentation index (FI; an index of restlessness that measures the extent of frequent interruption of sleep by physical movement), and minutes of WASO.

Secondary scoring of a subset of actigraphy data (9 of 29 individuals with DS) was in agreement with original scoring for the SE variable ($\rho = 1.0$, $p < .001$). A second assessment was administered in a subset of the DS sample after 2 years ($n = 9$); retesting analyses showed stability in the sleep measures over this time (SE Time 1 and Time 2, $\rho = 0.73$, $p = .01$).

Children's Sleep Habits Questionnaire

The CSHQ is a parent-completed sleep-screening instrument that has been used with a wide variety of populations, including preschoolers, children with developmental delay, and children with DS (Breslin, Edgin, Bootzin, Goodwin, & Nadel, 2011; Goodlin-Jones, Sitnick, Tang, Liu, & Anders, 2008). The CSHQ consists of 33 items relating to a number of key sleep domains and yields both a total score (total possible = 103, range = 33–103) and subscale scores, including a scale for SDB. Higher scores indicated poorer sleep behavior.

Assessment of Language

The MacArthur–Bates CDI

The MacArthur–Bates CDI: Words and Sentences form is a widely used parental report measure of language development (Fenson et al., 1993; Fenson et al., 1994). The CDI has often been used to measure early language development in DS (Mervis & Robinson, 2000; Singer Harris et al., 1997), is well validated across typical and atypical populations, and correlates with laboratory measures of vocabulary in children with DS with mental ages between 12 and 27 months (Miller, Sedey, & Miolo, 1995). The CDI: Words and Sentences form provides measures of

expressive vocabulary and level of productive grammatical complexity, an indication of the structures and morphemes that a child is using, and a section in which parents are asked to recall the three “longest” recent sentences uttered by their child. 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 in morphemes according to Systematic Analysis of Language Transcripts (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 (MLU).

Language ENvironment Analysis

The Language ENvironment Analysis (LENA) digital language processor (LENA Foundation, Boulder, CO) is a digital recorder that stores 16 continuous hours of the sound environment for later analysis by LENA software speech-identification algorithms or manual coding. The recorder fits into a small 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. Automated software analysis of the sound file separates speech-related sounds from environmental sounds, and identifies segments of speech as originating from either an adult male, an adult female, or the key child (i.e., the participant wearing the recorder). Variables of interest included total child vocalizations (speech-related key child babbles or words separated by at least 300 ms of background sound, media sound, other individual’s speech, or silence), parent or caregiver utterances (estimated number of adult words in adult speech segments), and conversational turns (number of times the child engaged in vocal interaction with an adult; Oller et al., 2010).

The utterances scored by the LENA need not be meaningful speech, but can be speech-like sounds. To code meaningful utterances we took advantage of the LENA’s full 16-hr recording of the actual sound environment. For each 16-hr period, the three 5-min segments with the highest child vocalization count (from the LENA analysis software) were hand-coded for length of the longest meaningful utterance in the entire 15-min segment (in morphemes). Coders were blind to the sleep status of the child. Utterances were classified based on previously established strategies for coding infant

vocalizations (Nathani & Oller, 2001); singing, repetitive speech, fixed vocal signals, and vegetative sounds were excluded from analysis. Length of utterance was calculated according to SALT morpheme transcription conventions (Miller & Chapman, 1993). We also validated the LENA automatic coding system in 10 children with DS, finding a correlation of $r = .73$ ($p < .05$) between hand-counted utterances and the LENA-generated utterances.

General Behavior, EF, and Autism Symptoms

Scales of Independent Behavior–Revised Early Development Form

The Scales of Independent Behavior–Revised (SIB–R; Bruininks, Woodcock, Weatherman, & Hill, 1996) was administered via parent-report checklist, and is designed as a measure of adaptive and problem behaviors. It has been normed for use with children and adults ages 3 months to 90 years, and has previously been reported to have adequate to high reliability and validity (Sattler, 2002). The SIB–R Early Development Form is a brief version of the checklist suitable for use with young children or individuals with developmental functioning below 8 years of age. The Early Development Form covers a range of functions including social and communication skills, motor skills, and daily living skills (e.g., eating, toileting). The SIB–R standard score provides a global assessment of the child’s day-to-day level of function.

Behavior Rating Inventory of Executive Function–Preschool

The Behavior Rating Inventory of Executive Function–Preschool (BRIEF–P) is a 63-item parent-report measure designed to assess EF in children ages 2–5 years. Items on the BRIEF–P comprise five EF domains: Inhibit, Shift, Emotional Control, Working Memory, and Planning/Organization. Scoring of the BRIEF–P yields a global composite T score and T scores from the individual subdomains. Higher scores on the subscales are indicative of higher levels of dysfunction in a particular domain. Previous studies have shown a unique pattern of strengths and weaknesses on the BRIEF–P in children with DS, including deficits in working memory and planning, but not in inhibition or emotional control (Lee et al., 2011). The BRIEF measures have been used extensively in individuals with DS, including their specific validation for use

in this population as reported by Edgin et al. (2010).

Autism Symptom Screener Questionnaires (Lifetime Social Communication Questionnaire and Modified Checklist for Autism in Toddlers)

On the basis of the work of Snow and Lecavalier (2008), which examined toddlers across the current study's age range, we assessed autism using a combination of the Modified Checklist for Autism in Toddlers (M-CHAT) and the Social Communication Questionnaire (SCQ) scores. In previous studies, these measures have been used in conjunction with the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999) and Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) to determine the population prevalence of autism and ASD in a sample of 123 children aged 2–11 years with DS (DiGuseppi et al., 2010). The SCQ has been used as young as 30 months and includes 40 items based on the content of the ADI-R (Snow & Lecavalier, 2008). In DiGuseppi et al. (2010), this measure displayed 100% sensitivity and 57.1% specificity in detecting autism using a cutoff score of 15. The M-CHAT is a checklist of items used as an autism screener in children between 16 and 30 months of age, and the clinical cutoff is three endorsed items overall or the endorsement of two critical items. DiGuseppi et al. (2010) found 81.8% sensitivity and 46.8% specificity for the M-CHAT in DS. In the current investigation, we present both the M-CHAT

raw score, which is the total of endorsed items, as well as the percent meeting the clinical cutoff on each measure.

Statistical Analysis

All statistical analyses were performed with SPSS 20.0 (IBM Corp., Armonk, NY).. To determine the relation between sleep disruption, language, and behavior in the DS population, we compared children with DS with low SE (actigraphy SE < 80%) to DS children with typical mean SE (SE ≥ 80%) and TD children. Table 1 shows the differences in sleep quality in these groups (DS poor sleep [DS PS], DS good sleep [DS GS], and TD) using analyses of variance (ANOVAs). If omnibus ANOVA tests were significant, individual group differences in sleep fragmentation, language, and EF between the high- and low- sleep groups and controls were analyzed using planned comparisons based on hypotheses generated from past work (*t* tests, significance *p* < .05). Other tests were considered post hoc and significant at *p* < .01 due to multiple comparisons. Our previous research (Breslin et al., 2014) detected large effect sizes for language and EF differences in relation to OSA diagnosis in school-age children (verbal IQ *d* = 0.91, EF *d* = 1.06), findings that were detected with a sample size similar to the current investigation.

Using this same analytic strategy, Table 2 shows the test of these groups' differences on clinical and background factors. Chi-square for dichotomous outcomes and individual group comparisons were

Table 1
Sleep Characteristics of Toddlers With DS and TD Toddlers

Measures, <i>M</i> (<i>SD</i>)	DS PS (SE < 80%) <i>n</i> = 19	DS GS (SE ≥ 80%) <i>n</i> = 10	TD <i>n</i> = 20	<i>F</i>	<i>p</i>	Group differences
Actigraphy variables						
Sleep efficiency across five nights (%)	74.35 (3.35)	83.66 (2.57)	85.09 (4.31)	46.43	< .001	DS PS < DS GS, TD
Average sleep time (min)	460.50 (47.94)	509.75 (47.67)	511.73 (48.51)	6.43	< .01	DS PS < DS GS, TD
Onset latency (min)	9.88 (5.90)	10.48 (10.45)	13.44 (10.59)	0.84	.44	—
Wake after sleep onset (min)	122.60 (18.07)	78.32 (18.42)	68.39 (23.74)	36.04	< .001	DS PS > DS GS, TD
Fragmentation index	35.29 (5.01)	25.54 (5.41)	25.50 (6.02)	18.23	< .001	DS PS > DS GS, TD
Children's Sleep Habits Questionnaire						
Sleep-disordered breathing	4.05 (1.47)	3.90 (0.99)	3.00 (0.00)	5.47	< .01	DS > TD
Daytime sleepiness	11.53 (2.39)	12.60 (1.65)	11.79 (2.92)	0.62	.54	—
Sleep duration	3.68 (1.16)	4.30 (1.42)	3.95 (1.72)	0.59	.56	—
Sleep anxiety	4.84 (1.26)	5.20 (1.23)	5.89 (1.45)	3.03	.06	—
Overall sleep disturbance	45.05 (7.22)	49.00 (8.03)	44.68 (5.90)	1.43	.25	—

Note. DS = individual sleep groups differed from TD, but not from each other; DS PS = Down syndrome poor sleepers (SE < 80%); DS GS = Down syndrome good sleepers (SE ≥ 80%); TD = typically developing.

Table 2

Clinical and Family Social Background of TD Toddlers and Toddlers With DS

Measures	DS PS (SE < 80%) (n = 19)	DS GS (SE > 80%) (n = 10)	TD (n = 20)	F/ χ^2	p	Group differences
Clinical characteristics						
Mean age, months (SD)	39.50 (10.08)	46.13 (9.63)	44.58 (10.28)	1.83	.17	—
% Male	68.4	80.0	70.0	0.46	.79	—
% White non-Hispanic	84.2	70.0	77.8	1.10	.89	—
Mean BMI (SD)	16.54 (2.30)	17.54 (2.48)	15.71 (1.02)	2.99	.06	—
% Tonsils and/or adenoids surgery	36.8	40.0	0.0	9.82	< .01	DS > TD
Social background factors						
% Family income < \$40,000	10.5	20.0	33.0	2.88	.24	—
Mean maternal education, years (SD)	17.74 (1.97)	18.10 (1.97)	17.72 (2.19)	0.13	.88	—

Note. One child in the DS GS group was diagnosed with atrioventricular heart defect. TD medical records showed no heart defects. Gestational age was ≥ 36 weeks in all DS and TD participants. Two TD participants did not report family income, ethnicity or mean maternal education. DS = individual sleep groups differed from TD, but not from each other; DS PS = Down syndrome poor sleepers (SE < 80%); DS GS = Down syndrome good sleepers (SE \geq 80%); BMI = body mass index; TD = typically developing.

then conducted with Fisher's exact test. In Tables 3 and 4 we examine the sleep groups in relation to parent-reported and objective language outcomes (Table 3) and measures of behavior (Table 4), first with ANOVA for continuous variables and chi-square for dichotomous outcomes. Post hoc tests of dichotomous outcomes were analyzed with Fisher's exact test. In the final section, the relation between the continuous variable of mean SE and key language outcomes was examined after control for potentially important behavioral predictors using linear and logistic regression.

Results

Sleep Characteristics

Based on actigraphy, a significant proportion of the young children with DS showed disturbed sleep. Specifically, 66% (19/29) of the DS sample had mean SE scores less than 80%, while only 15% (3/20) of the TD sample showed this level of disruption, $\chi^2(1, N = 49) = 12.21, p < .001$. To explore the relation between poor sleep efficiency and cognitive function, we split the groups into children with GS (SE > 80%: DS GS, $n = 10$), children with

Table 3

Vocabulary, Word Use, and Syntactic Development in DS and TD Toddlers and Toddlers with DS in Relation to Sleep

Measures, M (SD)	DS PS (SE < 80%) (n = 19)	DS GS (SE > 80%) (n = 10)	TD (n = 20)	F/ χ^2	p	Group differences
MacArthur-Bates CDI Vocabulary and Word Use						
Vocabulary production total score	85.47 (104.34)	275.50 (198.20)	605.10 (123.65)	71.03	< .001	DS PS < DS GS < TD
Word use total score	1.84 (1.61)	3.20 (1.99)	5.00 (0.00)	26.06	< .001	DS PS* < DS GS < TD
MacArthur-Bates CDI Syntactic and Morphological Development						
% Combining words	31.6	80.0	100.0	18.96	< .001	DS PS < DS GS, TD
Sentence length, morphemes	2.01 (1.89)	4.33 (3.96)	10.15 (5.11)	21.79	< .001	DS PS < DS GS < TD
Language ENvironment Analysis system						
Child vocalizations	1,305.89 (857.74)	1,560.40 (1,077.65)	2,924.74 (1,823.20)	7.36	< .01	DS < TD
Parent/caregiver utterances	8,311.26 (8,360.01)	12,228.90 (8,595.04)	11,680.37 (7,434.22)	1.14	.33	—
Conversational turns	262.74 (300.09)	366.30 (268.24)	561.47 (544.28)	2.49	.09	—
Length of longest utterance, morphemes	1.37 (1.34)	3.60 (3.78)	12.53 (6.36)	32.16	< .001	DS PS < DS GS < TD

Note. DS = individual sleep groups differed from TD, but not from each other; DS PS = Down syndrome poor sleepers (SE < 80%); DS GS = Down syndrome good sleepers (SE \geq 80%); CDI = Communicative Development Inventory; TD = typically developing.

*Nonsignificant trend, $p < .10$.

Table 4
Adaptive Behavior, Executive Function, and Autism Symptoms in TD Toddlers and Toddlers with DS in Relation to Sleep

Measures, <i>M</i> (<i>SD</i>)	DS PS (SE < 80%) (<i>n</i> = 19)	DS GS (SE > 80%) (<i>n</i> = 10)	TD (<i>n</i> = 20)	<i>F</i> / χ^2	<i>p</i>	Group differences
SIB-R standard score*	69.53 (27.37)	71.44 (24.39)	123.22 (13.85)	30.90	< .001	DS < TD
Behavior Rating Inventory of Executive Function–Preschool <i>T</i> Scores						
Global executive composite <i>T</i> score	57.84 (15.12)	54.40 (13.34)	47.84 (8.62)	3.09	.06	—
Inhibit <i>T</i> score	56.11 (13.05)	52.50 (11.57)	50.21 (9.38)	1.28	.29	—
Shift <i>T</i> score	52.53 (12.46)	48.20 (7.86)	44.26 (5.99)	3.65	.03	DS PS < TD, DS GS = TD
Emotional control <i>T</i> score	47.47 (8.51)	48.50 (10.95)	48.05 (7.79)	0.05	.95	—
Working memory <i>T</i> score	63.32 (17.57)	60.30 (14.42)	48.74 (9.15)	5.45	< .01	DS < TD
Planning/Organization <i>T</i> score	61.47 (18.74)	57.60 (14.18)	49.32 (8.89)	3.40	.04	DS < TD
Social Communication Questionnaire (SCQ) Lifetime						
SCQ raw score*	7.79 (4.58)	6.90 (3.04)	4.84 (2.48)	3.36	.04	—
% above clinical cutoff	10.5	0	0	3.19	.20	—
M-CHAT						
M-CHAT raw score*	2.06 (1.90)	1.60 (2.07)	0.58 (0.84)	4.13	.02	—
% above clinical cutoff	31.6	10.0	5.3	5.14	.08	—

Note. One TD participant did not complete the questionnaires. None of the TD participants had SCQ scores above the clinical cutoff of 15. Language results remained after controlling for M-CHAT scores in linear models (see Results). DS = individual sleep groups differed from TD, but not from each other; DS PS = Down syndrome poor sleepers (SE < 80%); DS GS = Down syndrome good sleepers (SE \geq 80%); M-CHAT = Modified Checklist for Autism in Toddlers; SIB-R = Scales of Independent Behavior–Revised; TD = typically developing.

*SCQ, M-CHAT, and SIB-R differences were considered exploratory and we set a significance level of $p < .01$.

low SE (SE < 80%: DS PS, $n = 19$), and TD children ($n = 20$). This cutoff was adopted based on its use in previous pediatric sleep research (Beebe et al., 2007; Gruber et al., 2007; Katz et al., 2002). In addition, this cut point falls close to the total sample's mean SE score (typical and DS combined $M = 80.11$, $SD = 6.79$), allowing for an adequate distribution of good and poor sleepers in each group.

The sleep characteristics of DS sleep groups and TD participants are described in Table 1. As shown in Table 1, group effects were found on a number of the actigraphy parameters. Planned comparisons using *t* tests showed that the DS PS group was significantly impaired across a number of actigraphy measures, demonstrating shorter average sleep times: DS PS versus DS GS, $t(27) = -2.65$, $p = .01$, and DS PS versus TD, $t(37) = -3.32$, $p < .01$; greater minutes of WASO: DS PS versus DS GS, $t(27) = 6.23$, $p < .001$, and DS PS versus TD, $t(37) = 7.99$, $p < .001$; and a higher FI: DS PS versus DS GS, $t(27) = 4.85$, $p < .001$, and DS PS versus TD, $t(37) = 5.51$, $p < .001$. As Table 1 shows, sleep onset latency did not differ across groups ($p = .44$).

Parents also reported significant levels of sleep disruption in the children with DS, with elevated SDB scores in both of the groups with DS as compared to the TD control group: DS PS versus TD,

$t(36) = 3.12$, $p < .01$, and DS GS versus TD, $t(27) = 4.01$, $p < .001$. However, we found no differences between the DS sleep groups on SDB scores: DS PS versus DS GS, $t(27) = 0.29$, $p = .77$. No other group effects were found from the omnibus ANOVA tests of CSHQ variables in Table 1, including ratings of daytime sleepiness ($p = .54$), sleep duration ($p = .56$), sleep anxiety ($p = .06$, nonsignificant trend), and the overall sleep disruption scale ($p = .25$).

Clinical and Social Background Factors

Table 2 shows the clinical and social background factors in each of the groups (DS PS, DS GS, and TD controls). The groups did not differ in mean age ($p = .17$), gender ($p = .79$), ethnicity ($p = .89$), BMI ($p = .06$, nonsignificant trend), mean years of maternal education ($p = .88$), or the percentage of families in each group with an income < \$40,000 ($p = .24$). As shown in Table 2, there was a significant group difference in tonsils and adenoids (TA) surgery status, $\chi^2(2, N = 49) = 9.82$, $p < .01$. Participants with DS were more likely to have undergone TA surgery at this age as compared to TD children: DS GS versus TD, Fisher's $p < .01$, and DS PS versus TD, Fisher's $p < .01$. The DS groups with poor and good sleep did not differ from each other on TA surgery

status: DS GS versus DS PS, Fisher's $p = 1.00$. While more minor heart defects were present, only one child (in the DS GS group) had an atrioventricular septal defect, and no children were diagnosed with tetralogy of fallot, two heart defects that might impact cognition (Visootsak, Hess, Bakeman, & Adamson, 2012).

Language Variables

Table 3 shows the differences in parent-reported and objective measures of vocabulary and syntax between the three groups. As reflected by the F values for group differences tested with ANOVAs in Table 3, the groups with DS were significantly impaired in relation to TD controls across most measures except parent and caregiver utterances ($p = .33$) and conversational turns from the LENA monitor ($p = .09$, nonsignificant trend).

While most of the language measures were impaired in both DS groups, some measures showed greater impairment in the sample with PS. The DS PS group was impaired in relation to DS GS on the MacArthur-Bates CDI vocabulary total score, $t(27) = -3.41$, $p < .01$, with 190 fewer words on average. The DS GS group was also impaired in relation to the TD group: DS GS versus TD, $t(27) = -5.53$, $p < .001$. Three children were at floor on the CDI vocabulary (2 DS PS, 1 DS GS) and no child achieved a ceiling score in any group. The "word use total score," a measure of the breadth of a child's vocabulary use, was also statistically different across groups, $p < .001$. Planned comparisons showed that both DS groups had lower mean word use total scores than the TD group: DS PS versus TD, $t(36) = -8.56$, $p < .001$, and DS GS versus TD, $t(27) = -4.01$, $p < .001$. A nonsignificant trend was found between the two groups with DS: DS PS versus DS GS, $t(27) = -1.99$, $p = .056$.

In terms of syntax, the percentage of children reported to be combining words differed across the DS sleep groups, $\chi^2(2, 48) = 21.45$, $p < .001$. Only 31.6% of children in the DS PS group were rated as combining words, while 80.0% of those in the DS GS group and 100.0% of the TD children were combining words: DS PS versus DS GS, Fisher's $p = .02$; DS GS versus TD, Fisher's $p = .11$; and DS PS versus TD, Fisher's $p < .001$. The DS PS group was impaired in relation to TD and DS GS, and DS GS and TD did not differ on this measure. The mean sentence lengths (in morphemes) from the CDI parent-reported longest utterances also differed between groups ($p < .001$) with shorter sentence lengths in the PS group as compared to the good

sleepers: DS PS versus DS GS: $t(27) = -2.15$, $p = .04$. The DS GS group differed from the TD group in sentence length: DS GS versus TD, $t(27) = -3.13$, $p < .001$.

Objective measures from the LENA language recordings showed a similar pattern. Consistent with the above results linking parent-reported language to sleep group differences, there was a significant difference between the DS PS and DS GS groups in the mean length of the longest meaningful utterance manually coded from the LENA recordings: DS PS versus DS GS, $t(27) = -2.34$, $p = .03$. The DS GS group also produced shorter utterances when compared to TD children: DS GS versus TD, $t(27) = -4.06$, $p < .001$. In validation of our manual coding of the longest meaningful utterance from the LENA recording, this measure was significantly related to parent-reported language from the CDI in the DS group: CDI sentence length, $\rho = 0.76$, $p < .001$, and CDI vocabulary total $\rho = 0.82$, $p < .001$.

While both DS groups showed significantly lower numbers of child vocalizations than the TD children (including babbles and nonmeaningful speech), the mean vocalizations did not differ across the DS sleep groups: DS PS versus TD, $t(36) = -3.50$, $p < .01$; DS GS versus TD, $t(27) = -2.16$, $p = .04$; and DS PS versus DS GS, $t(27) = -0.70$, $p = .49$.

Adaptive Behavior, EF, and Autism Symptoms

Table 4 displays group differences between DS PS, DS GS, and TD groups across the SIB-R, BRIEF, and autism screener inventories. Omnibus ANOVA tests showed significant group differences on a number of these measures, including deficits in adaptive behavior ($p < .001$) and EF, including the shift, working memory, and plan/organize T scores ($p < .05$ for all). Both DS groups showed poorer parent ratings of adaptive behavior on the SIB-R: DS PS versus TD, $t(35) = -7.47$, $p < .001$, and DS GS versus TD, $t(25) = -7.08$, $p < .001$, with no difference between the DS groups: DS PS versus DS GS, $t(26) = -0.18$, $p = .86$. The BRIEF shift T score was specifically elevated in the DS PS group in comparison to TD children: DS PS versus TD, $t(36) = 2.61$, $p = .01$, but the DS GS group did not differ from TD children, $t(27) = 1.51$, $p = .14$, or from the DS PS group, $t(27) = 0.99$, $p = .33$. A similar pattern was evident for the plan/organize T score. The DS PS group had elevated scores in comparison to TD children, $t(36) = 2.56$, $p = .02$, but the DS GS group did not differ in relation to TD chil-

dren, $t(27) = 1.94$, $p = .06$ (nonsignificant trend), or from the DS PS group: DS GS versus DS PS, $t(27) = 0.57$, $p = .57$. Both DS groups had poorer working memory T scores: DS PS versus TD, $t(36) = 3.21$, $p < .01$, and DS GS versus TD, $t(27) = 2.65$, $p = .01$, but did not differ from one another: DS PS versus DS GS, $t(27) = 0.47$, $p = .65$. As shown in Table 4, not all behavioral measures showed group differences across the sample of DS and TD children; there were no main effects of group on the BRIEF inhibit T score ($p = .29$), the emotional control T score ($p = .95$), and the Global executive composite (GEC) T score was nonsignificant at the trend level, $p = .06$.

Table 4 also shows the number of children exceeding the clinical cutoff on the SCQ and M-CHAT and mean ratings for each scale. As these findings were exploratory, they were evaluated for significance at $p < .01$. There were no statistically significant differences in mean autism symptoms or children above the clinical cutoff on these screeners at the $p < .01$ level. About 10.5% (2/19) of the DS PS group was over the clinical cutoff on the SCQ, while the other two groups had no participants who were significantly elevated ($p = .20$). Of the DS PS group, 31.6% were rated as clinically elevated on the M-CHAT, a value that was not statistically different from the DS GS group or the TD sample, which had 10.0% and 5.3% above the cutoff, respectively ($p = .08$, nonsignificant trend).

Control for Background Factor Differences

In the previous sections, we demonstrated specific differences in language function in poorly sleeping toddlers with DS. In analyses split on sleep disturbance using a clinically relevant cutoff (80% SE), we found language differences in DS groups that were statistically equivalent on a number of other measures, including social and medical background, autism symptoms, EF, and overall levels of speech sound production from the LENA. However, given the potential for children's behavioral profiles to relate to their language scores, we further examined if the significant relations between sleep and language remained after statistical control for possible associated variables using linear models. These additional analyses were conducted only in the groups with DS (DS PS and DS GS), and we focused on the CDI vocabulary production total score, the mean sentence length reported on the CDI, the number of children combining words, and the longest utterance from the LENA recording. The M-CHAT was used in the analyses as it

represented the most stringent test of autism spectrum disorders (ASD) symptoms (i.e., the greatest number of children in the clinical range) without including direct questions about speech development (as opposed to the SCQ). Using linear regression, we examined the effects of mean SE score over five nights, M-CHAT total score, BRIEF shift T score, and total child utterances from the LENA monitor (reflecting speech sound production and motivation) in predicting the CDI total vocabulary score. We obtained a significant model, $F(4, 24) = 8.17$, $p < .001$, accounting for 58% of the variance. Mean SE ($\beta = .53$, $p < .01$) and child vocalizations ($\beta = .46$, $p < .01$) significantly related to CDI vocabulary, but M-CHAT total score ($p = .35$) and the shift T score did not relate ($p = .92$).

Analyses of the other language variables revealed similar results. For CDI Mean length of utterance (MLU) we obtained a significant model, $F(4, 24) = 8.17$, $p < .01$, accounting for 42% of the variance. Mean SE ($\beta = .36$, $p = .03$) and child vocalizations ($\beta = .48$, $p < .01$) were significantly related to MLU, but M-CHAT total score ($p = .51$) and the shift T score did not relate ($p = .86$). Using logistic regression (model $\chi^2 = 12.20$, $p = .02$ with $df = 4$), we found that mean SE (Wald = 4.06, $p = .04$) and child vocalizations (Wald = 4.04, $p = .04$) both made a significant contribution to determining whether a child was classified as combining words. M-CHAT (Wald = 1.26, $p = .26$) and BRIEF shift T score (Wald = 0.05, $p = .82$) did not relate. Finally using the objective coding of longest utterance from the LENA monitor, we obtained a significant linear model, $F(4, 24) = 5.78$, $p < .01$, accounting for 49% of the variance. Mean SE ($\beta = .32$, $p = .04$) and child vocalizations ($\beta = .59$, $p < .01$) were significantly related to meaningful utterances, but M-CHAT total score ($p = .91$) and the shift T score did not relate ($p = .80$).

Discussion

In this study, we sought to elucidate the links between early sleep disruption, language development, and behavior in toddlers with DS ($M_{\text{age}} = 3.5$ years) as compared to a control group of TD children of this same age. In keeping with previous findings, the results suggest a high incidence of sleep problems in this group, above and beyond that of the general population and individuals with other developmental disorders (Ashworth et al., 2013; Ng et al., 2006). Sixty-six percent of our DS sample exhibited average sleep efficiencies

below 80%, as compared to a 15% in the TD sample. This rate of sleep disturbance is similar to the rate of clinical sleep abnormalities measured in other studies across this age range using PSG (Shott et al., 2006). Our findings indicate that sleep disruption and the correlation between poor sleep and language deficits has their origins earlier in development than previously detected (Breslin et al., 2014).

We found that the DS group with PS showed specific difficulties with expressive language (vocabulary and syntax), as measured by parent report on the CDI as well as through objective coding of language samples gathered with the LENA monitor, measures that were highly correlated. Most striking were the findings of a difference of 190 words of total vocabulary between the poor and good sleep groups with DS, and the fact that only 31.6% of children with DS in the PS group were combining words, as compared to 80.0% of good sleepers. The relation between sleep and language outcomes was found using two separate analysis techniques, including tests of these effects with separate groups of poor and good sleepers as well as with linear models using the continuous variable of SE. In total, the results of these analyses expand on our previous work revealing a 9-point difference in verbal IQ between school-age children with DS comorbid for and without OSA (Breslin et al., 2014). Our findings also support previous research suggesting that sleep disruption may have adverse effects on language development in children from the broader population (Dionne et al., 2011; Touchette et al., 2007).

Poorer language in children with DS was shown to relate to the level of sleep disruption, and this relation remained after controlling for a number of potentially confounding factors (i.e., autism symptoms, executive function, and motivation and ability to produce speech sounds). The groups exhibiting these differences were also equivalent in age, gender, social, and medical background factors (e.g., BMI). These results do not appear to be due to parent or caregiver response bias, as there were no significant group differences in the caregiver utterances measured by the LENA or any global differences in parent-reported functioning (e.g., adaptive behavior scores). Furthermore, the findings are not explained by differential level of motivation to produce language, as there were no sleep-related differences in the speech sound utterances produced during the LENA recording. Parents did not rate their children as exhibiting more daytime sleepiness, a finding that is consistent with past

work (Ashworth et al., 2013; Breslin et al., 2014). Considering that there were no EF differences between poor and good sleepers with DS, no indication of daytime sleepiness, and equivalent levels of child speech sound production, it does not appear that these results can be explained by a difference in the child's response style from sleep deprivation. Finally, the results cannot be explained by the inclusion of children with elevated autism symptoms in the PS sample, as the DS groups had statistically equivalent levels of autism symptoms on these screening instruments, and the results remained significant after controlling for ratings on the M-CHAT. However, while sleep quality did relate to variability in language within the DS group, it does not fully explain the extent of language disruption in DS, as the GS group with DS was also impaired in relation to the TD group across most measures.

Our findings show that sleep-related learning deficits may be quite specific to the language domain in toddlers with DS. More work is needed to determine the mechanisms underlying these links. Processes of memory consolidation occurring during SWS could be contributing to this relation, as SWS and the neurophysiological signatures relating to memory consolidation (e.g., sleep spindles) have been shown to be impaired in infants and young children with DS (Ellingson & Peters, 1980). A better understanding of the links between language learning and altered sleep physiology could potentially open new pathways to treat language dysfunction in DS, as methods to enhance SWS with noninvasive means are currently under development in typical adults (Ngo, Martinetz, Born, & Mölle, 2013; Oudiette, Santostasi, & Paller, 2013).

These results cannot prove a causal relation between disturbed sleep and language differences, but they do show correlations that were robust to control for other potentially confounding behavioral differences. Future work should assess language learning across periods of sleep and wake in DS, such that the causative mechanisms relating disturbed sleep to language deficits might be more clearly defined. Treatment studies, including continuous positive airway pressure interventions, could also support our understanding of the direction of these effects; the current study's data suggest that those studies should be initiated early in development.

While we found differences in language based on sleep quality, we did not find differences in EF between poor and good sleepers with DS. Given data from older children and adults showing robust

relations between sleep and EF, both in DS and in other populations, our null results in this domain are somewhat inconsistent with the past literature. Our failure to measure a correlation between EF and sleep within the group with DS could have two explanations. First, the BRIEF-P parent-report measure of EF was chosen based on its wide use and validation in this population (Edgin et al., 2010; Lee et al., 2011). While many laboratory tasks are not as thoroughly validated in young children with DS, the BRIEF-P may not capture EF in the same manner as laboratory tests (Toplak, West, & Stanovich, 2013). Another potential explanation lies in the fact that sleep disruption may influence EF to a greater degree later in development, as the prefrontal cortex continues to be wired and tuned (Beebe & Gozal, 2002). These relations would thus become more apparent as children age. Previous investigations have shown that parent reports of sleep in infancy may predict later EF at 4 years of age (Bernier et al., 2013). Given that our sample spanned a large age range, with our youngest subjects aged just over 24 months, it is possible that a longitudinal investigation tracking these children might be able to measure a later developing divergence in EF.

Several methodological limitations, including the small sample size, must be noted when considering results from this study. First, the use of a comprehensive diagnostic assessment battery for autism (ADI-R, ADOS, and clinical evaluation) would have been necessary to clarify the diagnostic status of each child, but was beyond the scope of the current study. The autism screening measures employed (M-CHAT and SCQ) have been widely used in individuals with DS and provide a strong estimate of behavioral and cognitive disturbance on their own. While the SCQ and M-CHAT have excellent sensitivity to detect autism, their specificity is not as good (leading to false positives). Despite these limitations, Guy et al. (2014) found that children born premature with false-positive screens on the M-CHAT were significantly more likely to demonstrate other language, cognitive, and socioemotional impairments of importance (see also Kuban et al., 2009, for similar findings). While we believe our current analyses provide more control for potentially confounding behavioral profiles than found in many previous investigations of the relations between sleep and language development (in DS or otherwise), future work should incorporate gold standard diagnostic instruments to explore these associations and further define sleep's role in the transition into an autism diagnosis in at-risk groups.

Another noteworthy limitation stems from a characteristic of our sleep assessment: Although the objective assessment of sleep using actigraphy is novel in this population and expands on parent-report measures, actigraphy cannot detect the presence of overnight hypoxia and respiratory difficulties that are indicative of OSA. While these results do highlight striking differences in the levels of sleep disturbance in DS, the primary source of these difficulties is unclear from this measurement alone (i.e., OSA, central apnea, or general fragmentation). Because of these limitations, actigraphy is not a substitute for PSG when delivering a medical diagnosis of OSA. Despite this fact, in the current investigation the use of actigraphy allowed us to assess sleep disturbances without the potential sampling bias stemming from the inherent difficulties in obtaining a full sleep study with PSG. Furthermore, previous PSG investigations of sleep-cognition relations in DS have suggested that level of oxygen desaturation is not the primary correlate of differences in cognition; rather, disturbances in SWS (i.e., from fragmentation) show higher correlations (Brooks et al., 2014).

Given the correlation between sleep disruption and language at this early age, these results serve to further emphasize the importance of good sleep habits, as well as early screening and treatment approaches for sleep disorders such as OSA, in all young children. As demonstrated here by the ratings on the Child Sleep Habits Questionnaire, which did not relate to actigraphy SE parameters, parent report of sleep problems are often unrelated to objective measures of sleep in DS, including estimates gathered in studies employing gold standard sleep assessments (i.e., laboratory PSG; Shott et al., 2006). The absence of predictive relations between parent report and sleep disturbance highlights the need for more sensitive and practical objective screening measures of sleep disruption in young children. Although current practice recommends children with DS undergo a baseline PSG sleep study by the age of 4 years (Bull & the Committee on Genetics, 2011), it seems likely that sleep problems may begin to manifest themselves earlier, potentially influencing how children start to express themselves with language.

Furthermore, a more thorough consideration of a child's sleep health may be crucial for understanding individual differences in response to behavioral and medical interventions. Yoder et al. (2014) recently demonstrated that toddlers with DS have poor vocabulary growth, but that they can benefit from high-frequency intervention. Future studies of

this nature may find a child's sleep status is an important determinant of intervention efficacy.

More broadly, our results interpreted in concert with findings from sleep-deprived TD children paint an alarming picture, suggesting that sleep disturbance is an often underrecognized, but likely highly influential, source of variability in young children's language development. On the basis of the current study's findings and others, we propose that infant and toddler sleep may be as important to consider when examining the antecedents of healthy cognitive development as many other widely acknowledged and researched early determinants, including self-regulation and environmental adversity.

References

- Abbeduto, L., Warren, S. F., & Conners, F. A. (2007). Language development in Down syndrome: From the prelinguistic period to the acquisition of literacy. *Mental Retardation and Developmental Disabilities Research Reviews*, *13*, 247–261. doi:10.1002/mrdd.20158
- Acebo, C., Sadeh, A., Seifer, R., Tzischinsky, O., Wolfson, A. R., Hafer, A., & Carskadon, M. A. (1999). Estimating sleep patterns with activity monitoring in children and adolescents: How many nights are necessary for reliable measures? *Sleep*, *22*, 95–103. Retrieved from <http://www.journalsleep.org/>
- Andreou, G., Galanopoulou, C., Gourgoulisanis, K., Karapetsas, A., & Molyvdas, P. (2002). Cognitive status in Down syndrome individuals with sleep disordered breathing deficits (SDB). *Brain and Cognition*, *50*, 145–149. doi:10.1016/S0278-2626(02)00019-2
- Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2013). Cross syndrome comparison of sleep problems in children with Down syndrome and Williams syndrome. *Research in Developmental Disabilities*, *34*, 1572–1580. doi:10.1016/j.ridd.2013.01.031
- Beebe, D. W., & Gozal, D. (2002). Obstructive sleep apnea and the prefrontal cortex: Towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *Journal of Sleep Research*, *11*, 1–16. doi:10.1046/j.1365-2869.2002.00289.x
- Beebe, D. W., Lewin, D., Zeller, M., McCabe, M., MacLeod, K., Daniels, S. R., & Amin, R. (2007). Sleep in overweight adolescents: Shorter sleep, poorer sleep quality, sleepiness, and sleep-disordered breathing. *Journal of Pediatric Psychology*, *32*, 69–79. doi:10.1093/jpepsy/jsj104
- Bernier, A., Beauchamp, M. H., Bouvette-Turcot, A. A., Carlson, S. M., & Carrier, J. (2013). Sleep and cognition in preschool years: Specific links to executive functioning. *Child Development*, *84*, 1542–1553. doi:10.1111/cdev.12063
- Breslin, J. H., Edgin, J. O., Bootzin, R. R., Goodwin, J. L., & Nadel, L. (2011). Parental report of sleep problems in Down syndrome. *Journal of Intellectual Disability Research*, *55*, 1086–1091. doi:10.1111/j.1365-2788.2011.01435.x
- Breslin, J., Spanò, G., Bootzin, R., Anand, P., Nadel, L., & Edgin, J. O. (2014). Obstructive sleep apnea and cognition in Down syndrome. *Developmental Medicine and Child Neurology*, *55*, 657–664. doi:10.1111/dmcn.12376
- Brooks, L. J., Olsen, M. N., Bacevice, A. M., Beebe, A., Konstantinopoulou, S., & Taylor, H. G. (2014). Relationship between sleep, sleep apnea, and neuropsychological function in children with Down syndrome. *Sleep and Breathing*, *19*, 197–204. doi:10.1007/s11325-014-0992-y
- Bruininks, R. H., Woodcock, R. W., Weatherman, R. F., & Hill, B. K. (1996). *Scales of Independent Behavior-Revised comprehensive manual*. Itasca, IL: Riverside.
- Bull, M. J., & the Committee on Genetics. (2011). Health supervision for children with Down syndrome. *Pediatrics*, *128*, 393–406. doi:10.1542/peds.2011-1605
- Chapman, R. S. (1995). Language development in children and adolescents with Down syndrome. In P. Fletcher & B. MacWhinney (Eds.), *The handbook of child language* (pp. 641–663). Oxford, UK: Blackwell.
- Chapman, R. (1997). Language development in children and adolescents with Down syndrome. *Mental Retardation and Developmental Disabilities Research Review*, *3*, 307–312. doi:10.1002/(SICI)1098-2779(1997)3:4<307:AID-MRDD5>3.0.CO;2-K
- Chen, C. C., Spanò, G., & Edgin, J. O. (2013). The impact of sleep disruption on executive function in Down syndrome. *Research in Developmental Disabilities*, *34*, 2033–2039. doi:10.1016/j.ridd.2013.03.009
- Churchill, S. S., Kieckhefer, G. M., Landis, C. A., & Ward, T. M. (2012). Sleep measurement and monitoring in children with Down syndrome: A review of the literature, 1960–2010. *Sleep Medicine Reviews*, *16*, 477–488. doi:10.1016/j.smrv.2011.10.003
- Colas, D., Valletta, J. S., Takimoto-Kimura, R., Nishino, S., Fujiki, N., Mobley, W. C., & Mignot, E. (2008). Sleep and EEG features in genetic models of Down syndrome. *Neurobiology of Disease*, *30*, 1–7. doi:10.1016/j.nbd.2007.07.014
- DiGuseppi, C., Hepburn, S., Davis, J. M., Fidler, D. J., Hartway, S., Lee, N. R., . . . Robinson, C. (2010). Screening for autism spectrum disorders in children with Down syndrome: Population prevalence and screening test characteristics. *Journal of Developmental & Behavioral Pediatrics*, *31*, 181–191. doi:10.1097/DBP.0b013e3181d5aa6d
- Dionne, G., Touchette, E., Forget-Dubois, N., Petit, D., Tremblay, R. E., Montplaisir, J. Y., & Boivin, M. (2011). Associations between sleep-wake consolidation and language development in early childhood: A longitudinal twin study. *Sleep*, *34*, 987–995. doi:10.5665/SLEEP.1148
- Dyken, M. E., Lin-Dyken, D. C., Poulton, S., Zimmerman, M. B., & Sedars, E. (2003). Prospective polysomno-

- graphic analysis of obstructive sleep apnea in Down syndrome. *Archives of Pediatrics & Adolescent Medicine*, 157, 655–660. doi:10.1001/archpedi.157.7.655
- Edgin, J. O., Mason, G. M., Allman, M. J., Capone, G. T., DeLeon, I., Maslen, C., . . . Nadel, L. (2010). Development and validation of the Arizona Cognitive Test Battery for Down syndrome. *Journal of Neurodevelopmental Disorders*, 2, 149–164. doi:10.1007/s11689-010-9054-3
- Ellingson, J. R., & Peters, J. F. (1980). Development of EEG and daytime sleep patterns in Trisomy-21 infants during the first year of life: Longitudinal observations. *Electroencephalography and Clinical Neurophysiology*, 50, 457–466. doi:10.1016/0013-4694(80)90012-7
- Fenson, L., Dale, P., Reznick, S., Bates, E., Thal, D., & Pethick, S. (1994). Variability in early communicative development. *Monographs of the Society for Research in Child Development*, 59(5). doi:10.2307/1166093
- Fenson, L., Dale, P., Reznick, S., Thal, D., Bates, E., Hartung, J., . . . Reilly, J. (1993). *MacArthur Communicative Development Inventories: Technical manual*. San Diego, CA: Singular Group.
- Fidler, D. J. (2005). The emerging Down syndrome behavioral phenotype in early childhood: Implications for practice. *Infants & Young Children*, 18, 86–103.
- Gaskell, M. G., Warker, J., Lindsay, S., Frost, R., Guest, J., Snowdon, R., & Stackhouse, A. (2014). Sleep underpins the plasticity of language production. *Psychological Science*, 25, 1457–1465. doi:10.1177/0956797614535937
- Gibson, D. (1978). *Down's syndrome: The psychology of mongolism*. Cambridge, UK: Cambridge University Press.
- Gomez, R. L., Bootzin, R. R., & Nadel, L. (2006). Naps promote abstraction in language-learning infants. *Psychological Science*, 17, 670–674. doi:10.1111/j.1467-9280.2006.01764.x
- Goodlin-Jones, B. L., Sitnick, S. L., Tang, K., Liu, J., & Anders, T. F. (2008). The Children's Sleep Habits Questionnaire in toddlers and preschool children. *Journal of Developmental & Behavioral Pediatrics*, 29, 82–88. doi:10.1097/DBP.0b013e318163c39a
- Gruber, R., Grizenko, N., Schwartz, G., Bellingham, J., Guzman, R., & Joobar, R. (2007). Performance on the continuous performance test in children with ADHD is associated with sleep efficiency. *Sleep*, 30, 1003–1009. Retrieved from <http://www.journalsleep.org/>
- Guy, A., Seaton, S. E., Boyle, E. M., Draper, E. S., Field, D. J., Manktelow, B. N., . . . Johnson, S. (2014). Infants born late/moderately preterm are at increased risk for a positive autism screen at 2 years of age. *Journal of Pediatrics*, 166, 269–275. doi:10.1016/j.jpeds.2014.10.053
- Heise, I., Fisher, S. P., Banks, G. T., Wells, S., Peirson, S. N., Foster, R. G., & Nolan, P. M. (2015). Sleep-like behavior and 24 hour rhythm disruption in the Tc1 mouse model of Down syndrome. *Genes, Brain and Behavior*, 14, 109–216. doi:10.1111/gbb.12198
- Henderson, L. M., Weighall, A. R., Brown, H., & Gaskell, M. G. (2012). Consolidation of vocabulary is associated with sleep in children. *Developmental Science*, 15, 674–687. doi:10.1111/j.1467-7687.2012.01172.x
- Honaker, S. M., Gozal, D., Bennett, J., Capdevila, O. S., & Spruyt, K. (2009). Sleep-disordered breathing and verbal skills in school-aged community children. *Developmental Neuropsychology*, 34, 588–600. doi:10.1080/87565640903133582
- Hupbach, A., Gomez, R. L., Bootzin, R. R., & Nadel, L. (2009). Nap-dependent learning in infants. *Developmental Science*, 12, 1007–1012. doi:10.1111/j.1467-7687.2009.00837.x
- Katz, E. S., Greene, M. G., Carson, K. A., Galster, P., Loughlin, G. M., Carroll, J., & Marcus, C. L. (2002). Night-to-night variability of polysomnography in children with suspected obstructive sleep apnea. *Journal of Pediatrics*, 140, 589–594. doi:10.1067/mpd.2002.123290
- Key, A. P., Molfese, D. L., O'Brien, L., & Gozal, D. (2009). Sleep-disordered breathing affects auditory processing in 5–7-year-old children: Evidence from brain recordings. *Developmental Neuropsychology*, 34, 615–628. doi:10.1080/87565640903133608
- Kuban, K. C., O'Shea, T. M., Allred, E. N., Tager-Flusberg, H., Goldstein, D. J., & Leviton, A. (2009). Positive screening on the Modified Checklist for Autism in Toddlers (M-CHAT) in extremely low gestational age newborns. *Journal of Pediatrics*, 154, 535–540. doi:10.1016/j.jpeds.2008.10.011
- Lee, N. R., Fidler, D. J., Blakeley-Smith, A., Daunhauer, L., Robinson, C., & Hepburn, S. (2011). Caregiver-report of executive functioning in a population-based sample of young children with Down syndrome. *American Journal on Intellectual and Developmental Disabilities*, 116, 290–304. doi:10.1352/1944-7558-116.4.290
- Levanon, A., Tarasiuk, A., & Tal, A. (1999). Sleep characteristics in children with Down syndrome. *Journal of Pediatrics*, 134, 755–760. doi:10.1016/S0022-3476(99)70293-3
- Lord, C., Rutter, M., DiLavore, P., & Risi, S. (1999). *Autism Diagnostic Observation Schedule manual*. Los Angeles, CA: Western Psychological Services.
- Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, 24, 659–685. doi:10.1007/BF02172145
- Meltzer, L. J., Montgomery-Downs, H. E., Insana, S. P., & Walsh, C. M. (2012). Use of actigraphy for assessment in pediatric sleep research. *Sleep Medicine Reviews*, 16, 463–475. doi:10.1016/j.smrv.2011.10.002
- Meltzer, L. J., Walsh, C. M., Traylor, J., & Westin, A. M. L. (2011). Direct comparison of two new actigraphs and polysomnography in children and adolescents. *Sleep*, 35, 159–166. doi:10.5665/sleep.1608
- Mervis, C. B., & Robinson, B. F. (2000). Expressive vocabulary ability of toddlers with Williams syndrome or Down syndrome: A comparison. *Developmental Neuropsychology*, 17, 111–126. doi:10.1207/S15326942DN1701_07
- Miano, S., Bruni, O., Elia, M., Scifo, L., Smerieri, A., Trovato, A., . . . Ferri, R. (2008). Sleep phenotypes of

- intellectual disability: A polysomnographic evaluation in subjects with Down syndrome and Fragile-X syndrome. *Clinical Neurophysiology*, 119, 1242–1247. doi:10.1016/j.clinph.2008.03.004
- Miller, J. F. (1988). The developmental asynchrony of language development in children with Down syndrome. In L. Nadel (Ed.), *The psychobiology of Down syndrome* (pp. 167–198). Cambridge, MA: MIT Press.
- Miller, J. F. (1999). Profiles of language development in children with Down syndrome. In J. Miller, M. Leddy, & L. A. Leavitt (Eds.), *Improving the communication of people with Down syndrome* (pp. 11–40). Baltimore, MD: Brookes.
- Miller, J., & Chapman, R. (1993). *SALT: Systematic Analysis of Language Transcripts: Basic SALT programs*. Madison: Language Analysis Laboratory, University of Wisconsin.
- Miller, J. F., Sedey, A. L., & Miolo, G. (1995). Validity of parent report measures of vocabulary development for children with Down syndrome. *Journal of Speech and Hearing Research*, 38, 1037–1044. doi:10.1044/jshr.3805.1037
- Nathani, S., & Oller, D. K. (2001). Beyond ba-ba and gu-gu: Challenges and strategies in coding infant vocalizations. *Behavior Research Methods, Instruments, & Computers*, 33, 321–330. doi:10.3758/BF03195385
- Ng, D. K., Hui, H. N., Chan, C. H., Kwok, K. L., Chow, P. Y., Cheung, J. M., & Leung, S. Y. (2006). Obstructive sleep apnoea in children with Down syndrome. *Singapore Medical Journal*, 47, 774–779. Retrieved from <https://www.sma.org.sg>
- Ngo, H. V. V., Martinetz, T., Born, J., & Mölle, M. (2013). Auditory closed-loop stimulation of the sleep slow oscillation enhances memory. *Neuron*, 78, 545–553. doi:10.1016/j.neuron.2013.03.006
- Nisbet, L. C., Phillips, N. N., Hoban, T. F., & O'Brien, L. M. (2014). Characterization of a sleep architectural phenotype in children with Down syndrome. *Sleep and Breathing*, 19, 1065–1071. doi:10.1007/s11325-014-1094-6
- O'Driscoll, D. M., Foster, A. M., Davey, M. J., Nixon, G. M., & Horne, R. S. (2010). Can actigraphy measure sleep fragmentation in children? *Archives of Disease in Childhood*, 95, 1031–1033. doi:10.1136/adc.2009.166561
- Oller, D. K., Niyogi, P., Gray, S., Richards, J. A., Gilkerson, J., Xu, D., . . . Warren, S. F. (2010). Automated vocal analysis of naturalistic recordings from children with autism, language delay, and typical development. *Proceedings of the National Academy of Sciences of the United States of America*, 107, 13354–13359. doi:10.1073/pnas.1003882107
- Oudiette, D., Santostasi, G., & Paller, K. A. (2013). Reinforcing rhythms in the sleeping brain with a computerized metronome. *Neuron*, 78, 413–415. doi:10.1016/j.neuron.2013.04.032
- Richdale, A. L. (1999). Sleep problems in autism: Prevalence, cause, and intervention. *Developmental Medicine & Child Neurology*, 41, 60–66. doi:10.1111/j.1469-8749.1999.tb00012.x
- Sattler, J. M. (2002). *Assessment of children: Behavioral and clinical applications* (4th ed.). San Diego, CA: Sattler.
- Shott, S. R., Amin, R., Chini, B., Heubi, C., Hotze, S., & Akers, R. (2006). Obstructive sleep apnea: Should all children with Down syndrome be tested? *Archives of Otolaryngology-Head & Neck Surgery*, 132, 432–436. doi:10.1001/archotol.132.4.432
- Singer Harris, N. G., Bellugi, U., Bates, E., Jones, W., & Rossen, M. (1997). Contrasting profiles of language development in children with Williams and Down syndrome. *Developmental Neuropsychology*, 13, 345–370. doi:10.1080/87565649709540683
- Snow, A. V., & Lecavalier, L. (2008). Sensitivity and specificity of the Modified Checklist for Autism in Toddlers and the Social Communication Questionnaire in preschoolers suspected of having pervasive developmental disorders. *Autism: The International Journal of Research and Practice*, 12, 627–644. doi:10.1177/1362361308097116
- Tamminen, J., Payne, J. D., Stickgold, R., Wamsley, E. J., & Gaskell, M. G. (2010). Sleep spindle activity is associated with the integration of new memories and existing knowledge. *Journal of Neuroscience*, 30, 14356–14360. doi:10.1523/JNEUROSCI.3028-10.2010
- Taylor, M. A., Schreck, K. A., & Mulick, J. A. (2012). Sleep disruption as a correlate to cognitive and adaptive behavior problems in autism spectrum disorders. *Research in Developmental Disabilities*, 33, 1408–1417. doi:10.1016/j.ridd.2012.03.013
- Toplak, M. E., West, R. F., & Stanovich, K. E. (2013). Practitioner review: Do performance-based measures and ratings of executive function assess the same construct? *Journal of Child Psychology and Psychiatry*, 54, 131–143. doi:10.1111/jcpp.12001
- Touchette, É., Petit, D., Séguin, J. R., Boivin, M., Tremblay, R. E., & Montplaisir, J. Y. (2007). Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. *Sleep*, 30, 1213–1219. Retrieved from <http://www.journalsleep.org/>
- Visootsak, J., Hess, B., Bakeman, R., & Adamson, L. B. (2012). Effects of congenital heart defects on language development in toddlers with Down syndrome. *Journal of Intellectual Disability Research*, 56, 1–6. doi:10.1111/j.1365-2788.2012.01619.x
- Weiss, A. R., Johnson, N. L., Berger, N. A., & Redline, S. (2010). Validity of activity-based devices to estimate sleep. *Journal of Clinical Sleep Medicine*, 6, 336–342. Retrieved from <http://www.aasmnet.org/jcsm/default.aspx>
- Williams, S. E., & Horst, J. S. (2014). Goodnight book: Sleep consolidation improves word learning via storybooks. *Frontiers in Psychology*, 5, 1–12. doi:10.3389/fpsyg.2014.00184
- Yoder, P., Woynaroski, T., Fey, M., & Warren, S. (2014). Effects of dose frequency of early communication intervention in young children with and without Down syndrome. *American Journal on Intellectual and Developmental Disabilities*, 119, 17–32. doi:10.1352/1944-7558-119.1.17