Running head: Sleep in infants/toddlers with neurodevelopmental disorders

**Sleep is atypical across neurodevelopmental disorders in infants and toddlers:**

**A cross-syndrome study**

Dean D'Souza1, Hana D’Souza2,3,4, Klára Horváth5,6, Kim Plunkett6, & Annette Karmiloff-Smith3,4

1Faculty of Science & Engineering, Anglia Ruskin University, Cambridge, UK

2Department of Psychology & Newnham College, University of Cambridge, Cambridge, UK

3Centre for Brain & Cognitive Development, Birkbeck, University of London, London, UK

4The LonDownS Consortium, London, UK

52nd Department of Paediatrics, Semmelweis University, Budapest, Hungary

6Department of Experimental Psychology, University of Oxford, Oxford, UK

**Abstract**

This cross-syndrome study focuses on sleep and its relationship with language development. Children with neurodevelopmental disorders present with language delay. Typical language development is constrained by numerous factors including sleep. Sleep is often disrupted in adolescents/adults with neurodevelopmental disorders. We therefore hypothesised that sleep may be disrupted, and correlate with language development, in infants/toddlers with neurodevelopmental disorders. To test our hypothesis, we obtained sleep and vocabulary size data from 75 infants/toddlers with one of three neurodevelopmental disorders (Down syndrome [DS], fragile X syndrome [FXS], Williams syndrome [WS]). Sleep was indeed disrupted in these children. It was also positively associated with receptive vocabulary size in the infants/toddlers with DS and WS (we could not test the relationship between sleep and language in FXS due to lack of power). We argue that disrupted sleep may be a common occurrence in very young children with neurodevelopmental disorders, and it may relate to their ability to acquire their first language.

**What this paper adds?**

This paper demonstrates that sleep is disrupted early in development in multiple neurodevelopmental disorders (Down syndrome [DS], fragile X syndrome [FXS], Williams syndrome [WS]). It also suggests that sleep is associated with early language development in DS and WS. It therefore raises the possibility that sleep may play a role in the emergence of the DS/WS phenotype and be an important target of intervention. As far as we are aware, no cross-syndrome study has hitherto investigated sleep (and the relationship between sleep and language) in such young participants with these neurodevelopmental disorders. Our study is important because phenotypes are emergent across developmental time; variations in sleep may contribute to the DS, FXS, and/or WS phenotype. Our study highlights a possible link between sleep and early language development across two neurodevelopmental disorders and offers a new—and possibly more treatable—target of early intervention.

**Keywords:** Sleep, language development, neurodevelopmental disorders, Down syndrome, fragile X syndrome, Williams syndrome

Sleep is the primary activity of, and crucial for, the developing infant (Mirmiran, Maas, & Ariagno, 2003; Touchette et al., 2007). It affects a range of physiological and cognitive processes, including language development. For example, one study found that 15-month-old infants who napped within 4 hours of exposure to an artificial language remembered the general grammatical pattern of the language 24 hours later, whereas 15-month-olds who had not napped showed no sign of remembering anything about the language (Hupbach, Gomez, Bootzin, & Nadel, 2009). Another study found that 3-year-old toddlers who napped after hearing stories remembered more novel words 2.5 hours later, 24 hours later, and 7 days later than 3-year-olds who did not nap – but the two groups did not differ on word retention when tested immediately after storytelling, demonstrating an effect of sleep consolidation on word learning (Williams & Horst, 2014). However, although a relationship between sleep and language development has been established in TD children, there has been very little focus on *very young children with disorders of known genetic origin*. Yet these children often present with language delay. Is the delay directly due to impaired (genetic) programming, as some research scientists and theorists suggest (e.g., Pinker, 1994)? Or might it indirectly result from bidirectional interactions between many diverse interdependent factors across multiple levels (e.g., genetic, cellular, neural networks, social) and timescales (e.g., moment-by-moment, developmental, evolutionary); factors as diverse as genes, culture, and *sleep* (D’Souza, D’Souza, & Karmiloff-Smith, 2016)? This is an important question because the former viewpoint implies that language delay is inevitable in children with neurodevelopmental disorders, whereas the latter hints at the possibility of early remediation. It is therefore imperative not only to investigate sleep and language ability across neurodevelopmental disorders, but also *early* in development; early intervention may lead to better outcomes (D’Souza, D’Souza, & Karmiloff-Smith, 2016).

There are currently very few studies on sleep and language development in infants/toddlers with disorders of known genetic origin. Edgin and colleagues (2015) reported poor sleep efficiency in 66% of 29 toddlers with Down syndrome (DS; mean age 42 months). They also found that the 19 toddlers with poor sleep efficiency and DS had significantly worse expressive language than the 10 toddlers with typical sleep efficiency and DS. This demonstrates an important relationship between variation in sleep efficiency and language development in DS. This finding was replicated in a much larger study of even younger children with DS (n = 66; mean age 29 months) (Fernandez et al., 2017). A smaller study of toddlers with a different neurodevelopmental disorder (Williams syndrome [WS]; n = 14; mean age 31 months) found a correlation between sleep duration and vocabulary size (Axelsson, Hill, Sadeh, & Dimitriou, 2013). However, the study relied on a parent report questionnaire for the sleep data. When Werner and colleagues (2008) directly compared agreement rates between a sleep questionnaire, sleep diary, and actigraphy, they found that the questionnaire was “not sufficient for any [sleep] measure variable” (p. 355). It would therefore be prudent to replicate this study using a sleep diary or actigraphy. Nevertheless, it is clear from these toddler studies that sleep is atypical and related to early language development in at least one neurodevelopmental disorder (DS).

What is unknown, however, is whether sleep problems in infants and toddlers are common across neurodevelopmental disorders. For instance, it is possible that sleep is particularly problematic in DS. Children with DS often present with obstructive sleep apnoea due to factors such as an improper cranial facial structure that constrains the airway, low muscle tone in the mouth and upper airway, a narrow nasopharyngeal area, and hypertrophy of adenoid and tonsillar tissues (Marcus, Keens, Bautista, von Pechmann, & Ward, 1991). These factors are likely to have cascading effects on language development. But they are less common in other neurodevelopmental disorders. It is therefore critical to directly compare different neurodevelopmental disorders early in development to answer the following questions: Is sleep disruption early in development syndrome-specific or syndrome-general? Is it related to early language development irrespective of syndrome-type?

The first question (‘Is sleep disruption early in development syndrome-specific or syndrome general?) has already been studied. Abel and Tonnsen (2017) asked mothers of children with WS (n = 19), Angelman syndrome (AS; n = 18), and Prader-Willi syndrome (PWS; n = 19) to complete a 12-item Brief Infant Sleep Questionnaire. They found that night-time sleep duration was significantly shorter in children with WS and AS (but not PWS) than in TD controls. They also found that night waking lasted longer in children with AS (but not WS or PWS) than in TD controls. The children with PWS did not differ from TD controls except for the fact that they fell asleep more quickly at bedtime (15 vs. 30 minutes). However, this study relied on a brief parent report questionnaire, so it is important to replicate the study using a sleep diary or actigraphy.

The second question has not hitherto been tackled in a cross-syndrome study. If sleep is disrupted *and* associated with early language delay across neurodevelopmental disorders, then this would hint that language delay is not predetermined but arises—at least in part—from variation in factors such as sleep. Furthermore, small variations in sleep may affect language development in atypically developing children more than in typically developing children. This is because sleep problems are a significant stressor in families of children with pervasive developmental disorders (Norton & Drew, 1994) and the interplay between stress, sleep, learning, and parent-child interaction may push the child into a different developmental state. Moreover, ameliorating sleep problems *early* in development may be more effective than only targeting language learning later in development.

In sum, sleep constrains language development in typically developing children. But very little is known about sleep across—or its relationship to language in—*early* atypical development. We seek to bridge this gap in our knowledge by measuring sleep variables in infants and toddlers with one of three neurodevelopmental disorders (Down syndrome [DS], fragile X syndrome [FXS], and Williams syndrome [WS]), and by ascertaining whether these sleep variables relate to measures of receptive and/or expressive language in DS and WS. DS was selected for comparison because children with DS present with obstructive sleep apnoea. FXS and WS were selected because they do not typically present with obstructive sleep apnoea. Children with FXS present with social anxiety (Cohen, Vietze, Sudhalter, Jenkins, & Brown, 1989), which may negatively affect their ability to acquire language, while children with WS are hyper-social (Mervis & Velleman, 2011), which may positively affect their language development. No cross-syndrome study has hitherto used sleep diaries to investigate the link between sleep and early language development. Our study is important because phenotypes are emergent across developmental time; variations in sleep may contribute to the DS, FXS, and/or WS phenotype. Our study may also highlight a relationship between sleep and language in young atypically developing populations, and offer a new—and possibly more treatable—target of early intervention.

**Methods**

**Participants**

The parents of 112 infants and toddlers took part in this study. Thirty-seven of the infants/toddlers were typically developing, while the remaining 75 had either Down syndrome (n = 30), fragile X syndrome (n = 15), or Williams syndrome (n = 30). All 30 infants/toddlers in the DS group were individually matched on age to the 30 infants/toddlers in the WS group. The 15 children in the FXS group were individually age-matched to 15 children in the DS/WS group. Although we would have liked to have recruited more infants/toddlers with FXS, FXS is often not diagnosed until later in development (Bailey, Raspa, Bishop, & Holiday, 2009). For the analyses, 30 typically developing (TD) controls were selected from the dataset of 37 TD infants/toddlers to closely match the ages of the atypically developing children. As a result, age did not significantly differ across the four groups, *F*3,101 = 0.43, *p* = .731.

The infants/toddlers with Down syndrome (DS), fragile X syndrome (FXS), and Williams syndrome (WS) had been clinically diagnosed and/or genetically tested respectively for full trisomy 21, mutation of the FMR1 gene, and deletion of the ELN gene. According to their parents, the typically developing (TD) toddlers presented with no developmental problems.

**Materials**

 The Sleep and Naps Oxford Research Inventory (SNORI; Horvath & Plunkett, 2016) and Oxford Communicative Developmental Inventory (OCDI; Hamilton, Plunkett, & Schafer, 2000) were used. The SNORI is an easy-to-use 10-day sleep diary. Caregivers indicate when their child is asleep by drawing in the SNORI a continuous line to a timescale (the timescale allows for 15-minute accuracy). They also draw a “down” arrow when they put their child to bed, and an “up” arrow when they wake their child up (see Figure 1). If the child wakes spontaneously, then this is indicated by the absence of a continuous line (rather than the presence of an “up” arrow). Caregivers note down in the SNORI the place and circumstances of their child’s sleep (e.g., in a pushchair, car) and highlight anything unusual that day that may have disrupted their child’s sleep pattern (e.g., illness, travelling, a loud noise). The SNORI is available to view online and download from the Oxford Babylab website (<http://www.psy.ox.ac.uk/research/oxford-babylab/research-overview/sleep/snoriv3-1.pdf>).

*[FIG. 1 HERE]*

The OCDI is a list of 416 words that are commonly acquired in infancy. For each word, the caregiver indicates whether their child can “understand” or “understand and say” the word. Only one of the 75 children with a neurodevelopmental disorder was able to understand (but not say) all 416 words. This child was 47 months old and had Williams syndrome. Nine typically developing children were also able to understand (and say) all 416 words. However, there was space in the OCDI for parents to include extra words that their child could say and/or understand, and each parent was encouraged to do so. There was no upper limit on the number of words the parents could report. The OCDI is a British English version of the American English MacArthur CDI, which has high internal consistency (.95-.96), test-retest reliability (.95), and concurrent validity (e.g., correlations between inventories scores and the Expressive One Word Picture Vocabulary Test ranged from .73 to .85) (Fenson et al., 1994). The OCDI is available to view online and download from the Oxford Babylab website (https://www.psy.ox.ac.uk/research/oxford-babylab/research-overview/oxford-cdi).

**Procedure**

Parents who visited our laboratory for another study were provided with the SNORI and OCDI. The parents were instructed to fill in the SNORI over 10-consecutive days and complete the OCDI within 14 days of starting the SNORI. They were asked to avoid starting the SNORI on a ‘special’ week (e.g., when the child is ill or when the family is travelling long distances).

**Measures**

Six sleep measures were taken using the SNORI: length of the main sleep period (‘bedtime duration’); time spent awake during the night; night-time sleep duration; sleep efficiency; daytime sleep (nap) duration; and number of naps (see Table 1 for descriptions).

*[TABLE 1 HERE]*

Two language measures were taken: receptive and expressive vocabularies. *Receptive vocabulary* was measured by counting the number of words in the OCDI that the infant could understand, while *expressive vocabulary* was measured by counting the number of words in the OCDI that the infant could understand and say (see Styles & Plunkett, 2009, for evidence that parents are good at estimating their child’s receptive and expressive vocabularies).

**Statistical analyses**

The SNORI data were manually coded and processed using custom MATLAB routines (see Horvath & Plunkett, 2016, for details). Our first step in exploring the data was to assess, for each group, whether any of the sleep variables (e.g., night-time sleep duration) was correlated with age. If a sleep variable was uncorrelated with age, then the second step for the analysis of that particular variable was to describe the sleep pattern in the group and use an analysis of variance (ANOVA) to ascertain whether the groups significantly differed on the sleep variable. Planned contrasts were used to compare the atypically developing groups with the TD control group.

If a sleep variable was correlated with age, then the second step for the analysis of that particular variable was to construct (ANCOVA-based) cross-sectional developmental trajectories for each group. The linear regressions of each group were then compared and evaluated to see whether the developmental trajectory of each group differed significantly in terms of their intercept (the level at which the sleep measure started) or gradient (the rate at which the sleep measure increased or decreased with age) (see Thomas et al., 2009, for details).

Age was included as a covariate in the developmental trajectories analysis for three reasons. First, age is highly correlated with some sleep measures and it was important to remove any variability that is accountable by age so the contribution of each sleep variable could be isolated. Second, including age as a covariate allowed us to ascertain whether the onset of any particular aspect of sleep was delayed. For example, if our analyses revealed that a sleep measure was significantly worse in the atypically developing groups yet increased over developmental time in all the groups at the same rate, then we could conclude that the developmental *pattern* is similar across groups but that developmental *onset* is delayed in the atypically developing groups. Third, including age allowed us to calculate whether rate of developmental change was different across groups. Thus, including age as a covariate tells us more about any differences we find between groups than simply comparing group means (Thomas et al., 2009).

Finally, the third step in our analyses was to use hierarchical regression analyses (controlling for age) to assess whether any of the sleep variables were associated with vocabulary size (specifically, OCDI receptive/expressive vocabulary scores).

**Results**

The results are provided in three sections. First, we assess the relationship between the sleep variables and age. Second, we describe sleep patterns (night-time sleep duration, time spent awake at night, sleep efficiency, daytime sleep duration, number of naps) in each group and examine whether there are differences between the groups in any of the sleep variables. Finally, for each group, we assess whether any of the sleep variables are associated with language comprehension and/or production.

**The relationship between age and sleep**

Correlations between age and each sleep variable were carried out to explore the data (see Table 2 for group characteristics). Interestingly, there was no significant relationship between age and night-time sleep duration in any of the four groups (TD: *τ* = .02, *p* = .872; DS: *τ* = .25, *p* = .054; FXS: *τ* = .05, *p* = .804; WS: *τ* = .13, *p* = .309 [Kendall’s tau was used because the data were positively skewed in some of the groups]). Nor was there a significant relationship between age and duration of time spent awake at night, nor between age and sleep efficiency, in any of the four groups (TD: *τ* = .10, *p* = .487; *τ* = -.10, *p* = .476; DS: *τ* = .12, *p* = .343; *τ* = -.13, *p* = .318; FXS: *τ* = .02, *p* = .920; *τ* = .10, *p* = .960; WS: *τ* = -.18, *p* = .174; *τ* = .18, *p* = .158; respectively).

There was, however, a significant relationship between age and duration of time spent napping in three (TD, FXS, WS) of the four groups, and a significant relationship between age and number of naps in all four groups (TD: *τ* = -.59, *p* < .001; *τ* = -.61, *p* < .001; DS: *τ* = -.43, *p* < .001; *τ* = -.29, *p* = .029[[1]](#footnote-1); FXS: *τ* = -.60, *p* = .002; *τ* = -.50, *p* = .0111; WS: *τ* = -.65, *p* < .001; *τ* = -.52, *p* < .001; respectively). The older the children were, the less time they spent napping and the fewer naps they had.

*[TABLE 2 HERE]*

**Sleep variables**

**Night-time sleep duration**

An ANOVA was carried out, with ‘group’ as the independent variable and ‘night-time sleep duration’ as the dependent variable. There was a significant effect of group on night-time sleep duration, *F*3,101 = 3.92, *p* = .011. Planned contrasts revealed that the TD infants had slept for longer than the infants and toddlers with DS/FXS/WS, *t*(101) = 3.36, *p* = .001. Multiple comparisons (three *t*-tests) failed to find any differences between the atypically developing groups (all, *p* > .744) (see Figure 2).

 *[FIG.2 HERE]*

***Figure 2.*** Night-time sleep duration for each participant group. TD = Typically-developing; DS = Down syndrome; FXS = fragile X syndrome; WS = Williams syndrome. During the night, the TD children slept for significantly longer than the atypically developing children.

**Time spent awake during bedtime**

An ANOVA was carried out, with ‘group’ as the independent variable and ‘time spent awake during bedtime’ as the dependent variable. There was a significant effect of group on time spent awake during bedtime, *F*3,101 = 7.40, *p* < .001. Planned contrasts revealed that the TD infants had spent more time asleep during bedtime than the infants and toddlers with DS/FXS/WS, *t*(101) = 4.49, *p* < .001. Multiple comparisons (three *t*-tests) failed to find any differences between the atypically developing groups (all, *p* > .371) (see Figure 3).

 *[FIG. 3 HERE]*

***Figure 3.*** Time spent awake at night for each participant group. TD = Typically-developing; DS = Down syndrome; FXS = fragile X syndrome; WS = Williams syndrome. The TD children spent significantly less time awake at night than the children with DS, FXS, and WS.

**Sleep efficiency**

Because the sleep efficiency data were proportional, we used the arcsine of the square root of the original values for our analyses. We ran an ANOVA with ‘group’ as the independent variable and ‘sleep efficiency’ as the dependent variable. There was a significant effect of group on sleep efficiency, *F*3,101 = 14.62, *p* < .001. Planned contrasts revealed that sleep efficiency was significantly better in the TD group than in the atypically developing groups, *t*(101) = 6.30, *p* < .001. However, multiple comparisons (three *t*-tests) failed to find any differences between the atypically developing groups (all, *p* > .264; Figure 4; see Figure 5 for examples of individual sleep patterns).



***Figure 4.*** Sleep efficiency (time spent asleep during night-time as a proportion of bedtime duration) for each participant group. TD = Typically-developing; DS = Down syndrome; FXS = fragile X syndrome; WS = Williams syndrome. Sleep efficiency was significantly greater in the TD group than in the DS, FXS, and WS groups.

 *[FIG. 4 HERE]*

*[FIG. 5 HERE]*

**Daytime sleep duration**

Because age was significantly correlated with daytime sleep duration, we compared the groups’ cross-sectional developmental trajectories by entering the age x daytime sleep duration interaction term as an independent variable.

***Comparing cross-sectional developmental trajectories***. For each disorder group, we constructed developmental trajectories relating daytime sleep duration to age and compared each pattern with the TD trajectory. Each model explained a significant proportion of the variance (all, *R*2 > .40). As expected, age predicted daytime sleep duration (all, *F* > 35.41, *p* < .001), indicating that the older children slept less than the younger children. However, neither the intercept nor the gradient significantly differed between atypically developing groups and the TD control group (all, *F* < 0.41, *p* > .525; see Figure 6).

 *[FIG. 6 HERE]*

***Figure 6.*** Developmental trajectories for daytime sleep duration for each participant group plotted against age (in months). TD = Typically-developing; DS = Down syndrome; FXS = fragile X syndrome; WS = Williams syndrome. The decrease over developmental time in daytime sleep duration was similar across the groups.

**Number of naps**

Although age was significantly correlated with number of naps, we could not compare the groups’ cross-sectional developmental trajectories because the data were non-normal (but see Figure 7 for a visual representation of the descriptive data).

 *[FIG. 7 HERE]*

***Figure 7.*** Mean number of naps for each participant group plotted against age (in months). TD = Typically-developing; DS = Down syndrome; FXS = fragile X syndrome; WS = Williams syndrome.

**Does sleep predict vocabulary size?**

Hierarchical regression analyses were carried out for each group – except the FXS group, which had only 15 participants, and the TD group, because some of the TD children were at ceiling on the CDI (see Table 3 for descriptive data). Five of the 30 families with DS did not complete the CDI within 14 days and were thus excluded from these analyses. To control for the nonlinear effect of age (which correlates with vocabulary size and some sleep variables), age squared was entered as a predictor first (Model 1), followed by either night-time sleep duration, total awakening time, or sleep efficiency (Model 2, forced entry). The outcome variable was either language comprehension or language production.

*[TABLE 3 HERE]*

**Night-time sleep duration.** For language comprehension in DS, age accounted for 50% of the variance in vocabulary size (adjusted *R*2 = .48). However, when night-time sleep duration was included as a predictor (Model 2), 59% of the variance in vocabulary size was explained (adjusted *R*2 = .55). This change (*ΔR*2 = .08) was significant, *F*1,22 = 4.45, *p* = .046. After accounting for age, for every two minutes of sleep time, language comprehension increased by one word in DS (*B* = 0.73; *t*(22)= 2.11, *p* = .046; Table 4; see also Tables SI-1 and SI-2 in Supplementary Information for correlation matrices).

For language comprehension in WS, age accounted for 54% of the variance in vocabulary size (adjusted *R*2 = .53). However, when night-time sleep duration was included as a predictor (Model 2), 60% of the variance in vocabulary size was explained (adjusted *R*2 = .58). This change (*ΔR*2 = .06) was significant, *F*1,27 = 4.29, *p* = .048. After accounting for age, for every two minutes of sleep time, language comprehension increased by one word in WS (*B* = 0.47; *t*(27)= 2.07, *p* = .048; Table 4).

*[TABLE 4 HERE]*

For language production in DS, age accounted for 32% of the variance in vocabulary size (adjusted *R*2 = .29). When night-time sleep duration was included as a predictor (Model 2), 36% of the variance in vocabulary size was explained (adjusted *R*2 = .30). This change (*ΔR*2 = .04) was not significant, *F*1,22 = 1.41, *p* = .247.

For language production in WS, age accounted for 49% of the variance in vocabulary size (adjusted *R*2 = .47). However, when night-time sleep duration was included as a predictor (Model 2), 55% of the variance in vocabulary size was explained (adjusted *R*2 = .52). This change (*ΔR*2 = .06) was not statistically significant but trending, *F*1,27 = 3.83, *p* = .061 (Table 5).

*[TABLE 5 HERE]*

**Other sleep variables.** For both language comprehension and language production, neither Model 2Awakening time nor Model 2Sleep efficiency significantly improves upon Model 1Age in DS or WS (all, *ΔR*2 < .05, *p* > .170). Nor did Model 2Daytime (nap) sleep duration significantly improve upon Model 1Age in DS or WS for language comprehension (DS: *ΔR*2 < .01, *p* = .881; WS: *ΔR*2 = .06, *p* = .055) or language production (DS: *ΔR*2 = .01, *p* = .670; WS: *ΔR*2 = .05, *p* = .102). We did not relate number of naps to language development, while controlling for age, because the data were non-normal.

**Summary**

Night-time sleep, but not daytime nap duration, is atypical in infants and toddlers with one of three neurodevelopmental disorders (DS, FXS, WS). The data also suggest that night-time sleep duration is associated with language ability in infants and toddlers with DS/WS. However, if we apply a Bonferroni-correction to the separate regression analyses, then none of the regressions would be statistically significant. It is therefore crucial that this aspect of the study is replicated.

**Discussion**

We found that night-time sleep, but not daytime nap duration, is atypical in infants and toddlers with one of three neurodevelopmental disorders. Why might nap duration not differ across groups? It is possible that daytime sleep is strongly constrained by social practices (e.g., formal education, parenting). In any case, during the night the infants with DS/FXS/WS slept less and woke for longer than the TD controls. Hence, our DS data replicate findings that young children with DS have poor sleep efficiency (Edgin et al., 2015; Fernandez et al., 2017) and our WS data replicate findings that children with WS have shorter night-time sleep and longer periods of wakefulness at night (Axelsson et al., 2013). Our WS data also replicate Abel and Tonnsen’s (2017) finding that sleep duration is relatively short in WS. Unlike Abel and Tonnsen (2017), however, we (like Axelsson et al., 2013) also found that night waking duration is longer in WS than in TD controls. Abel and Tonnsen reported that night awakenings lasted 3 minutes in total (median) for TD controls and 5 minutes in total (median) for WS. In our data, night awakenings lasted for about 3 minutes (median = 0; mean = 3.19) in TD controls but for six times longer (18 minutes) in WS (median = 17.60 mins; mean = 29.00 mins). This may reflect a difference in sample sizes (19 vs. 30), distributions of ages, and/or methodology (parent recall of how long their child spent awake over the past week vs. an ongoing 10-day sleep diary).

It is interesting that Abel and Tonnsen found no difference in sleep duration and night waking duration between children with Prader-Willi syndrome (PWS) and TD controls. Sleep-related disordered breathing (SDB) is very common in PWS (e.g., obstructive sleep apnoea has been diagnosed in 90% of children with PWS [Canora et al., 2018] while sleep disorders in general have been diagnosed in 70% of adults with PWS [Ghergan et al., 2017]), which suggests that the high prevalence of daytime sleepiness reported in PWS could be the result of disrupted night-time sleep. Therefore, Abel and Tonnsen’s findings raise the possibility that night awakenings in PWS are less likely to be noticed by parents than night awakenings in WS. More research is needed. But based on our cross-syndrome data and the wider literature, we suggest that short night-time sleep and/or poor sleep efficiency is a common characteristic of neurodevelopmental disorders.

We also found that night-time sleep duration was predictive of receptive vocabulary size in DS and WS. This dovetails findings by Axelsson and colleagues (2012), who also found that sleep duration explains a significant portion of variance in CDI ‘understands and says’ scores in WS. If we had used ‘age’ (like Axelsson et al., 2012) rather than ‘age squared’, then we too would have found that sleep duration predicts ‘understands and says’ scores (*B* = 0.48, *SE* = 0.23, *β* = .27, *ΔR*2 = .07, *p* = .047). Controlling for age squared, we found that sleep duration significantly predicts CDI ‘understands’ scores (*p* = .048) and shows a trend towards explaining CDI ‘understands and says’ scores (*p* = .061).

However, night-time sleep duration was not predictive of language *production* in DS. This was unexpected, because when Edgin and colleagues (2015) compared nineteen 39.5-month-olds with DS and low sleep efficiency (< .80) to ten 46.1-month-olds with DS and relatively high sleep efficiency (≥ .80), they found that the children with slow sleep efficiency produced significantly fewer words than the children with relatively high sleep efficiency (language comprehension was not reported). So, why would night-time sleep duration be associated with receptive but not expressive vocabulary size in DS in our study? One possibility is that language production is more variable than language comprehension—especially in DS (e.g., see Table 3)—and therefore a larger sample size was required to detect an effect. Another reason why our results differ from Edgin et al.’s is that although their two DS groups and TD control group did not significantly differ from each other on age (*p* = .17), the children with DS in the relatively high sleep efficiency group not only had a better vocabulary but also were (as expected) older by half a year. Sleep efficiency improves with age in children with DS (Fernandez et al., 2017), as does vocabulary size (Zampini & D’Odorico, 2013). So, some of the variability in sleep efficiency and language ability may have been the result of differences in chronological age. While Edgin et al. did also examine the findings with linear models in addition to groupings, the effect may have been smaller if age was factored into the analysis (in our study, age was entered first and accounted for a large proportion of the variation; the sleep variables were entered second).

Why was only sleep *duration* related to vocabulary size in DS and WS? One straightforward explanation is that (1) infants and toddlers with DS/WS are not spending sufficient time asleep, hence they benefit from extra sleep, and (2) sleep quality is generally inadequate in DS/WS and thus variation in night-time awakenings or sleep efficiency may not indicate a particularly disruptive sleep period. For example, it has been shown that sleep structure in older children with WS substantially differs from that of TD. Children with WS (median age of 8.4 years) have worse sleep efficiency, less REM sleep duration, and more slow wave sleep (Mason et al., 2011). Moreover, a quantitative EEG analysis suggests that sleep in adolescents and adults with WS can be characterised by accelerated thalamocortical activity (Bodizs, Gombos, & Kovacs, 2012). Thalamocortical activity is associated with sleep spindles, which are in turn associated with sleep-dependent learning (Tamminen, Payne, Stickgold, Wamsley, & Gaskell, 2010). Indeed, Ashworth at al. (2017) found that the consolidation of novel words did not benefit from sleep in WS, which might be due to its altered microstructure. It is possible that, in WS, sleep does not itself much enhance sleep-dependent memory consolidation, but longer sleep durations may improve other socio-cognitive functions important for vocabulary development, such as mood and attention. Alternatively, it is possible that sleep quality, and thus sleep-dependent memory consolidation, improves during the night in WS/DS. For example, children with WS (median age of 7.3 years) were found to have shallower drops in cortisol levels and a less pronounced increase in melatonin at bedtime than TD controls (Sniecinska-Cooper et al., 2014) – which hints at the possibility that they require more sleep-time to reach deeper levels of sleep. To test these hypotheses, we suggest that future studies use EEG to relate sleep stages and neural oscillatory activity to language development in WS and DS.

**Conclusion**

Night-time sleep is disrupted in infants and toddlers with neurodevelopmental disorders. Moreover, night-time sleep duration is associated with language ability in infants and toddlers with DS and WS. Sleep may therefore play a significant role in the emergence of the DS/WS phenotype. It is important to note that the analyses *linking sleep duration to receptive language* yielded barely significant results, so these findings need to be replicated in a larger sample before firm conclusions can be drawn. Future studies should ascertain whether improving sleep in infants/toddlers with DS/WS results in improvements in language (and cognitive) development.

**Acknowledgements**

We are very grateful for the contributions families have made towards this study. The study was funded by The Waterloo Foundation (Grant 2027-3399), Autour des Williams (France), and British Academy (SRG\171226). Recruitment was supported by Down Syndrome Education In- ternational, the Fragile X Society, and the Williams Syndrome Foundation. HD is a Beatrice Mary Dale Research Fellow supported by Newnham College, University of Cambridge, the Baily Thomas Charitable Fund, and the Isaac Newton Trust.

**References**

Abel, E. A., & Tonnsen, B. L. (2017). Sleep phenotypes in infants and toddlers with neurogenetic syndromes. *Sleep Medicine*, *38*, 130-134.

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2017). A cross-syndrome study of the differential effects of sleep on declarative memory consolidation in children with neurodevelopmental disorders. *Developmental Science*, *20*(2), e12383.

Axelsson, E. L., Hill, C. M., Sadeh, A., & Dimitriou, D. (2013) Sleep problems and language development in toddlers with Williams syndrome. *Research in Developmental Disabilities*, *34*(11), 3988-3996.

Bailey, D. B., Raspa, M., Bishop, E., & Holiday, D. (2009). No change in the age of diagnosis for fragile X syndrome: findings from a national parent survey. *Pediatrics*, *124*(2), 527-533.

Bódizs, R., Gombos, F., & Kovács, I. (2012). Sleep EEG fingerprints reveal accelerated thalamocortical oscillatory dynamics in Williams syndrome. *Research in Developmental Disabilities*, *33*(1), 153-164.

Canora, A., Franzese, A., Mozzillo, E., Fattorusso, V., Bocchino, M., & Sanduzzi, A. (2018). Severe obstructive sleep disorders in Prader-Willi syndrome patients in southern Italy. *European Journal of Pediatrics*, 177(9), 1367-1370.

Cohen, I. L., Vietze, P. M., Sudhalter, V., Jenkins, E. C., & Brown, W. T. (1989). Parent‐Child Dyadic Gaze Patterns in Fragile X Males and in Non‐fragile X Males with Autistic Disorder. *Journal of Child Psychology and Psychiatry*, *30*(6), 845-856.

Dionne, G., Touchette, E., Forget-Dubois, N., Petit, D., Tremblay, R.E., Montplaisir, J., & Boivin, M. (2011). Associations between sleep-wake consolidation and language development in early childhood: A longitudinal twin study. *Sleep*, 34, 987–995.

D’Souza, D., D’Souza, H., & Karmiloff-Smith, A. (2017). Precursors to language development in typically and atypically infants and toddlers: the importance of embracing complexity. *Journal of Child Language*, *44*(3), 591-627.

Edgin, J. O., Tooley, U., Demara, B., Nyhuis, C., Anand, P., & Spanò, G. (2015). Sleep Disturbance and Expressive Language Development in Preschool‐Age Children With Down Syndrome. *Child Development*, *86*(6), 1984-1998.

Fernandez, F., Nyhuis, C. C., Anand, P., Demara, B. I., Ruby, N. F., Spanò, G., ... & Edgin, J. O. (2017). Young children with Down syndrome show normal development of circadian rhythms, but poor sleep efficiency: a cross-sectional study across the first 60 months of life. *Sleep Medicine*, *33*, 134-144.

Ghergan, A., Coupaye, M., Leu-Semenescu, S., Attali, V., Oppert, J. M., Arnulf, I., ... & Redolfi, S. (2017). Prevalence and Phenotype of Sleep Disorders in 60 Adults With Prader–Willi Syndrome. *Sleep*, *40*(12), zsx162.

Hamilton, A., Plunkett, K., & Schafer, G. (2000). Infant vocabulary development assessed with a British communicative development inventory. *Journal of Child Language*, *27*(3), 689-705.

Horváth, K., & Plunkett, K. (2016). Frequent daytime naps predict vocabulary growth in early childhood. *Journal of Child Psychology and Psychiatry*, *57*(9), 1008-1017.

Hupbach, A., Gomez, R. L., Bootzin, R. R., & Nadel, L. (2009). Nap-dependent learning in infants. *Developmental Science*, *12*(6), 1007-1012.

Marcus, C. L., Keens, T. G., Bautista, D. B., von Pechmann, W. S., & Ward, S. L. D. (1991). Obstructive sleep apnea in children with Down syndrome. *Pediatrics*, *88*(1), 132-139.

Mervis, C. B., & Velleman, S. L. (2011). Children with Williams Syndrome: Language, Cognitive, and Behavioral Characteristics and their Implications for Intervention. *Perspectives on Language Learning and Education*, *18*(3), 98–107.

Mirmiran, M., Maas, Y. G., & Ariagno, R. L. (2003). Development of fetal and neonatal sleep and circadian rhythms. *Sleep Medicine Reviews*, *7*(4), 321-334.

Norton, P., & Drew, C. (1994). Autism and potential family stressors. *The American Journal of Family Therapy*, *22*(1), 67-76.

Pinker, S. (1994). *The language instinct*. New York: Morrow.

Sniecinska-Cooper, A. M., Iles, R. K., Butler, S. A., Jones, H., Bayford, R., & Dimitriou, D. (2015). Abnormal secretion of melatonin and cortisol in relation to sleep disturbances in children with Williams syndrome. *Sleep Medicine*, *16*(1), 94-100.

Styles, S., & Plunkett, K. (2009). What is ‘word understanding’ for the parent of a one-year-old? Matching the difficulty of a lexical comprehension task to parental CDI report. *Journal of Child Language*, *36*(4), 895-908.

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*(43), 14356-14360.

Thomas, M. S. C., Annaz, D., Ansari, D., Serif, G., Jarrold, C., & Karmiloff-Smith, A. (2009). Using developmental trajectories to understand developmental disorders. *Journal of Speech, Language, and Hearing Research*, *52*, 336-358

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*(9), 1213-1219.

Werner, H., Molinari, L., Guyer, C., & Jenni, O. G. (2008). Agreement rates between actigraphy, diary, and questionnaire for children's sleep patterns. *Archives of Pediatrics & Adolescent Medicine*, *162*(4), 350-358.

Williams, S. E., & Horst, J. S. (2014). Goodnight book: sleep consolidation improves word learning via storybooks. *Frontiers in Psychology*, *5*, 184.

Zampini, L., & D'Odorico, L. (2013). Vocabulary development in children with Down syndrome: Longitudinal and cross-sectional data. *Journal of Intellectual and Developmental Disability*, *38*(4), 310-317.

1. This result would not survive a Bonferroni correction for multiple comparisons. [↑](#footnote-ref-1)