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Sleep is atypical across neurodevelopmental disorders in infants and toddlers: A cross-syndrome study

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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. This 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.

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1. Introduction

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 h of exposure to an artificial language remembered the general grammatical pattern of the language 24 h 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 h later, 24 h 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, 2017)? 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 et al., 2017).

There are currently very few studies on sleep and language development in infants/toddlers with disorders of known genetic origin. Edgin et al. (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, Molinari, Guyer, and Jenni (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 min). 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 hypersocial (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