

# Wake up to the benefits of timely management of sleep problems in toddlers with Williams Syndrome

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This commentary relates to Gwilliam, Joyce, and Dimitriou [1] and their longitudinal work on sleep problems in toddlers with Williams syndrome (WS). WS is a rare and sporadic genetic disorder caused by a small deletion of genes on chromosome 7 [2]. Individuals with WS experience a range of medical and developmental difficulties and sleep disturbances are highly prevalent. The aim, here, is to address why early identification of sleep problems could be beneficial for children with WS and their families. The specific sleep difficulties reported in children with WS will be outlined and the importance of early, syndrome-specific sleep support will be discussed, with reference to clinical outcomes.

Sleep plays a fundamental role in healthy development and promotes optimal cognitive and daytime functioning. Sleep disturbances are associated with a range of negative outcomes. For children with typical development (TD), these include compromised cognitive functioning, increased behavioral problems and emotional dysregulation [3,4]. For children with neurodevelopmental disorders, it is probable that sleep difficulties compound their existing functioning difficulties; described by Owens [5] (p. 541) as a 'double jeopardy'.

In TD, early sleep difficulties are predictive of future disturbances [6]; yet, implementing early and brief sleep interventions has been reported to have a high success rate for improving sleep outcomes [7,8]. Treating sleep problems also provides demonstrable benefits for cognitive and behavioral functioning, with even moderate improvements in sleep patterns resulting in improved functioning [9,10]. Conversely, modest sleep debt on a regular basis may result in children becoming chronically sleep deprived, which can affect development [11]. Furthermore, longitudinal studies have revealed that there is an association between sleep in early childhood and cognitive and behavioral functioning at school age [12,13]. Crucially, the relationship between sleep and cognitive functioning appears to intensify over time [11]. This provides strong evidence that treating sleep problems as early as possible will minimize the adverse effects of sleep loss on functioning and long-term development.

In TD, almost a third of children experience sleep difficulties in the pre-school years [14,15]. Sleep patterns change with age and follow a distinct developmental trajectory. By school-age, there is a reduction in reported sleep difficulties; although these remain for almost one fifth of children [16]. In general, by school-age, sleep quality is improved and total sleep duration is shorter, but notably, more consolidated.

For children with WS, the developmental trajectory of sleep difficulties presents differently. Growing evidence indicates that sleep problems emerge as early as the toddler years, with parent-reported short sleep durations and long settling times [17,18]. Objective measures corroborate this and worryingly, unlike in TD, there is no indication of maturational improvement [1]. Thus, where sleep problems tend to be transient in TD, they become chronic in WS; Sleep difficulties emerge in early childhood, remain common at school-age, manifesting in short sleep durations, bedtime resistance, long sleep latencies and frequent night waking [19] and persist into adulthood [20]. Consequently, there is a high prevalence of individuals with WS experiencing sleep difficulties throughout life, which is reflected in the inclusion of *sleep issues* in the official clinical guidelines for the management of Williams Syndrome [21].

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It is unknown as to what extent sleep disturbances may contribute to the range of cognitive and behavioral difficulties associated with WS, which include mild to moderate intellectual disability, visuospatial difficulties, poor executive functioning, attention problems and high levels of anxiety [22-24]. The specific interplay between both sleep & cognition, and sleep & behavior, remains unclear, with bidirectionality a distinct possibility. Studies are increasingly linking sleep disturbances with functioning difficulties in children with developmental disorders or those with an intellectual disability [25-27]; more frequent and severe sleep problems are associated with greater cognitive and behavioral difficulties [26]. Thus, it is feasible that there is an additive effect of sleep problems on functioning difficulties for individuals with WS, and, by treating sleep difficulties there is the potential to improve cognitive and behavioral outcomes.

de Magalhaes G, et al. [28] explored the associations between sleep and language development and behavior problems in 2-year-olds with WS. Night-time sleep duration was positively associated with language development [28], consistent with other findings [18,29]. Previous studies have examined the link between sleep disturbances and behavioral problems in children with WS but no significant associations were observed [18,30]. In contrast, de Magalhaes G, et al. [28] found that, in addition to a high proportion of children with WS experiencing behavioral difficulties, problems were significantly greater for children who screened positive for a Sleep-Related Breathing Disorder or excessive daytime tiredness. The authors proposed that the demonstrable link highlights the importance of assessing sleep problems early in life as they could contribute to, or exacerbate, behavior problems.

Functioning difficulties are not the only concern associated with sleep problems. There are potential health risks associated with poor sleep in children, including in the cardiovascular and immune systems [5]. This could be of particular concern in the WS population, as cardiovascular disease is present in approximately 84% of cases.

Furthermore, sleep disruption also impacts wider family life. Meltzer and Montgomery-Downs [31] highlighted the importance of viewing children's sleep problems within a family context. Often there is a direct relationship between childhood sleep problems and quality and quantity of parental sleep [5]; compromising parental daytime functioning and increasing the risk of parental stress, mood and quality of life [32]. This potential is certainly present for parents of toddlers with WS, who reported high levels of involvement in their child's sleep and frequently viewed it to be problematic, yet received limited professional support [1]. Feasibly, due to professionals lacking knowledge about WS, a source of stress for parents of children with WS [33]. Practitioner knowledge is crucial for sleep support as parents may not appreciate the extent to which untreated sleep problems will negatively impact multiple facets of their child's development.

A growing body of research is demonstrating that genetic disorders, such as WS, have their own unique sleep profile, with potentially differing causal mechanisms [17,34]. This indicates that despite sleep problems displaying common features, such as frequent night waking or bedtime resistance, it is likely that the nature of sleep problems are varied. This recognition is the first step in providing syndrome-specific sleep support but, consequently, treating sleep difficulties is more complex than it may appear. Generalizing sleep management from the TD population will not be applicable for individuals with WS. A thorough understanding of the unique

features and individual sleep profile of WS is required. Without this, health professionals will not have the necessary tools to effectively manage and treat sleep difficulties.

Mason et al. [30] suggested that a behavioral intervention could be considered for managing and treating sleep difficulties in WS. By promoting good sleep hygiene, more specifically a consistent bedtime routine, they proposed that self-soothing skills might improve, increasing sleep efficiency. Arguably, positive sleep hygiene should always be used as a first line of treatment because, even if measures are not sufficient to treat sleep problems, success of other interventions would be limited if poor sleep habits are not addressed [35,36]. A recent review exploring the effectiveness of behavioral sleep interventions on treating sleep problems in rare genetic neurodevelopmental disorders, including WS, found some positive treatment effects but highlighted the need for more studies in the area [37].

In conjunction with behavioral measures, pharmacological management of sleep difficulties in children with WS could be considered and has had some success. Martens et al. [38] identified that, from a large sample of individuals with WS (513), a quarter had taken medication to help with sleep, at some stage. Melatonin was the most commonly used medication and it was widely reported to be helpful (91%). Further evidence is needed to determine in what ways it was helpful; most likely it would improve sleep onset difficulties but the impact on sleep duration and night waking requires more exploration. Furthermore, increased levels of respiratory-related arousals in children with WS could indicate an intrinsic sleep-disrupter, such as obstructive sleep apnea [30]; overnight polysomnography could be appropriate to screen for problems and specific treatment, such as assessment for adenotonsillectomy, could be required.

Longitudinal studies are needed to assess the effectiveness of any management of sleep problems in WS. This would also help address our ability to determine whether treating sleep difficulties in the early years could affect the developmental sleep trajectory in WS, and, in what ways this might subsequently impact development.

In summary, our understanding of the individual WS sleep profile is growing. The recent evidence identifying sleep problems to be present in toddlers with WS demands attention. The pre-school years constitute a period of rapid cognitive and behavioral development, reflected in huge anatomical and physiological brain growth [39]. Not only could sleep disturbances confound existing functioning difficulties, but age will likely magnify effects. Thus, management of sleep problems at an early age, using a targeted and syndrome-specific approach, will lead to a greater opportunity for maximizing children's developmental potential and improving clinical outcomes, as well as enhancing quality of life for the entire family.

## References

1. Gwilliam K, Joyce A, Dimitriou D. Early manifestation of sleep problems in toddlers with Williams syndrome using a mixed method longitudinal approach. *Research in Developmental Disabilities*. 2020 Sep 1;104:103658.
2. Ewart AK, Morris CA, Atkinson D, Jin W, Sternes K, Spallone P, et al. Hemizygoty at the elastin locus in a developmental disorder, Williams syndrome. *Nature Genetics*. 1993 Sep;5(1):11-6.
3. Astill RG, Van der Heijden KB, Van IJzendoorn MH, Van Someren EJ.

- Sleep, cognition, and behavioral problems in school-age children: A century of research meta-analyzed. *Psychological Bulletin*. 2012 Nov;138(6):1109.
4. Sadeh A, Gruber R, Raviv A. Sleep, neurobehavioral functioning, and behavior problems in school age children. *Child Development*. 2002 Mar;73(2):405-17.
  5. Owens J. Classification and epidemiology of childhood sleep disorders. *Sleep Medicine Clinics*. 2007 Sep 1;2(3):353-61.
  6. Simard V, Nielsen TA, Tremblay RE, Boivin M, Montplaisir JY. Longitudinal study of preschool sleep disturbance: the predictive role of maladaptive parental behaviors, early sleep problems, and child/mother psychological factors. *Archives of Pediatrics & Adolescent Medicine*. 2008 Apr 1;162(4):360-7.
  7. Mindell, J. A., Kuhn, B., Lewin, D. S., Meltzer, L. J., Sadeh, A., & American Academy of Sleep, M. (2006). Behavioral treatment of bedtime problems and night wakings in infants and young children. *Sleep*, 29(10), 1263-1276. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/17068979>
  8. Sadeh A. Cognitive-behavioral treatment for childhood sleep disorders. *Clinical Psychology Review*. 2005 Jul 1;25(5):612-28.
  9. Gruber R, Somerville G, Bergmame L, Fontil L, Paquin S. School-based sleep education program improves sleep and academic performance of school-age children. *Sleep Medicine*. 2016 May 1;21:93-100.
  10. Sadeh A, Gruber R, Raviv A. The effects of sleep restriction and extension on school age children: What a difference an hour makes. *Child Development*. 2003 Mar;74(2):444-55.
  11. Buckhalt JA. Children's sleep, sleepiness, and performance on cognitive tasks. *WMF Press Bulletins*. 2011 Jan 1;2011(2):1.
  12. Kocovska D, Rijlaarsdam J, Ghassabian A, Jaddoe VW, Franco OH, Verhulst FC, et al. Early childhood sleep patterns and cognitive development at age 6 years: the Generation R Study. *Journal of Pediatric Psychology*. 2017 Apr 1;42(3):260-8.
  13. Touchette É, Petit D, Séguin JR, Boivin M, Tremblay RE, Montplaisir JY. Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. *Sleep*. 2007 Sep 1;30(9):1213-9.
  14. Galland BC, Taylor BJ, Elder DE, Herbison P. Normal sleep patterns in infants and children: a systematic review of observational studies. *Sleep Medicine Reviews*. 2012 Jun 1;16(3):213-22.
  15. Mindell JA, Owens JA, Carskadon MA. Developmental features of sleep. *Child and Adolescent Psychiatric Clinics of North America*. 1999 Oct 1;8(4):695-725.
  16. Sadeh A, Raviv A, Gruber R. Sleep patterns and sleep disruptions in school-age children. *Developmental Psychology*. 2000 May;36(3):291.
  17. Abel EA, Tonnsen BL. Sleep phenotypes in infants and toddlers with neurogenetic syndromes. *Sleep Medicine*. 2017 Oct 1;38:130-4.
  18. Axelsson EL, Hill CM, Sadeh A, Dimitriou D. Sleep problems and language development in toddlers with Williams syndrome. *Research in Developmental Disabilities*. 2013 Nov 1;34(11):3988-96.
  19. Ashworth A, Hill CM, Karmiloff-Smith A, Dimitriou D. Cross syndrome comparison of sleep problems in children with Down syndrome and Williams syndrome. *Research in Developmental Disabilities*. 2013 May 1;34(5):1572-80.
  20. Goldman SE, Malow BA, Newman KD, Roof E, Dykens EM. Sleep patterns and daytime sleepiness in adolescents and young adults with Williams syndrome. *Journal of Intellectual Disability Research*. 2009 Feb;53(2):182-8.
  21. Williams Syndrome Guideline Development Group. (2017). Management of Williams Syndrome: A Clinical Guideline. Retrieved from [https://williams-syndrome.org.uk/wp-content/uploads/2018/07/williams\\_syndrome\\_guidelines\\_pdf.pdf](https://williams-syndrome.org.uk/wp-content/uploads/2018/07/williams_syndrome_guidelines_pdf.pdf)
  22. Morris CA. The behavioral phenotype of Williams syndrome: A recognizable pattern of neurodevelopment. In *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* 2010 Nov 15 (Vol. 154, No. 4, pp. 427-431). Hoboken: Wiley Subscription Services, Inc., A Wiley Company.
  23. Royston R, Waite J, Howlin P. Williams syndrome: recent advances in our understanding of cognitive, social and psychological functioning. *Current Opinion in Psychiatry*. 2019 Mar 1;32(2):60-6.
  24. Udwin O, Yule W. A cognitive and behavioural phenotype in Williams syndrome. *Journal of Clinical and Experimental Neuropsychology*. 1991 Mar 1;13(2):232-44.
  25. Mughal R, Hill CM, Joyce A, Dimitriou D. Sleep and cognition in children with fetal alcohol spectrum disorders (FASD) and children with autism spectrum disorders (ASD). *Brain Sciences*. 2020 Nov;10(11):863.
  26. Richdale A, Francis A, Gavidia-Payne S, Cotton S. Stress, behaviour, and sleep problems in children with an intellectual disability. *Journal of Intellectual and Developmental Disability*. 2000 Jan 1;25(2):147-61.
  27. Wiggs L, Stores G. Severe sleep disturbance and daytime challenging behaviour in children with severe learning disabilities. *Journal of Intellectual Disability Research*. 1996 Dec;40(6):518-28.
  28. de Magalhães CG, O'Brien LM, Mervis CB. Sleep characteristics and problems of 2-year-olds with Williams syndrome: relations with language and behavior. *Journal of Neurodevelopmental Disorders*. 2020 Dec;12(1):1-6.
  29. D'Souza D, D'Souza H, Horváth K, Plunkett K, Karmiloff-Smith A. Sleep is atypical across neurodevelopmental disorders in infants and toddlers: a cross-syndrome study. *Research in Developmental Disabilities*. 2020 Feb 1;97:103549.
  30. Mason TB, Arens R, Sharman J, Bintliff-Janisak B, Schultz B, Walters AS, et al. Sleep in children with Williams syndrome. *Sleep Medicine*. 2011 Oct 1;12(9):892-7.
  31. Meltzer LJ, Montgomery-Downs HE. Sleep in the family. *Pediatric Clinics*. 2011 Jun 1;58(3):765-74.
  32. Sadeh A, Mindell JA, Owens J. Why care about sleep of infants and their parents?. *Sleep Medicine Reviews*. 2011 Oct 1;15(5):335-7.
  33. Ashworth M, Palikara O, Van Herwegen J. Comparing parental stress of children with neurodevelopmental disorders: The case of Williams syndrome, Down syndrome and autism spectrum disorders. *Journal of Applied Research in Intellectual Disabilities*. 2019 Sep;32(5):1047-57.
  34. Agar G, Brown C, Sutherland D, Coulborn S, Oliver C, Richards C. Sleep disorders in rare genetic syndromes: a meta-analysis of prevalence and profile. *Molecular Autism*. 2021 Dec;12(1):1-7.
  35. Heussler HS, Hiscock H. Sleep in children with neurodevelopmental difficulties. *Journal of Paediatrics and Child Health*. 2018 Oct;54(10):1142-7.
  36. Jan JE, Owens JA, Weiss MD, Johnson KP, Wasdell MB, Freeman RD, et al. Sleep hygiene for children with neurodevelopmental disabilities. *Pediatrics*. 2008 Dec 1;122(6):1343-50.

37. McLay L, Roche L, France KG, Blampied NM, Lang R, France M, et al. Systematic review of the effectiveness of behaviorally-based interventions for sleep problems in people with rare genetic neurodevelopmental disorders. *Sleep Medicine Reviews*. 2019 Aug 1;46:54-63.
38. Martens MA, Seyfer DL, Andridge RR, Coury DL. Use and effectiveness of sleep medications by parent report in individuals with Williams syndrome. *Journal of Developmental & Behavioral Pediatrics*. 2017 Nov 1;38(9):765-71.
39. Brown TT, Jernigan TL. Brain development during the preschool years. *Neuropsychology Review*. 2012 Dec;22(4):313-33.