

The relationship between autism spectrum disorder and sleep

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INTRODUCTION

This issue of *Sleep Science* contains 2 reports related to autism spectrum disorder (ASD), an extremely important and relatively frequent neurodevelopmental disorder. This condition is characterized by impaired reciprocal social interaction and communication, as well as restricted and repetitive patterns of behaviors or interest. It affects 1 in every 40 to 59 children in the United States, with prevalence rates doubling between 2000-2002 and 2010-2012¹⁻³. Sleep disturbances are some of the marked challenges faced by young people with ASD, their families and caregivers. Approximately 50% to 80% of children and adolescents with ASD suffer from sleep problems⁴ in comparison to 20-30% in neurotypical (NT) children⁴⁻⁷.

The usual sleep-related complaints and symptoms among ASD children are insomnia, bedtime settling issues, sleep anxiety, night waking, poor sleep quality and sleep-disordered breathing^{5,8}. Problems initiating and maintaining sleep are one of the most common concurrent clinical complaints and are less likely to diminish with age compared with NT children^{9,10}.

These sleep difficulties commonly faced by children with ASD can produce a significant decrease in the quality of life of all family members as a consequence of sleep deprivation. As sleep is a behavioral and emotional regulator, sleep fragmentation or deprivation can worsen behavioral disturbances in children with ASD¹¹⁻¹³, possibly triggering disruptive or inflexible behavior and anxiety¹⁴⁻²⁰. Greater variation in sleep duration and timing have been found to predict subsequent disruptive daytime behavior²¹. Parents of children with ASD and sleep problems may, thus, have to deal with 2 consequences: firstly, their child's behavior problems derived from their sleep issues and secondly, the consequences of their own sleep deprivation.

One important question is whether the sleep difficulties of children with ASD also affect their siblings as well as their parents. Understanding the experiences of this population is essential as the relationship that an individual with ASD has with a sibling is typically their longest relationship, and it can have a substantial impact on emotional, behavioral, and psychological outcomes²². However, few studies have examined the sleep of the siblings of children with ASD (ASD-Sib). In this issue of *Sleep Science*, Naeen et al. provided very interesting data on the sleep of the immediate family of individuals with ASD. The authors investigated 64 children with ASD, 80 of their siblings and 80 NT children using a sleep-wake diary, a school sleep habit questionnaire and a childhood autism spectrum test. Surprisingly, the comparison revealed no significant differences between the children with ASD and their siblings, nor between these 2 groups and the control subjects in terms of their sleep profiles.

These results are contrary to those of some previous studies, demonstrating that this is a very complex issue, which probably depends on how siblings deal with the altered family functioning secondary to ASD²³. In 2012, Chou et al. reported that ASD-Sib have a higher risk of early insomnia and parasomnias compared to NT children²⁴. Shivers et al. (2019) published a meta-analysis about the degree to which ASD-Sibs function similarly or differently compared to siblings of NT people and to the siblings of individuals with

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other disabilities. They described that there were specific areas of functioning in which ASD-Sibs fared worse, such as internalizing behavior problems, psychological functioning, beliefs, social functioning, and the sibling relationship²⁵. Recent data from Taylor et al.²⁶ presented a genetic role for sleep issues in ASD siblings. They investigated etiological links between ASD and difficulties initiating and maintaining sleep in 15,279 child and adolescent ASD twin pairs. The authors found that monozygotic co-twins of ASD individuals were most at risk of difficulties initiating and maintaining sleep compared to the reference group, followed by dizygotic co-twins and full siblings. Their results suggest that shared genetic mechanisms could underlie ASD and sleep difficulties. The take home message of the study is that more attention needs to be paid to the care of the siblings of young individuals with ASD. They may not only be directly affected by the family concerns involving their siblings but also indirectly by a shared underlying genetic link.

In this issue of *Sleep Science*, Cebreros-Paniagua et al. investigated sleep microstructure in children with Asperger's Syndrome (AS). According to the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5)²⁷, AS is part of the broad spectrum of neurodevelopmental disorders that comprise ASD. Different levels of severity ranging from childhood autism with language impairment to so-called "high level" autism can be found in ASD. The authors observed a statistically significant decrease in the intrinsic frequency of sleep spindles in different brain regions in the AS group in relation to the NT development group, which may reflect the immaturity in brain regions related to the integration of sleep spindles.

Recently, Gorgoni²⁸ et al. reviewed 18 articles published from 2006 to 2019 in respect of their findings on EEG microstructural sleep patterns and their possible relationship with cognitive functioning in children and adolescents with neurodevelopmental disorders. The authors did not notice a specific microstructural sleep EEG pattern in AS, or any relationship between the pattern they found and diurnal functioning. Some studies have shown a decrease in spindle density in different regions of the ASD brain individuals, according to the age group analysed. ASD adults have exhibited that variation only in the central region^{29,30}, whereas in ASD children, the problem is specifically localized in the right prefrontal area^{6,31}. The change in spindle activity observed in the study by Cebreros-Paniagua et al. could be a consequence of altered thalamo-cortical processes involved in spindle production in ASDs. The regional differences between children and adults could be associated with the atypical brain development that characterizes autism³². The observed central and prefrontal K-complex decrease in children with AS⁶ may represent an index of perturbation of the sleep protective mechanisms that involve K-complexes³³. Alternatively, reduced K-complex density in the central and prefrontal regions may indicate possible neurodegenerative processes^{34,35}. Some other findings³⁶⁻³⁹ suggest that changes in slow wave activity in ASD mirror the atypical cortical maturation detected in

this population³², which was associated with thalamo-cortical alterations³⁷ and a specific pattern in distinct age ranges.

To conclude, studies into the relationship between sleep problems and ASD are still at an early stage. Further research focusing on understanding and modifying the factors which contribute to sleep problems in ASD could make a significant contribution to improving the quality of life of this population. The studies described here published in this issue of *Sleep Science* represent a relevant contribution to help in this effort.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

REFERENCES

- Centers for Disease Control and Prevention (CDC). Autism spectrum disorder: data & statistics. Atlanta: CDC; 2016; available from: <http://www.cdc.gov/ncbddd/autism/data.htm>
- Christensen DL, Baio J, Van Naarden Braun K, Bilder D, Charles J, Constantino JN, et al; Centers for Disease Control and Prevention (CDC). Prevalence of autism spectrum disorder among children aged 8 years—autism and developmental disabilities monitoring network, 11 sites, United States, 2012. *MMWR Surveill Summ.* 2016;65(3):1–23. doi: 10.15585/mmwr.ss6503a1. Erratum in: *MMWR Morb Mortal Wkly Rep.* 2016;65(15):404. Corrected and republished in: *MMWR Morb Mortal Wkly Rep.* 2018;67(45):1279.
- Kogan MD, Vladutiu CJ, Schieve LA, Ghandour RM, Blumberg SJ, Zablotsky B, et al. The prevalence of parent-reported autism spectrum disorder among US children. *Pediatrics.* 2018;142(6):e20174161. doi: 10.1542/peds.2017-4161
- Miano S, Bruni O, Elia M, Trovato A, Smerieri A, Verrillo E, et al. Sleep in children with autistic spectrum disorder: a questionnaire and polysomnographic study. *Sleep Med.* 2007;9(1):64–70. doi: 10.1016/j.sleep.2007.01.014
- Goldman SE, Surdyka K, Cuevas R, Adkins K, Wang L, Malow BA. Defining the sleep phenotype in children with autism. *Dev Neuropsychol.* 2009;34(5):560–73. doi: 10.1080/87565640903133509
- Lambert A, Tessier S, Rochette AC, Scherzer P, Mottron L, Godbout R. Poor sleep affects daytime functioning in typically developing and autistic children not complaining of sleep problems: a questionnaire-based and polysomnographic study. *Res Autism Spectr Disord.* 2016;23:94–106.
- Johnson KP, Zarrinpar P. Autism Spectrum Disorder and Sleep. *Child Adolesc Psychiatric Clin N Am.* 2021;30(1):195–208. doi: 10.1016/j.chc.2020.08.012
- Turner KS, Johnson CR. Behavioral Interventions to Address Sleep Disturbances in Children with Autism Spectrum Disorders: A Review. *TECSE.* 2012;33(3): 144–152. doi:10.1177/0271121412446204
- Ming X, Brimacombe M, Chaaban J, Zimmerman-Bier B, Wagner GC. Autism spectrum disorders: concurrent clinical disorders. *J Child Neurol.* 2008;23(1):6–13. doi: 10.1177/0883073807307102
- Hodge D, Carollo TM, Lewin M, Hoffman CD, Sweeney DP. Sleep patterns in children with and without autism spectrum disorders: developmental comparisons. *Res Dev Disabil.* 2014; 35(7):1631–8. doi: 10.1016/j.ridd.2014.03.037
- Lambert A, Tessier S, Chevrier E, Scherzer P, Mottron L, Godbout R. Sleep in children with high functioning autism: polysomnography, questionnaires and diaries in a non-complaining sample. *Sleep Med.* 2013;14(suppl 1):e137–8. doi:10.1016/j.sleep.2013.11.310
- Kirkpatrick B, Louw JS, Leader G. Efficacy of parent training incorporated in behavioral sleep interventions for children with autism spectrum disorder and/or intellectual disabilities: a systematic review. *Sleep Med.* 2019; 53: 141–152. doi: 10.1016/j.sleep.2018.08.034
- Vriend JL, Corkum PV, Moon EC, Smith IM. Behavioral Interventions for Sleep Problems in Children with Autism Spectrum Disorders: Current Findings and Future Directions. *J Pediatr Psychol.* 2011; 36(9): 1017–29. doi: 10.1093/jpepsy/jsr044

14. Arazi A, Meiri G, Danan D, Michaelovski A, Flusser H, Menashe I, et al. Reduced sleep pressure in young children with autism. *Sleep*. 2020;43(6):zsz309. doi: 10.1093/sleep/zsz309
15. Maquet P. The role of sleep in learning and memory. *Science*. 2001; 294(5544):1048-52. doi: 10.1126/science.1062856
16. Mazurek MO, Sohl K. Sleep and behavioral problems in children with autism spectrum disorder. *J Autism Dev Disord*. 2016; 46(6), 1906-15. doi: 10.1007/s10803-016-2723-7
17. Carmassi C, Palagini L, Caruso D, Masci I, Nobili L, Vita A, et al. Systematic Review of Sleep Disturbances and Circadian Sleep Desynchronization in Autism Spectrum Disorder: Toward an Integrative Model of a Self-Reinforcing Loop. *Front Psychiatry*. 2019;10:366. doi: 10.3389/fpsy.2019.00366
18. Gagnon K, Godbout R. Melatonin and Comorbidities in Children with Autism Spectrum Disorder. *Curr Dev Disord Rep*. 2018;5(3):197-206. doi: 10.1007/s40474-018-0147-0
19. Keogh S, Bridle C, Siriwardena NA, Nadkarni A, Laparidou D, Durrant SJ, et al. Effectiveness of non-pharmacological interventions for insomnia in children with Autism Spectrum Disorder: A systematic review and meta-analysis. *PLoS One*. 2019;14(8):e0221428. doi: 10.1371/journal.pone.0221428
20. Malow BA, Adkins KW, Reynolds A, Weiss SK, Loh A, Fawkes D, et al. Parent-based sleep education for children with autism spectrum disorders. *J Autism Dev Disord*. 2014; 44(1):216-28. doi: 10.1007/s10803-013-1866-z
21. Cohen S, Fulcher BD, Rajaratnam SMW, Conduit R, Sullivan JP, St Hilaire MA, et al. Sleep patterns predictive of daytime challenging behavior in individuals with low-functioning autism. *Autism Res*. 2018;11(2):391-403. doi: 10.1002/aur.1899
22. Cicirelli, VG. Sibling relationships across the life span. 1995. New York: Plenum Press.
23. Meadan H, Stoner JB, Angell ME. Review of literature related to the social, emotional, and behavioral adjustment of siblings of individuals with Autism Spectrum Disorder. *J Dev Phys Disabil*. 2010;22(1), 83-100. doi:10.1007/s10882-009-9171-7
24. Chou MC, Chou WJ, Chiang HL, Wu YY, Lee JC, Wong CC, et al. Sleep problems among Taiwanese children with autism, their siblings and typically developing children. *Res Autism Spectr Disord*. 2012;6(2):665-72. doi:10.1016/j.rasd.2011.09.010
25. Shivers CM, Jackson JB, McGregor CM. Functioning among typically developing siblings of individuals with autism spectrum disorder: a meta-analysis. *Clin Child Fam Psychol Rev*. 2019;22(2):172-96. doi:10.1007/s10567-018-0269-2. PMID: 30178117.
26. Taylor MJ, Larsson H, Lundström S, Lichtenstein P, Butwicka A. Etiological links between autism and difficulties in initiating and maintaining sleep: a familial co-aggregation and twin study. *J Child Psychol Psychiatry*. 2021. Jul 1. doi: 10.1111/jcpp.13473. Epub ahead of print.
27. Battle DE. Diagnostic and Statistical Manual of Mental Disorders (DSM). *Codas*. 2013;25(2):191-2. doi: 10.1590/s2317-17822013000200017
28. Gorgoni M, Scarpelli S, Reda F, Gennaro LD. Sleep EEG oscillations in neurodevelopmental disorders without intellectual disabilities. *Sleep Med Rev*. 2020;49:101224. doi: 10.1016/j.smrv.2019.101224
29. Limoges E, Mottron L, Bolduc C, Berthiaume C, Godbout R. Atypical sleep architecture and the autism phenotype. *Brain*. 2005;128(Pt 5):1049-61. doi: 10.1093/brain/awh425.
30. Godbout R, Bergeron C, Limoges E, Stip E, Mottron L. A laboratory study of sleep in Asperger's syndrome. *Neuroreport*. 2000;11(1):127-30. doi: 10.1097/00001756-200001170-00025
31. Tessier S, Lambert A, Chicoine M, Scherzer P, Soulieres I, Godbout R. Intelligence measures and stage 2 sleep in typically-developing and autistic children. *Int J Psychophysiol*. 2015;97(1):58-65. doi: 10.1016/j.ijpsycho.2015.05.003
32. Courchesne E, Campbell K, Solso S. Brain growth across the lifespan in autism: age-specific changes in anatomical pathology. *Brain Res*. 2011;1380: 138-45. doi: 10.1016/j.brainres.2010.09.101
33. Parrino L, Vaudano AE. The resilient brain and the guardians of sleep: new perspectives on old assumptions. *Sleep Med Rev* 2018;39:98-107. doi: 10.1016/j.smrv.2017.08.003
34. De Gennaro L, Gorgoni M, Reda F, Lauri G, Truglia I, Cordone S, et al. The fall of K-complex in Alzheimer disease. *Sci Rep*. 2017;7:39688. doi: 10.1038/srep39688
35. Reda F, Gorgoni M, Lauri G, Truglia I, Cordone S, Scarpelli S, et al. In search of sleep biomarkers of Alzheimer's disease: K-complexes do not discriminate between patients with Mild Cognitive Impairment and healthy controls. *Brain Sci* 2017;7(5):51. doi: 10.3390/brainsci7050051
36. Gorgoni M, D'Atri A, Scarpelli S, Reda F, De Gennaro L. Sleep electroencephalography and brain maturation: developmental trajectories and the relation with cognitive functioning. *Sleep Med*. 2020;66:33-50. doi: 10.1016/j.sleep.2019.06.025
37. Lehoux T, Carrier J, Godbout R. NREM sleep EEG slow waves in autistic and typically developing children: morphological characteristics and scalp distribution. *J Sleep Res*. 2019;28(4):e12775. doi: 10.1111/jsr.12775
38. Rochette A-C, Soulieres I, Berthiaume C, Godbout R. NREM sleep EEG activity and procedural memory: a comparison between young neurotypical and autistic adults without sleep complaints. *Autism Res*. 2018;11(4):613-23. doi: 10.1002/aur.1933
39. Lázár AS, Lázár ZI, Bíró A, Gyóri M, Tárnok Z, Prekip C, et al. Reduced fronto-cortical brain connectivity during NREM sleep in Asperger syndrome: an EEG spectral and phase coherence study. *Clin Neurophysiol*. 2010;121(11): 1844-54. doi: 10.1016/j.clinph.2010.03.054