



## Journal Review

# What's new in paediatric sleep medicine?

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**Source:** Sharma M, Aggarwal S, Madaan P, Saini L, Bhutani M. Impact of COVID-19 pandemic on sleep in children and adolescents: A systematic review and meta-analysis. *Sleep Med.* 2021 Aug;84:259-267. doi: 10.1016/j.sleep.2021.06.002. Epub 2021 Jun 11. PMID: 34182354.

The authors conduct a systematic review and meta-analysis to study the prevalence and pattern of sleep disturbances in children and adolescents with or without pre-existing neurobehavioral disorders during the COVID-19 pandemic. Among the studies reviewed, five studies were in preschool children, two were in children with pre-existing neurobehavioral disorders, and the remaining were in school going children and adolescents. The outcome measures used for sleep were markedly heterogeneous across the studies. The prevalence of sleep problems in children and adolescents during the COVID-19 pandemic is alarming. Preschool children had a trend toward relatively fewer sleep disturbances due to home confinement measures in comparison with pre-pandemic times. Sleep duration recommendations were not met in nearly half of healthy children. However, these conclusions need to be seen in light of limited literature on the topic, few included studies done in heterogeneous populations, and dubious quality of inferences drawn from these studies which were predominantly online surveys.

**Source:** Petruzzelli MG, Matera E, Giambersio D, Marzulli L, Gabellone A, Legrottaglie AR, Margari A, Margari L. Subjective and electroencephalographic sleep parameters in children and adolescents with autism spectrum disorder: A systematic review. *J Clin Med.* 2021 Aug 30;10(17):3893. doi: 10.3390/jcm10173893. PMID: 34501341; PMCID: PMC8432113.

Sleep problems have commonly manifested in children and adolescents with autism spectrum disorder (ASD) with a complex and multifactorial interaction between clinical and etiological components. These disorders are associated with functional impairment and provoke significant physical and mental affliction. Data collected from 20 survey result reports showed that children and adolescents with ASD experienced a higher rate of sleep abnormalities than in typically developing children. The macrostructural sleep parameters that were consistent with subjective parent reported measures unveil a greater percentage of nighttime signs of insomnia. Sleep microstructure patterns, in addition, pointed toward the bidirectional relationship between brain dysfunctions and sleep problems in children with ASD. It would be worthwhile in future studies to examine how factors, such as age, cognitive level, or ASD severity, could be related to ASD sleep abnormalities. Future research should directly assess whether sleep alterations could represent a specific marker for atypical brain development in ASD.

**Source:** Alibabaei Z, Jazayeri S, Vafa M, Feizy Z, Sajadi Hezaveh Z. The association between dietary patterns and quality and duration of sleep in children and adolescents: A systematic review. *Clin Nutr ESPEN.* 2021 Oct;45:102-110. doi: 10.1016/j.clnesp.2021.07.012. Epub 2021 Jul 28. PMID: 34620305.

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Dietary pattern has been represented as a contributor to the duration and quality of sleep. This study aimed to review the evidence on this relation among children and adolescents. Fourteen publications (12 cross sectional, one cohort, and one clinical trial) were identified. Findings from most studies suggested that long sleep duration was consistently associated with healthy dietary patterns, such as “Vegetables and Healthy Proteins,” “Traditional,” and “Fruit and Vegetables.” Results were more mixed and inconclusive regarding the quality of sleep, with two studies supporting, two studies disapproving, and one study neutral about the association between better sleep quality and healthier dietary patterns. The association between diet and sleep seemed to be affected by confounders and covariates, including sex, physical activity, and screen time. Longer sleep duration appears to be associated with healthier dietary pattern. However, various results in regard to the relation between dietary patterns and sleep quality preclude definitive conclusions.

**Source:** Fangupo LJ, Haszard JJ, Reynolds AN, Lucas AW, McIntosh DR, Richards R, Camp J, Galland BC, Smith C, Taylor RW. Do sleep interventions change sleep duration in children aged 0–5 years? A systematic review and meta-analysis of randomized controlled trials. *Sleep Med Rev*. 2021 Oct;59:101498. doi: 10.1016/j.smrv.2021.101498. Epub 2021 Apr 30. PMID: 34029803.

This review investigated whether randomized controlled trials attempting to improve sleep or prevent sleep problems in 0–5 year olds influenced nocturnal sleep duration, daytime naps, or 24 h sleep. Overall, sleep interventions increased nocturnal sleep duration by a mean of 9 min per night when compared with no sleep intervention. Increases were predominantly seen in sleep only, rather than multicomponent interventions. Total 24 h sleep duration tended to increase by a similar amount (8.6 min [95% CI -2.7–19.8,  $I^2 = 59\%$ ]), but this was mainly only seen in studies that assessed sleep using diaries. There was no evidence that interventions changed daytime sleep duration. Future studies should involve sleep only rather than multicomponent interventions and use objective sleep measures.

**Source:** Perpétuo C, Diniz E, Veríssimo M. A systematic review on attachment and sleep at preschool age. *Children (Basel)*. 2021 Oct 7;8(10):895. doi: 10.3390/children8100895. PMID: 34682160; PMCID: PMC8534890.

Sleep is a biological process that impacts nearly every domain of a child’s life. Sleep-wake regulation influences and it is highly influenced by developmental variables related to parent-child relationships, such as attachment. The main goal of this systematic review was to analyse and integrate the findings of empirical studies investigating the relations between attachment and sleep in preschool age, a period marked by important developmental changes that challenge both attachment system and sleep-wake regulation.

Overall, the findings were not consistent, with some studies reporting significant associations between attachment security and sleep quality, as well as between attachment insecurity and sleep problems, whereas others did not find significant associations. The results are discussed in light of the available theoretical models and integrated in the context of measurement approaches to attachment and sleep heterogeneity, aiming to guide future research on the topic.

**Source:** Kirkham EM, Leis AM, Chervin RD. Weight gain in children after adenotonsillectomy: Undesirable weight gain or catch-up growth? *Sleep Med*. 2021 Sep;85:147-149. doi: 10.1016/j.sleep.2021.07.010. Epub 2021 Jul 14. PMID: 34329898.

Obesity and obstructive sleep apnea (OSA) are consequential conditions with significant overlap in the paediatric population. Early studies documented catch-up growth in underweight children after adenotonsillectomy, but more recent studies have suggested that normal and even overweight children may experience excess weight gain after adenotonsillectomy. The authors perform a secondary analysis of Childhood Adenotonsillectomy Trial data to test whether there was an effect of early adenotonsillectomy on undesirable weight gain, defined as an increase in body mass index (BMI) Z score in an already overweight or obese child or a change from baseline normal or underweight to a follow-up BMI Z score classified as overweight. Forty-three percent experienced undesirable weight gain. A similar percentage of children in both arms experienced undesirable weight. Neither unadjusted nor adjusted regression analysis demonstrated a significant effect of adenotonsillectomy on undesirable weight gain. They conclude that adenotonsillectomy may not be an independent risk factor for undesirable weight gain in children.

**Source:** Bassetti CLA, Kallweit U, Vignatelli L, Plazzi G, Lecendreux M, Baldin E, Dolenc-Groselj L, Jennum P, Khatami R, Manconi M, Mayer G, Partinen M, Pollmächer T, Reading P, Santamaria J, Sonka K, Dauvilliers Y, Lammers GJ. European guideline and expert statements on the management of narcolepsy in adults and children. *Eur J Neurol*. 2021 Sep;28(9):2815-2830. doi: 10.1111/ene.14888. Epub 2021 Jun 25. PMID: 34173695.

Narcolepsy is an uncommon hypothalamic disorder of presumed autoimmune origin that usually requires lifelong treatment. This paper aims to provide evidence-based guidelines for the management of narcolepsy in both adults and children. The European Academy of Neurology (EAN), European Sleep Research Society, and European Narcolepsy Network (EU-NN) nominated a task force of 18 narcolepsy specialists. According to the EAN recommendations, 10 relevant clinical questions were formulated in PICO format. Following a systematic review of the literature (performed in Fall 2018 and updated in July 2020), recommendations were

developed according to the GRADE approach. A total of 10,247 references were evaluated, 308 studies were assessed, and 155 finally included. The main recommendations can be summarized as follows: (i) Excessive daytime sleepiness in adults – scheduled naps, modafinil, pitolisant, sodium oxybate (SXB), solriamfetol (all strong), methylphenidate, and amphetamine derivatives (both weak); (ii) cataplexy in adults – SXB, venlafaxine, clomipramine (all strong), and pitolisant (weak); (iii) excessive daytime sleepiness in children – scheduled naps, SXB (both strong), modafinil, methylphenidate, pitolisant, and amphetamine derivatives (all weak); and (iv) cataplexy in children – SXB (strong) and antidepressants (weak). Treatment choices should be tailored to each patient's symptoms, comorbidities, tolerance, and risk of potential drug interactions. The management of narcolepsy involves non-pharmacological and pharmacological approaches with an increasing number of symptomatic treatment options for adults and children that have been studied in some detail.

**Source:** Myette RL, Feber J, Blinder H, Bendiak GN, Foster BJ, MacLean JE, Constantin E, Katz SL. Blood pressure variability in children with obesity and sleep-disordered breathing following positive airway pressure treatment. *Paediatr Res*. 2021 Nov 16. doi: 10.1038/s41390-021-01841-8. Epub ahead of print. PMID: 34785780.

Obese youth with sleep-disordered breathing is treated with positive airway pressure to improve sleep and cardiovascular status. While improvements in sleep parameters have been confirmed, a study by Katz *et al.* showed no major improvement in ambulatory blood pressure. The aim of this ancillary study was to analyse short-term blood pressure variability, following positive airway pressure treatment, as a more sensitive marker of cardiovascular health. The authors analysed 24 h blood pressure variability data in 17 children, taken at baseline and after 12 months of treatment. These data were derived from an already published prospective, multicentre cohort study conducted in 27 youth (8–16 years) with obesity who were prescribed 1 year of positive airway pressure for moderate-severe sleep-disordered breathing. Significant decreases were found in 24 h systolic blood pressure ( $P = 0.040$ ) and nighttime diastolic blood pressure ( $p = 0.041$ ) average real variability, and diastolic blood pressure ( $P = 0.035$ ) weighted standard deviation. Significant decreases were noted in nighttime diastolic blood pressure time rate variability ( $P = 0.007$ ). Positive airway pressure treatment resulted in a significant decrease in blood pressure variability, suggesting a clinically significant improvement of sympathetic nerve activity in youth with obesity and sleep-disordered breathing. Cardiovascular variability, as measured by blood pressure variability, is improved in children following positive airway pressure treatment. Future studies aimed at analysing target organ damage in this

patient population will allow for a better understanding as to whether alterations in blood pressure variability translate to decreasing target organ damage in children, as seen in adults.

**Source:** Manousaki D, Barnett TA, Mathieu ME, Maximova K, Simoneau G, Harnois-Leblanc S, Benedetti A, McGrath JJ, Henderson M; QUALITY Cohort Collaborative Group. Tune out and turn in: The influence of television viewing and sleep on lipid profiles in children. *Int J Obes (Lond)*. 2020 May;44(5):1173-1184. doi: 10.1038/s41366-020-0527-5. Epub 2020 Mar 13. PMID: 32203106.

Physical activity is beneficial to lipid profiles; however, the association between sedentary behaviour and sleep and paediatric dyslipidaemia remains unclear. The study aims to investigate whether sedentary behaviour or sleep predicted the lipid profiles in children over a 2-year period. Six hundred and thirty children from the QUALITY cohort, with at least one obese parent, were assessed prospectively at ages 8–10 and 10–12 years. Measures of sedentary behaviour included self-reported TV viewing and computer/video game use. Adiposity was assessed using DEXA scans. Twenty-four hour dietary recalls yielded estimates of carbohydrate and fat intake. Outcomes included fasting total cholesterol, triglycerides, HDL, and LDL cholesterol. Multivariable models were adjusted for adiposity and diet. At both Visit 1 (median age 9.6 years) and Visit 2 (median age 11.6 years), children were of normal weight (55%), overweight (22%), or obese (22%). Every additional hour of TV viewing at Visit 1 was associated with a 7.0% triglyceride increase and 2.6% HDL decrease at Visit 2; findings remained significant after adjusting for adiposity and diet. Every additional hour of sleep at Visit 1 predicted a 4.8% LDL decrease at Visit 2, after adjusting for fat intake; this association became non-significant once controlling for adiposity. So possibly, longer screen time during childhood appears to deteriorate lipid profiles in early adolescence, even after accounting for other major lifestyle habits. There is preliminary evidence of a deleterious effect of shorter sleep duration, which should be considered in further studies.

**Source:** Barceló A, Morell-Garcia D, Ribot C, De la Peña M, Peña-Zarza JA, Alonso-Fernández A, Giménez P, Piérola J. Vitamin D as a biomarker of health in snoring children: A familial aggregation study. *Pediatr Res*. 2021 Jun 8. doi: 10.1038/s41390-021-01612-5. Epub ahead of print. PMID: 34103676.

Hypovitaminosis D is a common health problem. The purpose of this study was to investigate the inter-relationship between serum 25-hydroxyvitamin D (25(OH)D) levels and paternal and maternal Vitamin D status in a sample of snoring children. The authors selected 137 participants for whom serum 25(OH)D had been measured and underwent overnight polysomnography evaluation. Serum glucose, lipids, liver enzymes, parathyroid hormone, insulin, and

glycated haemoglobin were also measured. Glucose and insulin levels were used to estimate insulin resistance with the homeostasis model assessment (HOMA-IR). Vitamin D insufficiency (<30 ng/mL) and deficiency (<20 ng/mL) were found in 40.9 and 17.5% of children, respectively. After adjustments for age, BMI Z-score, and seasonality, the odds ratio for risk of Vitamin D insufficiency according to the Vitamin D status of parents was as follows: OR (95% CI): Paternal insufficiency 15.1 (2.7–35.7),  $P = 0.002$ ; maternal insufficiency 7.2 (2.4–22),  $P = 0.001$ . When children with Vitamin D deficiency were analysed separately, serum 25(OH)D concentration was found to be associated with the apnea-hypopnea index ( $r = -0.647$ ,  $P = 0.009$ ) and respiratory arousal index ( $r = -0.669$ ,  $P = 0.034$ ). Family patterns of Vitamin D could be helpful for the early identification of snoring children at risk of metabolic and/or sleep disturbances. Significant associations were found between serum 25(OH)D concentrations in children and their parents. An inverse association between 25(OH)D levels and OSA severity was detected in deficient Vitamin D children. Children with insufficient and deficient Vitamin D status tended to have a worse metabolic profile, so strategies are needed to improve Vitamin D status.

**Source:** Ando A, Ohta H, Yoshimura Y, Nakagawa M, Asaka Y, Nakazawa T, Mitani Y, Oishi Y, Mizushima M, Adachi H, Kaneshi Y, Morioka K, Shimabukuro R, Hirata M, Ikeda T, Fukutomi R, Kobayashi K, Ozawa M, Takeshima M, Manabe A, Takahashi T, Mishima K, Kusakawa I, Yoda H, Kikuchi M, Cho K. Sleep maturation influences cognitive development of preterm toddlers. *Sci Rep.* 2021 Aug 5;11(1):15921. doi: 10.1038/s41598-021-95495-5. PMID: 34354199; PMCID: PMC8342419.

A recent study on full-term toddlers demonstrated that daytime nap properties affect the distribution ratio between nap and

nighttime sleep duration in total sleep time but does not affect the overall total amount of daily sleep time. However, there is still no clear scientific consensus as to whether the ratio between naps and nighttime sleep or just daily total sleep duration itself is more important for healthy child development. In the current study, to gain an answer to this question, the authors examined the relationship between the sleep properties and the cognitive development of toddlers born prematurely using actigraphy and the Kyoto scale of psychological development test. A total of 101 premature toddlers of approximately 1.5 years of age were recruited for the study. Actigraphy units were attached to their waist with an adjustable elastic belt for 7 consecutive days and a child sleep diary was completed by their parents. The study showed “no” significant correlation between either nap or nighttime sleep duration and cognitive development of the preterm toddlers. In contrast, it was found that stable daily wake time was significantly associated with better cognitive development, suggesting that sleep regulation may contribute to the brain maturation of preterm toddlers.

#### Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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