

## How Many Children with ADHD Have Sleep Apnea or Periodic Leg Movements on Polysomnography?

Comment on Sangal RB; Owens J; Sangal J. Patients With Attention-Deficit/Hyperactivity Disorder Without Observed Apneic Episodes in Sleep or Daytime Sleepiness Have Normal Sleep on Polysomnography. *SLEEP* 2005; 28(9):1143-1148

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IN THIS ISSUE OF *SLEEP*, SANGAL, OWENS AND SANGAL REPORT FINDING NO SIGNIFICANT OBSTRUCTIVE SLEEP APNEA OR PERIODIC LEG MOVEMENTS among 40 children studied with polysomnography prior to a trial of atomoxetine vs. methylphenidate for Attention-Deficit/Hyperactivity Disorder (ADHD).<sup>1</sup> Exclusion criteria included reports of restless legs at bedtime, snoring with observed apneas, or snoring with excessive daytime sleepiness. However, only 1 subject was excluded prior to polysomnography for meeting any one of these criteria (snoring with sleepiness), and the authors therefore conclude that obstructive sleep apnea and periodic leg movement disorder are not common findings or etiological factors in ADHD patients.

An important strength of this study that distinguishes it from many previous reports is that children were assessed prospectively to identify DSM-IV-defined ADHD. The authors further corroborated the DSM-IV-based diagnosis with 2 validated assessment instruments. As the authors note, prior sleep research using milder criteria for hyperactivity has generated results applicable to many children, but perhaps not those who meet full DSM-IV criteria for ADHD. Existing literature often addresses neurobehavioral morbidity of sleep disorders in children as a monolithic entity assumed to have uniform etiologies and responsiveness to treatment, whereas future research may well prove otherwise.

The inability of Sangal and colleagues to identify more evidence of sleep apnea or periodic leg movements on polysomnography does seem at first to be surprising in light of previous studies that suggest close links between hyperactive behavior and both types of sleep pathology. The authors point out that these discrepancies could result from differences in how hyperactivity was defined, or from confounds and other limitations in selected previous studies that the authors reviewed. However, other reasons for the discrepant results may also exist.

For example, the new study defines obstructive sleep apnea by an apnea/hypopnea index (AHI) > 5 per hour of sleep. The authors defend this choice at some length, but the International Classification of Sleep Disorders, 2<sup>nd</sup> Edition (published after the current report was written) requires only an AHI > 1 to diagnose

pediatric obstructive sleep apnea.<sup>2</sup> The authors' arguments in favor of a higher AHI are not unreasonable, especially in a study that monitored airflow by nasal pressure rather than thermistors, but the point is that experts can – and often do – disagree on what level of polysomnographic abnormality defines treatable sleep apnea in children. Furthermore, a literature spanning more than 20 years shows that clinically-significant hyperactivity can appear in children who have essentially no apneas or hypopneas but do have the excessively-negative esophageal pressures of upper airway resistance syndrome,<sup>3</sup> or other signs of subtle SDB such as nocturnal tachypnea.<sup>4</sup> If the new study had still excluded more subtle signs but had at least used ICSD-2 definitions, the title of the manuscript might have been quite different, perhaps “Most children with ADHD have obstructive sleep apnea on polysomnography.” Among the 40 subjects, 57.5% had an AHI > 1.

Discrepancies between the current findings and those previously published could also arise from the choice of polysomnographic definitions for significant periodic leg movements during sleep. The paper does not specify how periodic leg movements were defined. Moreover, use of a periodic leg movement arousal index, rather than the simpler periodic leg movement index, is explained as consistent with a 1995 American Academy of Sleep Medicine practice parameter on insomnia in adults. However, the ICSD-2 adopts the more common periodic leg movement index in its criteria for both pediatric periodic limb movement disorder and restless legs syndrome.<sup>2</sup> Literature on periodic leg movements suggests that they may not cause associated arousals,<sup>5,6</sup> which in turn may not exacerbate the clinical significance of the leg movements: in adults, at least, periodic leg movements with arousals predict slightly less sleepiness, not more, on next-day Multiple Sleep Latency Tests.<sup>7</sup> In short, the polysomnographic measure of leg movements used in the new study does not facilitate comparison with most previous reports on this phenomenon, periodic limb movement disorder, or restless legs syndrome.

Two other methodological issues merit consideration. The parent drug study sought participants without primary sleep disorders, but the report does not discuss how recruitment was carried out, or specify how many families approached about the study declined to participate in any part of it. The reader cannot judge how many ADHD children never met the investigators specifically because a clinician or family member had already diagnosed or suspected a primary sleep disorder. In addition to the possibility of selection bias, the lack of control subjects also makes interpretation of the results more difficult. The authors note that one previous controlled investigation found SDB in 50% of 34

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ADHD children,<sup>8</sup> but question the choice of an AHI > 1 as the cut-off to define SDB because 22% of the control subjects also met this criterion. However, another study, published just after the current report was accepted for publication, prospectively confirmed DSM-IV-defined ADHD in 88 children aged 6 – 12 and found an AHI > 1 in 50 (57%), whereas among 27 controls only 1 subject (4%) reached the same threshold.<sup>9</sup> Among the ADHD children, 17 (19%) had an AHI > 5. In addition, 9 ADHD children but no controls had more than 5 periodic leg movements per hour of sleep. The authors conclude, in contrast to Sangal et al, that “ADHD based on DSM-IV [does] not differentiate between children with or without sleep disorders.”<sup>9</sup>

Taken together, these 3 selected studies<sup>1,8,9</sup> from a growing relevant literature may be telling us something quite important. Although their conclusions differ on the extent to which SDB-linked hyperactivity resembles DSM-IV-defined ADHD, they all suggest that mild SDB -- even in the range reflected by an AHI between 1 and 5, and sometimes less -- rather than more severe SDB may be particularly common in children with ADHD compared to controls. In part, this may be because milder SDB is likely to be much more common than more severe SDB. Another speculative explanation is that more severe SDB could cause enough daytime sleepiness or other health problems to mask hyperactivity in some cases. Perhaps intermittent hypoxemia, associated with more severe SDB but neither mild SDB nor unrelated sleep disorders, can change the observed behavioral phenotype. A link between mild SDB and hyperactivity might explain why polysomnographic measures of SDB severity do not correlate with the severity of the behavior, in the current study or in previous reports,<sup>9-14</sup> whereas reported snoring repeatedly demonstrates associations with hyperactive behavior and ADHD.<sup>11,15-17</sup>

Few clinicians doubt the merit of treatment for severe pediatric SDB or restless legs syndrome with periodic leg movements, but less consensus exists in numerous milder cases about what findings suggest risks to health, behavior, or quality of life. Additional controlled studies are clearly needed to examine polysomnographic methods and develop new ones that best predict outcomes and response to treatment. Long-term longitudinal studies also are critical in developing children, whose behavioral morbidity from current sleep problems may not appear until years later.<sup>18</sup> In the meantime, clinicians (and insurers) are probably well-advised to maintain skepticism about any simple, strict cut-offs. Precise polysomnographic criteria may be a necessity in research, but their subsequent application to an individual patient in a clinical setting may do more harm than good. The distributions of the AHI and the periodic leg movement index in the population are unlikely to form bi-modal curves. Good clinical sense must be used to combine many different clues beyond these indices to arrive at a diagnosis and recommendation that may have years of positive impact for a child and his or her family.

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## REFERENCES

1. Sangal RB, Owens J, Sangal J. Patients with attention-deficit/hyperactivity disorder without observed apneic episodes in sleep or daytime sleepiness have normal sleep on polysomnography. *Sleep*. 2005;28:1143-1148.

2. Hauri PJ, Sateia MJ, eds. *International Classification of Sleep Disorders*. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
3. Guilleminault C, Winkle R, Korobkin R, Simmons B. Children and nocturnal snoring-- evaluation of the effects of sleep related respiratory resistive load and daytime functioning. *Eur J Pediatr*. 1982;139:165-71.
4. Guilleminault C, Li K, Khramtsov A, Palombini L, Pelayo R. Breathing patterns in prepubertal children with sleep-related breathing disorders. *Arch Pediatr Adolesc Med*. 2004;158:153-61.
5. Karadeniz D, Ondze B, Besset A, Billiard M. EEG arousals and awakenings in relation with periodic leg movements during sleep. *J Sleep Res*. 2000;9:273-7.
6. El-Ad B, Chervin RD. The case of a missing PLM. *Sleep*. 2000;23:450-1.
7. Chervin RD. Periodic leg movements and sleepiness in patients evaluated for sleep-disordered breathing. *Am J Resp Crit Care Med*. 2001;164:1454-8.
8. Golan N, Shahar E, Ravid S, Pillar G. Sleep disorders and daytime sleepiness in children with attention-deficit/hyperactive disorder. *Sleep*. 2004;27:261-6.
9. Huang YS, Chen NH, Li HY, Wu YY, Chao CC, Guilleminault C. Sleep disorders in Taiwanese children with attention deficit/hyperactivity disorder. *J Sleep Res*. 2005;13:269-77.
10. Chervin RD, Archbold KH. Hyperactivity and polysomnographic findings in children evaluated for sleep-disordered breathing. *Sleep*. 2001;24:313-20.
11. O'Brien LM, Holbrook CR, Mervis CB et al. Sleep and neurobehavioral characteristics of 5- to 7-year-old children with parentally reported symptoms of attention-deficit/hyperactivity disorder. *Pediatrics*. 2003;111:554-63.
12. Melendres CS, Lutz JM, Rubin ED, Marcus CL. Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. *Pediatrics*. 2004;114:768-75.
13. Mulvaney SA, Goodwin JL, Morgan WJ, Rosen GM, Quan SF, Kaemingk KL. Behavior problems associated with sleep disordered breathing in school-aged children -- the Tucson Children's Assessment of Sleep Apnea Study. *J Pediatr Psychol*. 2005;doi:10.1093/jpepsy/jsj035:1-9.
14. Beebe DW, Wells CT, Jeffries J, Chini B, Kalra M, Amin R. Neuropsychological effects of pediatric obstructive sleep apnea. *Journal of the International Neuropsychological Society*. 2004;10:962-75.
15. Chervin RD, Dillon JE, Bassetti C, Ganoczy DA, Pituch KJ. Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep*. 1997;20:1185-92.
16. Chervin RD, Archbold KH, Dillon JE et al. Inattention, hyperactivity, and symptoms of sleep-disordered breathing. *Pediatrics*. 2002;109:449-56.
17. Gottlieb DJ, Vezina RM, Chase C et al. Symptoms of sleep-disordered breathing in 5-year-old children are associated with sleepiness and problem behaviors. *Pediatrics*. 2003;112:870-7.
18. Chervin RD, Ruzicka DL, Archbold KH, Dillon JE. Snoring predicts hyperactivity four years later. *Sleep*. 2005;28:885-90.