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Sleep Medicine 4 (2003) 271–272

**SLEEP  
MEDICINE**

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Editorial

## Sleep problems, stimulants, and ADHD: true, true, unrelated?

The swirling relationship between sleep problems, stimulants, and attention deficit hyperactivity disorder (ADHD) is not a trivial clinical issue. Sleep disturbance was once a diagnostic criterion for ADHD [1]. The impact of disturbed daytime functioning based on nocturnal symptoms is central to the relevance of sleep medicine in pediatrics. ADHD is the most common neuropsychiatric diagnosis in children, and stimulants have represented the medication group of choice in children with ADHD for many years. For a long time, insomnia has been a frequently reported side effect associated with stimulant therapy [2]; yet, most research claiming such relationships between sleep problems, ADHD, and stimulants are based on parent-report data. Parent surveys have reported, for instance, that a majority of children with ADHD have greater sleep difficulty than normally developing children [3]. Stimulants have been interpreted as a serious confounder of sleep problems in children with ADHD. Based on a parent questionnaire, Stein [4] reported frequent nighttime waking in 25% of children with ADHD on stimulant medication compared with 9% of non-medicated ADHD children.

In order to reduce rater bias, more objective measures, ranging from sleep logs to actigraphy to polysomnography (PSG), have been initiated. A study of 30 boys with untreated ADHD utilized multiple sleep latency tests (MSLTs) and computerized reaction time tests following PSG and found significant differences in sleep latencies and reaction times compared with controls, implicating a deficit in alertness in the ADHD children [5]. Others have suggested underlying restless legs syndrome (RLS) with periodic limb movement disorder [6], and sleep-disordered breathing including snoring and sleep apnea [7,8] as important co-morbidities associated with ADHD.

In the current issue of *Sleep Medicine*, O'Brien et al. [9] report on their systematic evaluation of sleep characteristics in children with ADHD, with analysis of questionnaire results and overnight PSG stratified for ADHD children on stimulant medication, non-medicated ADHD children, and controls. Furthermore, they extract their results from both a referred sleep clinic population and a community group. Eighty-seven ADHD children are studied: 53 stimulant-medicated, 34 non-medicated, and 53 controls. On subjective measures, the ADHD subjects had more nightmares and enuresis than controls, and the medicated ADHD

patients had more restless sleep than controls. Objectively, there was a decrease in the amount of rapid eye movement (REM) sleep in ADHD, although to a questionable clinically significant degree ( $24.1 \pm 6.5\%$  in controls versus  $20.3 \pm 6.5\%$  in medicated and  $20.5 \pm 8.1\%$  in non-medicated subjects). There was no difference in subjective sleep or objective measures with the use of stimulant medication in ADHD children compared with non-medicated ADHD children. While periodic leg movements (PLM) were present in over 10% of each studied group, there was no difference in the PLM index between ADHD medicated, ADHD non-medicated, and control subjects.

Are the results valid? The demographics for the ADHD medicated, ADHD non-medicated, and control groups were similar, except for increased male predominance in the ADHD medicated group. No clear differences were present in either the demographics or PSG values between the clinic medicated and non-medicated groups, or between the community medicated and non-medicated groups. The community group did have more spontaneous arousals than the clinic population, but this was true for both the stimulant treated and non-medicated ADHD children. A more pressing problem in the current study is the lack of a formal diagnostic assessment for each investigated subject. Patients were classified as ADHD if a parent responded affirmatively on a sleep laboratory questionnaire, 'Does your child have ADHD?' Parents were asked to list any medications for ADHD/hyperactivity that their child was taking at that time. Only the Conners Parent Rating Scale was used to corroborate a reported diagnosis of ADHD in the community population. These strategies seem far from adequate in properly identifying children who may fulfill DSM-IV diagnostic criteria for ADHD. In addition, patients are identified from retrospective chart review; subsequently, the pre-entry data is minimal. We do not know if non-medicated ADHD children were previously medicated, and even withdrawn from stimulants because of perceived sleep problems. This could have inadvertently led to a higher risk population of non-medicated ADHD children for sleep disturbances, thus offsetting any potential difference in sleep disruptions in stimulant-treated versus non-treated subjects in this study. Further, there is no indication that PSG interpretation was done by blinded evaluators. These factors introduce potential for bias in patient selection and PSG results.

Notwithstanding these reservations, this observational cohort study provides intriguing preliminary documentation of an insignificant role of stimulants in producing sleep disturbances in children with ADHD. O'Brien et al. should be lauded for their systematic methodology and incorporation of clinic and community samples with medicated, non-medicated, and control groups. Neurologic or psychiatric control groups would be helpful to ascertain whether any influence of ADHD or stimulants on sleep are endemic to ADHD per se or the presence of a neurologic or psychiatric disorder. Prospective randomized double-blind, placebo-controlled, clinical trials are sorely missing in this area. Studies of stimulant medication effects on sleep of control children are needed, but pose very real logistical difficulties. Differential effects of different stimulants, long versus short acting preparations, or repeat daily dosing on sleep remain unanswered. The stakes for these issues were raised with reports of sudden death on the combination of methylphenidate and clonidine [10], which may have represented exaggerated claims [11], yet had an impact on clinicians reaching for sedating products in ADHD children having terrible sleep problems and daytime dysfunction. Now that a non-stimulant medication, atomoxetine, [12] has been approved by the Food and Drug Administration for the treatment of ADHD, it is even more pressing to ascertain whether stimulants, other medications for ADHD, or neuropsychiatric disorders themselves have a significant impact on children's sleep characteristics.

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Received 19 March 2003; Accepted 26 March 2003

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