How Can We Better Leverage the Nocturnal Polysomnogram in the Diagnosis of Childhood-Onset Narcolepsy?

Commentary on Reiter et al. Usefulness of a nocturnal SOREMP for diagnosing narcolepsy with cataplexy in a pediatric population. SLEEP 2015;38:859–865.

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Idiopathic narcolepsy generally has onset during childhood and adolescence, though there may be a delay of several years before a firm diagnosis is established. In the United Kingdom, the time between onset of clinical symptoms and establishment of a definitive diagnosis of narcolepsy was reported to be 10.5 years.1 Children are not able to accurately express the subjective experiences of cataplexy, hypnagogic hallucinations, or sleep paralysis. This can lead to a delay in diagnosis. In adults, the presence of a sleep-onset REM period on the nocturnal polysomnogram is over 97% specific for the diagnosis of narcolepsy with cataplexy.2 While the possible utility of the nocturnal sleep onset REM period (nSOREMP) in facilitating the diagnosis of NC in children has been briefly discussed,3–5 the sensitivity and specificity of the nSOREMP in enabling a diagnosis of childhood narcolepsy-cataplexy has not been evaluated in a large series of subjects. Further, both children with suspected narcolepsy and their parents may find the multiple sleep latency test (MSLT) a stressful experience, which might per se impact sleep onset latency, particularly during the afternoon hours. During the late afternoon, children sometimes become restless, and not emotionally disposed to cooperating for the 4th or 5th nap of the MSLT. Further, when it comes to diagnosing narcolepsy, the specificity of the childhood MSLT-derived information is limited—Carskadon et al. found that one or two SOREMPs could be detected in 48% and 16% respectively of otherwise healthy adolescents.6 Given these limitations of the MSLT in children, are there other, under-evaluated biomarkers within the nocturnal polysomnogram that could aid in the diagnosis of narcolepsy? This clinically relevant question is addressed in this issue by the study of SLEEP by Reiter and colleagues.7

Reiter et al. conducted a retrospective study of 210 children who had undergone nocturnal polysomnography and MSLT at the Boston Children’s Hospital. After excluding subjects with variables that could confound the test results, they were able to analyze the remaining group of 148 subjects. The cohort was ethnically diverse. Patients were categorized into four groups: narcolepsy with cataplexy (N+C), narcolepsy without cataplexy (N-C), other hypersomnias (H) and “Other.” Subjects with N+C had shorter sleep onset latencies as compared to the other three categories (all P values ≤ 0.003). Patients with N+C also exhibited significantly shorter nocturnal REM latencies as compared to the Hypersomnia (H) and Other groups, though not in comparison with the N-C category. Further, the sleep-onset REM period (nSOREMP) was very specific for the diagnosis of N+C (97.3%; 95% CI: 92.2%–99.4%). The sensitivity of the nSOREMP was only moderate 54.8% (95% CI: 38.7%–70.2%). Overall, the positive predictive value of the nSOREMP for diagnosis of N+C was 88.5% (95% CI: 69.8%–97.4%). If patients showed very short nocturnal REM latencies, they were also more likely to exhibit significantly more sleep-onset REM periods on the MSLT. The investigators have thus validated an important tenet pertaining to narcolepsy—when the pressure to quickly enter into REM sleep appears during the daytime, it also becomes evident during night sleep. This finding was also found in a 2012 paper by Rao et al.8 This biomarker of quick transition into REM sleep in the night sleep of narcolepsy could have potential pharmaco-therapeutic implications, as pharmacological agents that enhance slow wave sleep might perhaps serve to delay the appearance of REM sleep both during the night and daytime.

The results of the Reiter study,7 while important, have some limitations, which are acknowledged by the authors. The retrospective design of the study is understandable, given the small number of childhood narcolepsy patients, even at large academic sleep centers. The composition of the control groups could however have been improved. For instance, subjects with behavioral sleep problems were included as controls. This might artificially embellish specificity values of the MSLT in the narcolepsy group. It is unclear why behavioral insomnia patients were subjected to the MSLT. It would have been helpful to include in the comparison group some children with depression, as they can also manifest an early transition to REM sleep, though not to the degree as narcolepsy.9,10

When nocturnal REM latency is significantly shortened, it suggests the possibility of narcolepsy. The absence of an nSOREMP, however, does not exclude narcolepsy—for instance, the patient may have experienced an nSOREMP prior to hook up and initiation of the polysomnogram, as children with narcolepsy are overwhelmingly sleepy. On balance, however, the authors and their study have made an important contribution towards facilitating early diagnosis of childhood narcolepsy.

CITATION

DISCLOSURE STATEMENT
Dr. Kotagal has indicated no financial conflicts of interest.

REFERENCES