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A Narcolepsy Detection Paradigm: Automated Nocturnal Detection and Notification of Sleep Onset Rapid Eye Movement Periods

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Introduction

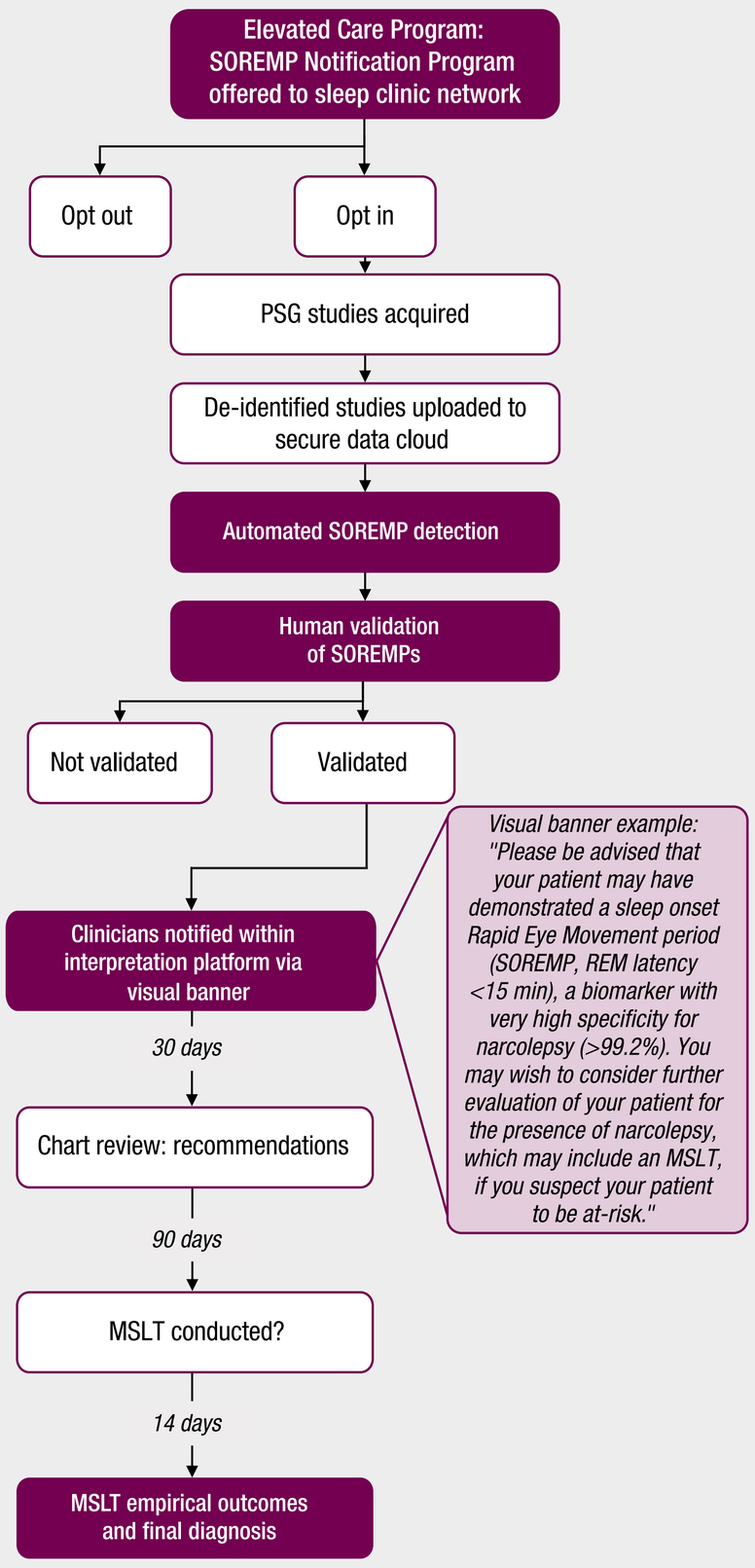
- Narcolepsy often remains undiagnosed for many years following symptom onset, likely due, in part, to a combination of limited narcolepsy-specific education for clinicians and it being a rare disorder, as well as it having substantial medical comorbidities, including sleep disorders, that may be associated with similar symptoms[1]
- Rapid eye movement (REM) sleep detected by polysomnography (PSG) occurring within 15 minutes of nocturnal sleep (sleep onset REM period; SOREMP) is a known biomarker for hypocretin-deficient narcolepsy (NT1)[2]
- Recent revisions of the CNS Hypersomnias diagnostic criteria (*ICSD–Third Edition-Text Revision*; published March 2023) underscored the significance of the NT1 biomarker, such that the presence of a nocturnal SOREMP is now sufficient for diagnosing NT1 if cataplexy is also present[3]
- Despite this progressive nosological modification, among patients who undergo diagnostic sleep testing, as few as 4% with a SOREMP receive further evaluation for narcolepsy, suggesting that the PSG SOREMP biomarker either largely goes unnoticed or is not recognized as an important indicator of narcolepsy[4]
- To enhance identification and clinician visibility of nocturnal SOREMP episodes, an automated process was developed to detect and advise sleep clinicians of SOREMPs occurring during overnight PSG

Objective

- To evaluate the impact of automated SOREMP notification on clinician recommendations for hypersomnia evaluation that included a multiple sleep latency test (MSLT)

Methods

Figure 1. Study Design

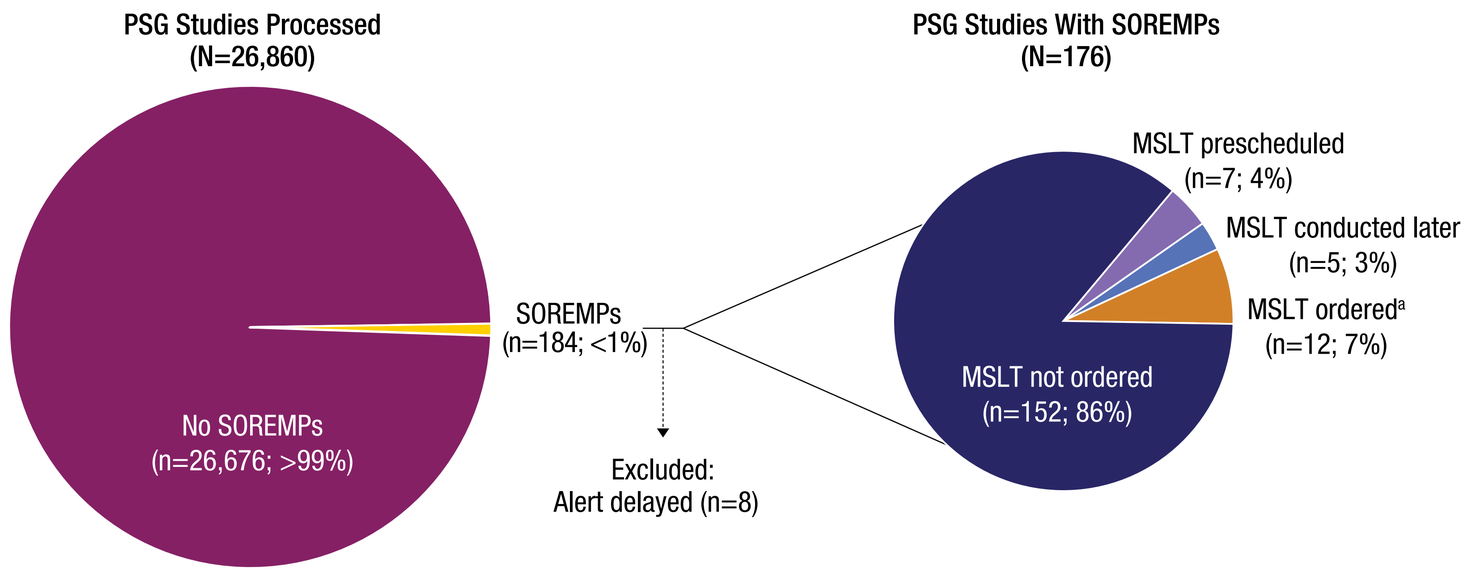


MSLT, multiple sleep latency test; PSG, polysomnography; REM, rapid eye movement; SOREMP, sleep onset rapid eye movement period.

- Sleep studies were processed over 5 years

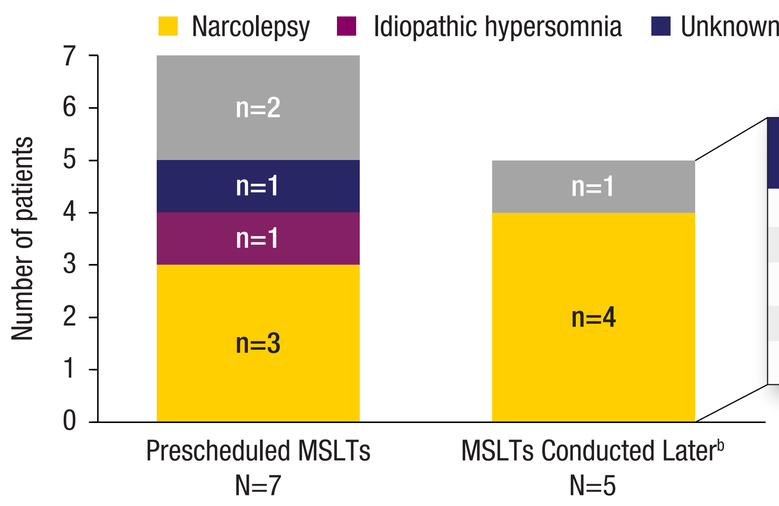
Results

Figure 2. Based on the Automated SOREMP Notification Program, 24 Patients (14%) Were Recommended for Further Narcolepsy Evaluation (MSLT)



[a]MSLT scheduled, n=2; patient refused, n=3; no follow-up from patient, n=7.
MSLT, multiple sleep latency test; PSG, polysomnography; SOREMP, sleep onset rapid eye movement period.

Figure 3. When Conducted, MSLTs Most Often Supported a Narcolepsy Diagnosis

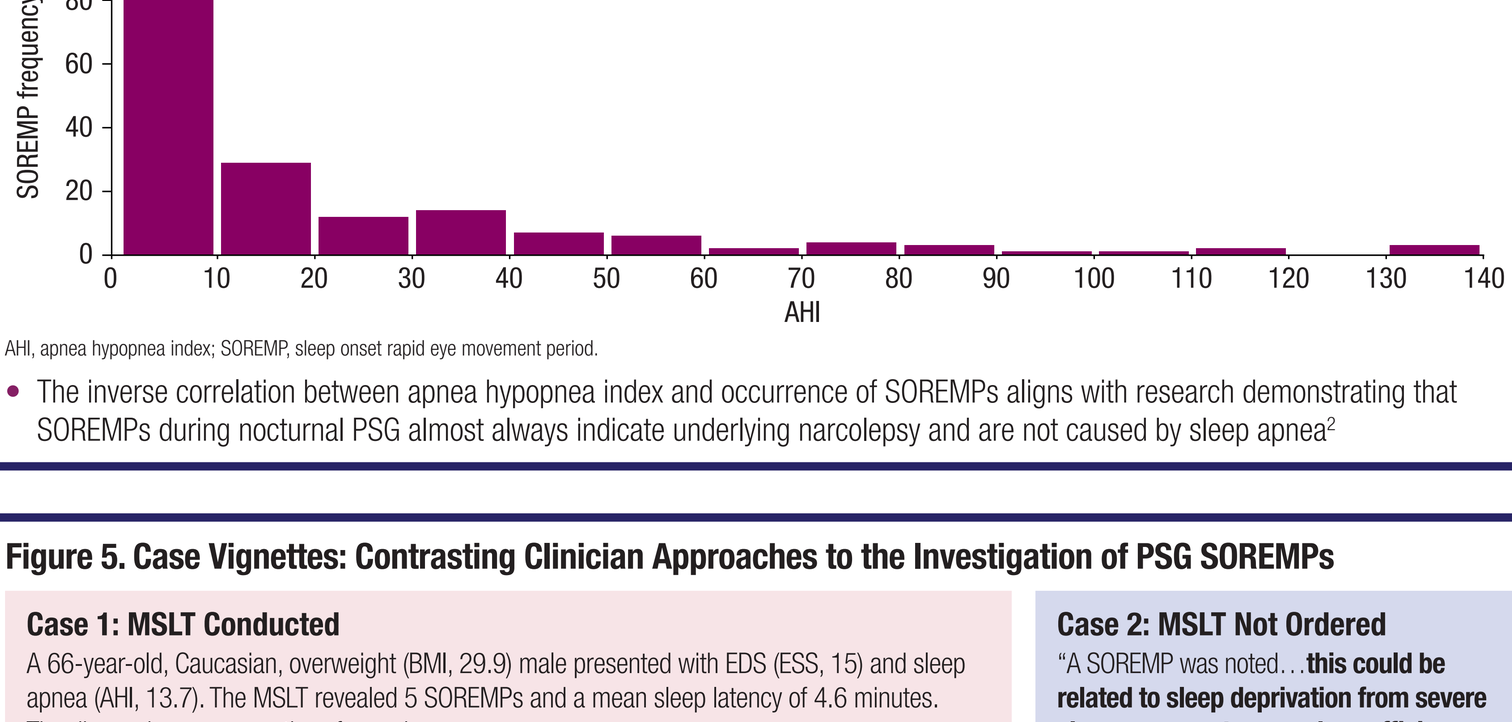


MSLT	SOREMPs (n)	Mean Sleep Latency (min)
Normal MSLT	0	11.7
Narcolepsy #1	5	4.6
Narcolepsy #2	3	3.0
Narcolepsy #3	2	4.7
Narcolepsy #4	3	0.4

[a]Diagnosis unknown due to inaccessible MSLT.
[b]Based on recommendation for further evaluation by the automated SOREMP notification program.
MSLT, multiple sleep latency test; SOREMP, sleep onset rapid eye movement period.

- Of the 24 patients who were recommended for further evaluation, 5 had subsequent MSLTs conducted, 7 had MSLTs prescheduled (the following morning), and 12 had MSLTs ordered (which have yet to occur)
- Of the 5 MSLTs that were conducted based on recommendations from automated PSG screening, the majority were consistent with narcolepsy
  - Four patients (80%) had numbers of SOREMPs and mean sleep latency values from MSLT that supported the narcolepsy diagnosis
  - One patient (20%) had a normal MSLT

Figure 4. SOREMPs Occurred More Frequently Among Patients With Lower AHI



AHI, apnea hypopnea index; SOREMP, sleep onset rapid eye movement period.

- The inverse correlation between apnea hypopnea index and occurrence of SOREMPs aligns with research demonstrating that SOREMPs during nocturnal PSG almost always indicate underlying narcolepsy and are not caused by sleep apnea[2]

Figure 5. Case Vignettes: Contrasting Clinician Approaches to the Investigation of PSG SOREMPs

Case 1: MSLT Conducted

A 66-year-old, Caucasian, overweight (BMI, 29.9) male presented with EDS (ESS, 15) and sleep apnea (AHI, 13.7). The MSLT revealed 5 SOREMPs and a mean sleep latency of 4.6 minutes. The diagnosis was supportive of narcolepsy.

"MSLT is supportive of narcolepsy, but these findings can be seen in other medical conditions."

Case 2: MSLT Not Ordered

"A SOREMP was noted…**this could be related to sleep deprivation from severe sleep apnea or to poor sleep efficiency.** If severe drowsiness persists in spite [of] proper treatment of sleep apnea, consider an MSLT."

Case 3: MSLT Not Ordered

"REM onset was very short, and short onset REM periods can be associated with narcolepsy, though an isolated short onset REM period on a PSG is not adequate to make this diagnosis, **and *[patient]* is out of the typical age group for narcolepsy.** If any suspicion for narcolepsy is found after further evaluation, a repeat PSG immediately followed by an MSLT would be used to evaluate further."

AHI, apnea hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; MSLT, Multiple Sleep Latency Test; PSG, polysomnography; REM, rapid eye movement; SOREMP, sleep onset REM period.

Conclusions

- This study implemented real-time identification and subsequent clinician notification of nocturnal SOREMPs using a novel detection paradigm
  - This methodology resulted in the recommendation of further narcolepsy evaluation (MSLT) for 24 patients (14%), 17 of whom may have otherwise not have had an MSLT ordered
  - Subsequent MSLTs resulted in a narcolepsy diagnosis rate of 80% in patients in whom narcolepsy was not suspected
- Contrary to popular supposition, evidenced by the predominance of SOREMPs in those with low AHI, our data suggest that sleep apnea is not etiologic for nocturnal SOREMPs
- The high narcolepsy diagnosis rate observed in patients with unexpected PSG SOREMP episodes underscores the specificity of this biomarker and gives reason for clinicians to increase referral rates for subsequent MSLTs
- This is a call to action for medical providers to critically evaluate patients who exhibit SOREMPs on nocturnal PSG, as this provides a unique opportunity to identify and treat narcolepsy

References: 1. Thorpy MJ, Krieger AC. *Sleep Med.* 2014;15:502-7. **2.** Andlauer O, et al. *JAMA Neurol.* 2013;70:891-902. **3.** American Academy of Sleep Medicine. *International Classification of Sleep Disorders - Third Edition, Text Revision* (ICSD-3-TR). 2023. **4.** Cairns A, Bogan R. *Sleep Med.* 2017;32:150-6.

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