

SLEEP MEDICINE PEARLS

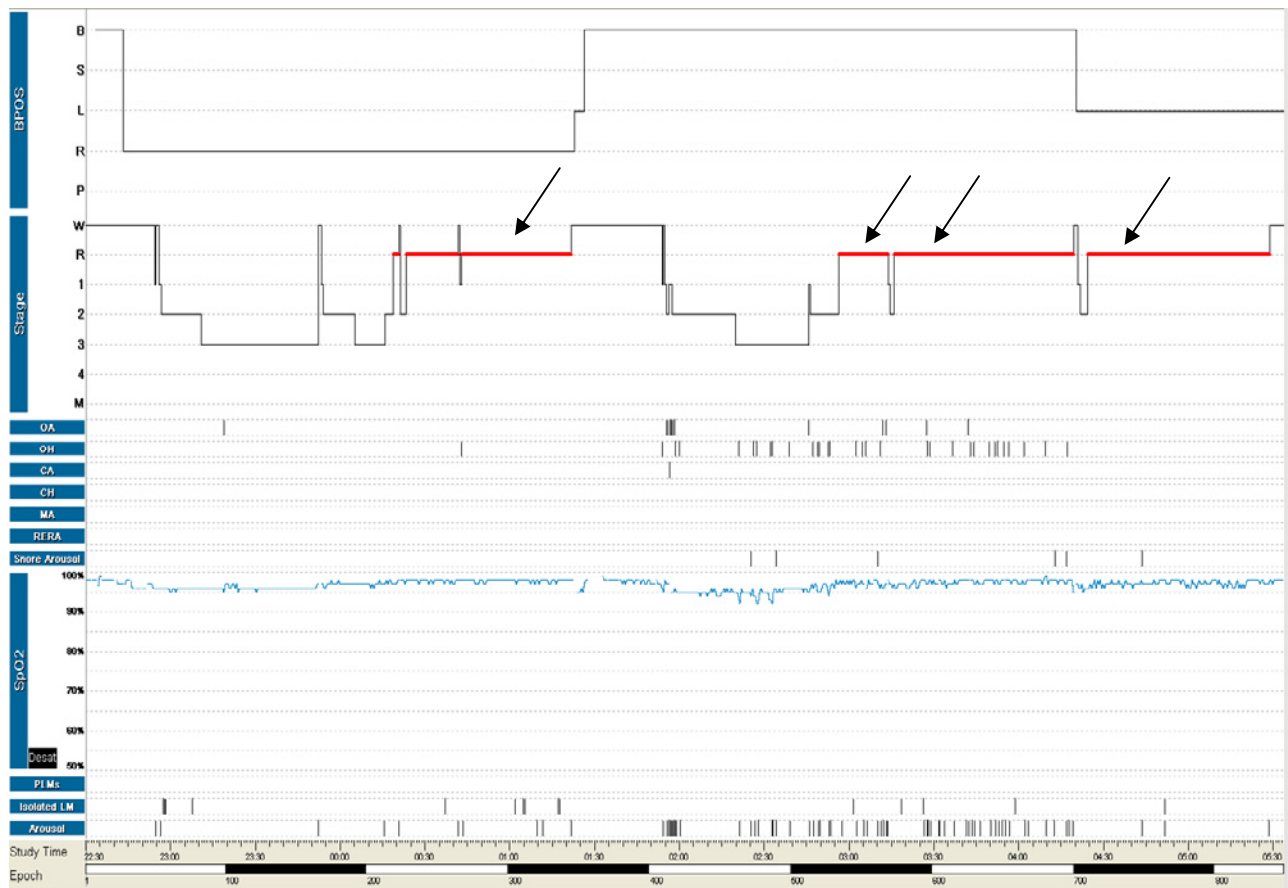
## A Sleepy Patient with REM Rebound

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A 25-year-old male presented to the sleep clinic with a chief complaint of excessive daytime somnolence and witnessed nocturnal “choking episodes” dating back a few years. His Epworth Sleepiness Scale score was 13. His usual bed time and rise time were 23:00 and 07:00, respectively. There was no history of snoring, and the patient denied a history of cataplexy,

hypnopompic/hypnagogic hallucinations, or sleep paralysis. Six weeks prior to his sleep study, his primary care physician had prescribed paroxetine 20 mg daily, and 2 weeks prior to the study, trazodone 50 mg at bedtime had been added to his medication regimen. These medications were prescribed to treat depression with comorbid anxiety that had been present for many



**Figure 1**—Hypnogram showing the summary of sleep stages for the sleep period. Note the large amount of REM sleep (as designated by R in the y axis) with the arrows pointing to these areas of interest.

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**Table 1**—Diagnostic Polysomnogram Summary of Sleep Time Statistics, Sleep Stage Statistics and Respiratory Event Statistics

Polysomnographic Variable	Result
Lights off (time)	22:34
Lights on (time)	05:33
Time in bed (min)	420
Total sleep time NREM (min)	152
Total sleep time REM (min)	205
Wake after sleep onset (min)	36
Sleep efficiency (%)	85
Latency to sleep (min)	21
Latency to REM (min)	83
Percentage N1 sleep to total sleep time (%)	1
Percentage N2 sleep to total sleep time (%)	19
Percentage N3 Sleep to total sleep time (%)	22
Percentage of REM sleep to total sleep time (%)	58
Overall apnea-hypopnea index (events/hour)	7.6
Supine apnea-hypopnea index (events/hour)	17.8
REM apnea-hypopnea index (events/hour)	6.4

**Table 2**—Results of the Multiple Sleep Latency Test

Nap	Time	Sleep Latency (minutes)	REM Latency (minutes)
I	07:11	16	-
II	09:12	5	-
III	11:08	13	8*
IV	13:11	18.5	5*
V	15:01	20	-
Mean sleep latency		14.5	

Despite having an overall normal mean sleep latency, it was noted that in nap III and nap IV demonstrated sleep onset REM periods (SOREMP) (\*).

years but were not currently treated. In spite of a regular sleep schedule of 8 h per night, he often fell asleep on the job. The patient noted that his excessive daytime sleepiness predated the use of the antidepressants. His family history was positive for a father with obstructive sleep apnea. His physical examination revealed normal vital signs with a body mass index of 23.5. Head, ears, eyes, nose and throat examination were unremarkable, as was the cardiopulmonary examination.

An overnight diagnostic polysomnogram (PSG) was obtained with the hypnogram shown in Figure 1 and a summary of pertinent results in Table 1.

A multiple sleep latency test (MSLT) was ultimately obtained following the PSG to evaluate objectively his severity of somnolence (Table 2).

**Question: What additional information would be important to request from the patient to help explain the findings seen on the PSG and MSLT?**

**Answer: A list of any medications or recreational drugs recently started or stopped. One may consider drug screening to ensure that the findings are not pharmacologically induced. Sleep logs for 1 week prior to the MSLT to assess prior sleep-wake schedules can sometimes be helpful to look for insufficient sleep.**

## DISCUSSION

Although clinical depression can present with hypersomnia, our patient's complaint of nocturnal choking episodes warranted further polysomnographic evaluation to rule out sleep disordered breathing as a contributing cause. In addition to the mild sleep disordered breathing seen on the polysomnogram, the significant increase in the percentage of REM sleep on his hypnogram, termed *REM rebound*, and the 2 SOREMPs seen on MSLT were important findings of the case. Each of these will be addressed in turn.

In healthy adults, REM sleep makes up 20% to 25% of total sleep time. REM sleep occurs every 90-120 min of a night's sleep and increases in duration with each period of REM. There may be 4 to 5 periods of REM sleep per night.<sup>1</sup> In our patient, by contrast, 58% of the total sleep time was made up of REM sleep. There are several causes of the increased REM sleep percentage, as seen in Table 3.<sup>1-8</sup>

The patient's report of disabling hypersomnia appeared out of proportion to his overnight PSG findings, and thus we elected to perform and interpret the MSLT despite that some of the MSLT guidelines were not precisely met.<sup>9,10</sup> MSLT guidelines suggest a minimum 2-week withdrawal period from any drugs with side effects that disrupt sleep, including alcohol, antidepressants, or narcotics;<sup>9,10</sup> however, it was felt upon consultation with the primary care physician that his psychiatric state did not permit stopping his antidepressant medications. MSLT guidelines suggest the first nap start 1.5 to 3 h after the termination of the preceding nocturnal study and at least 360 min of nocturnal sleep need to be recorded for meaningful MSLT results. Although AASM guidelines are routinely followed in our sleep laboratory, an inadvertent early "Light On" resulted in a sleep time of 357 min, which we believe still permitted meaningful clinical interpretation of the data in this case. Our patient had a mean sleep latency of 14 min, which falls into the normal range despite his complaints of excessive hypersomnolence. Note that the mean sleep latency may have been skewed by the fact that the patient was not able to nap during nap V. Our patient also experienced 2 SOREMPs during the study. While 2 or more SOREMPs could raise a question of narcolepsy, this diagnosis also requires a mean sleep latency of < 8 min, which our patient did not have. SOREMPs can occur in other clinical situations as well, as seen in Table 4.<sup>1-8</sup>

We conducted further questioning to explain the surprising amount of REM sleep and the presence of SOREMPs in the context of his normal mean sleep latency. Although he did not report changes in his medication regime to us prior to the PSG or MSLT, he disclosed at a later date that he had discontinued the paroxetine and trazodone 3 days prior to his PSG because of side effects, and that he then restarted these medications the night of the PSG because of increasing anxiety about the hospital stay. In addition, increasing anxiety also led the patient to take diazepam 5 mg the night prior to the PSG and 5 mg on the

**Table 3**—Causes of an Increased REM Sleep Percentage on PSG

REM sleep deprivation
Withdrawal of REM-suppressing medications (ie. selective serotonin reuptake inhibitors)
Withdrawal of REM-suppressing recreational drugs (ie. ethanol, cocaine)
Depression
Patients undergoing CPAP titration

**Table 4**—Causes of Sleep Onset REM Periods on MSLT

Narcolepsy
Obstructive sleep apnea
Withdrawal of REM-suppressing medications (ie. selective serotonin reuptake inhibitors)
Depression
Delayed sleep phase syndrome
REM sleep rebound from REM sleep deprivation

morning of the MSLT; this was discovered on his urine toxicology screen on the day of the MSLT. Interestingly, there was no increase in the number of sleep spindles on the overnight PSG or on the MSLT, which have been previously been associated with diazepam administration.<sup>11</sup> Upon reflection, the patient's anxiety may also have contributed to his longer mean sleep latency, as he was preoccupied with leaving the hospital in the afternoon and could not fall asleep during the last nap.

The key take-away from this case is that a large amount of REM sleep seen on a PSG and SOREMPs seen on an MSLT can be caused by a withdrawal of REM suppressing medications, and does not necessarily indicate narcolepsy.<sup>1-4,8</sup> In our patient, the abrupt withdrawal of paroxetine and trazodone most likely led to these dramatic findings. Our diagnosis is complicated by the confounding factors of the patient's depression, which can also increase REM sleep,<sup>1,7-9</sup> and the patient's mild sleep apnea, which can lead to SOREMPs on MSLT the following day.<sup>1,4,5</sup> However, the severity of the REM rebound is unlikely to be explained by these issues alone. Given the multiple confounding variables, a decision was made to repeat the patient's PSG and MSLT when his psychiatric state was more stable and the medications could be withdrawn safely.

## PEARLS

1. In the face of a sleep study showing REM rebound, patients should be questioned not only about current medications and recreational drug use but also any alteration made to the medication or sleep routine in the weeks prior to testing
2. Routine drug screening and drug levels may be helpful to confirm that the MSLT findings are not pharmacologically induced.
3. The presence of 2 SOREMPs should not automatically be equated with the diagnosis of narcolepsy.
4. A REM rebound phenomenon should be part of the differential diagnosis when a high percentage of REM sleep is seen in a polysomnogram, especially in the context of high sleep efficiency.

## DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.

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