NEW RESEARCH

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Sodium Oxybate-Induced Sleep Driving and Sleep-Related Eating Disorder

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CASE REPORTS

Hypnosedative-induced complex behaviors have gained increased attention in recent years as a potential complication of benzodiazepines and benzodiazepine-receptor agonist use. Sodium oxybate (SO), the sodium salt of γ-hydroxybutyrate, an inhibitory neurotransmitter, has been associated with dose-dependent rates of somnambulism; however, there is limited information about complex motor behaviors with SO. We describe a patient with narcolepsy-cataplexy who experienced one episode of sleep-driving and at least two sleep-related eating episodes with therapeutic doses of SO.

Keywords: Sodium oxybate, sleep related eating disorder, sleep driving, parasomnia, narcolepsy

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Sodium oxybate (SO) is approved for the treatment of excessive daytime sleepiness (EDS) and cataplexy in patients with narcolepsy.[1] Most common side effects include nausea, dizziness, headache, vomiting, somnolence, and urinary incontinence.[1-3] Somnambulism has been reported to occur in 0.4% to 5.7% of patients in a dose-dependent manner.[1,3] A recent safety publication on SO reported one patient with recurrent episodes of sleep-eating and one episode of sleep-driving resulting in a motor vehicle accident[3]; however, there is limited information in the literature concerning complex motor behaviors associated with SO. We describe the second case of sleep-driving and sleep-related eating disorder (SRED).

REPORT OF CASE

A 42-year-old gentleman with narcolepsy-cataplexy and moderate obstructive sleep apnea returned to our sleep clinic with persistent complaints of excessive daytime sleepiness (EDS). His past medical history was remarkable for obesity, depression, and hypertension. He often avoided eating at work for fear of worsening EDS. His persistent EDS was a frequent source of stress at work. Upon arriving home, he sometimes consumed large quantities of food at bedtime and in the middle of the night. His Patient Health Questionnaire-9 score was 17, consistent with moderately severe depressive symptoms. There was no previous history of seizures, childhood parasomnias, family history of parasomnias, or active alcohol use. His current medications included bupropion, modafinil, and dextroamphetamine.

Other etiologies of EDS were excluded after verification of positive airway pressure (PAP) compliance. Adequate sleep duration was confirmed by actigraphy over 2 weeks. Physical examination revealed a body mass index of 34 kg/m^2 and unremarkable neurological exam.

To treat his residual EDS, SO 4.5 g/night was initially prescribed and titrated over 6 weeks to 8 g/night. Two weeks after reaching the dose of 8 g/night, he reported a total of 6 parasomnia episodes. He drove to a convenience store 3 blocks away and he was awakened by the store clerk while purchasing a candy bar. Two other times, he awakened with chocolate bars smeared on his face. His other behaviors during sleep included showering fully dressed, vomiting while seated on the toilet, and urinating on his computer. Most of these occurred in the early morning hours after the second SO dose. He was amnestic for these events.

A comprehensive workup for de novo parasomnia was negative. PAP polysomnography (PSG) was repeated on SO (8 g nightly) and 2 weeks after discontinuation. PSG sleep variables are provided in **Table 1**. PAP pressure requirements were equivalent in both studies. There were no parasomnias or focal EEG abnormalities observed on either study. SO was restarted and slowly titrated to 7 g/night without recurrence of parasomnias and resolution of bedtime food cravings during one year of follow-up. SO dose was increased to 8 g nightly for one week but he experienced 2 more somnambulistic episodes, after which the dose was reduced to 7 g nightly.

DISCUSSION

Parasomnia episodes occur during complete or partial arousals while transitioning from N3 sleep to a lighter stage of NREM sleep and can be primed by medications. Episodes of sleep-related eating and sleep-related driving have mostly been linked to use of benzodiazepines and, more recently, benzodiazepine-receptor agonists.[4] A review of the literature revealed limited reports of SO-induced parasomnias with only one documented case of sleep-related driving and eating.[3] A key difference between the first report and our patient's episode was that the former involved the use of alcohol on the night of the episode.

Table 1—PSG parameters with and without SO

Sleep Parameters	PAP study with SO	PAP study without SO
TST	513.0	421.0
SE	95.2	92.5
SOL	1.5	2.0
REM latency	418.5	112.5
WASO	1.0	27.5
N1	4.0	2.0
N2	41.4	45.4
N3	49.3	20.6
REM	5.4	32.0

TST, total sleep time; SE, sleep efficiency; SOL, sleep onset latency; WASO, wake after sleep onset. TST, SOL, WASO, and REM latency are reported in minutes. SE, N1, N2, N3, and REM are reported as percentages of TST.

Many factors are important for the predisposition, priming, and precipitation of NREM parasomnias in adults. Complex interactions exist in patients with mental illness, comorbid sleep disorders, stress, medications, and parasomnias.[5] Lam et al. reported that patients with depressive spectrum disorders have significantly higher one year prevalence of somnambulism and SRED than patients with other psychiatric diagnoses. The association of depression and parasomnias may be mediated through a common trigger (life stress) or worsening sleep disturbances or be due to the side effects of medications used to treat either.

Although our patient did not have a known predisposition for parasomnias, he had at least three important priming factors: (1) Increased work-related stress, (2) increased depression with resultant poor sleep quality and nocturnal arousals, and (3) the introduction of SO, further increasing the potential for parasomnias by augmenting N3 sleep. After the second nightly dose of SO, the duration of N3 sleep increases and is most profound during the latter half of the night, which correlates with the timing of our patient's clinical events.[2] A number of other possible events could have precipitated his parasomnias including early-morning PAP noncompliance with respiratory-event related arousals, arousals related to back pain, or environmental factors. Polypharmacy has often been noted in medication-induced parasomnia case reports but we are not aware of drug-drug interactions between bupropion and SO.[4]

SRED is a recently recognized parasomnia combining features of somnambulism and eating disorders. As illustrated by our patient, subjects may have nocturnal arousals followed by compulsive eating with partial or complete amnesia for the event. Our patient's preexisting nighttime binge eating with preserved recall is consistent with a history of nocturnal eating syndrome. It is currently controversial if nocturnal eating syndrome and SRED are disorders which lie on a continuum or are two distinct clinical entities.[6] SO treatment, increased stress, and depression may have permitted the expression of a latent subclinical eating disorder.

We believe that the delayed emergence of parasomnia activity (2 weeks after reaching 8 g nightly) may support a physiologic mechanism (further enhancement of N3 sleep) coupled with partial arousals related to psychosocial stressors and depression. The emergence of complex motor activities with the higher doses of SO coincided with heightened work-related stress and depressive symptoms. The one year of follow-up of SO use (at 7 g) without parasomnia recurrence suggests that multiple factors were necessary to culminate in complex motor behaviors. The recurrence of parasomnia upon SO re-challenging at higher dose (8 g) suggests that SO was an important priming factor and is in agreement with dose-related somnambulism rates noted in SO safety studies.[1]

In conclusion, SO may prime for complex parasomnia activity in susceptible patients. This potential adverse event is particularly important to discuss with patients who sleep alone to prevent injuries. Further research is necessary to elucidate the mechanism of SO-induced complex motor behaviors.

ABBREVIATIONS:

SO, sodium oxybate
SRED, sleep-related eating disorder
EDS, excessive daytime sleepiness
PAP, positive airway pressure
PSG, polysomnography

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