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CASE REPORTS

Acute Insomnia Following Surgery of the Ventralis Intermedius Nucleus of the Thalamus for Tremor

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Abstract: Stereotactic surgery with lesioning or deep brain stimulation directed to the ventralis intermedius nucleus of the thalamus is a well-recognized treatment for medically intractable tremor. A patient developed the rare complication of severe insomnia, easy awakening, and lack of slow-wave sleep after thalamotomy/deep brain stimulation implantation. This complication underscores the role of thalamic regulation on initiation and maintenance of sleep.

Keywords: Thalamus, insomnia, thalamotomy, deep brain stimulation, tremor

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Stereotactic surgery with lesioning or deep brain stimulation (DBS) directed to the ventralis intermedius nucleus of the thalamus is a well-recognized treatment for medically intractable tremor.[1] We report a case of severe insomnia following thalamotomy of the ventralis intermedius nucleus and DBS.

REPORT OF CASE

A 66-year-old man without history of dyssomnia or mood disorder presented for surgical treatment of disabling resting and action tremor from an overlap syndrome of Parkinson disease and familial essential tremor. In November 2003, a DBS electrode was stereotactically implanted in the left ventralis intermedius nucleus with effective tremor reduction. When intraoperative high-frequency stimulation failed to control the left-sided tremor, a thalamotomy of the right ventralis intermedius nucleus was performed with radiofrequency lesioning during awake neurologic testing. (Figure 1). Postoperatively, the patient achieved excellent tremor control bilaterally.

The first night, however, he could not sleep. Within the next week, he developed worsening akathisia that was initially attributed to abrupt self-discontinuation of carbidopa-levodopa. Insomnia persisted, and behavior declined despite drug resumption and trials of temazepam and zolpidem.

He was admitted in an agitated state on postoperative week 4, demonstrating profound hypervigilance during wakefulness, short sleep latency when quiet, and an inability to maintain sleep.

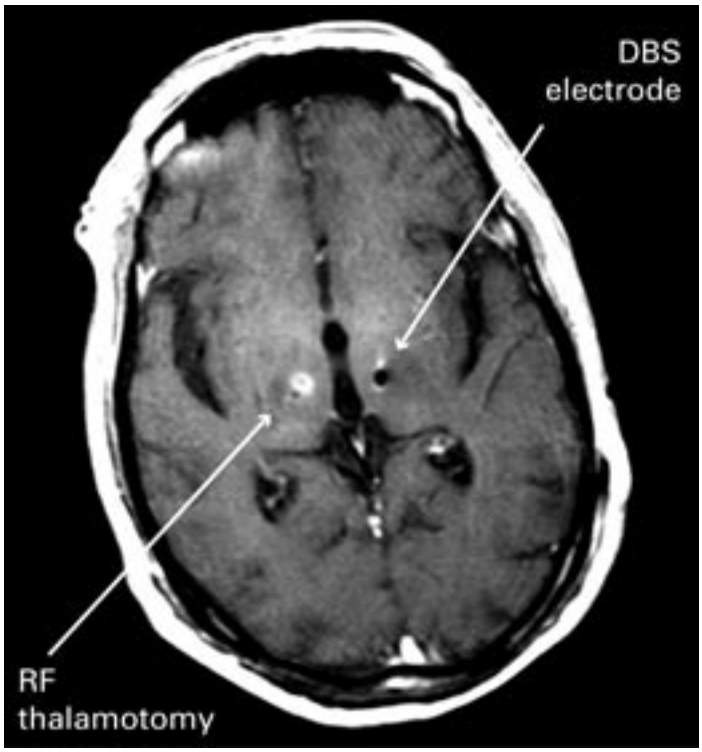

Figure 1—Fast fluid-attenuated inversion recovery magnetic resonance imaging 43 days after bilateral stereotactic surgery directed to the ventralis intermedius nucleus of the thalamus. Note the left-sided deep brain stimulation electrode and the right-sided radiofrequency lesion. AC-PC distance = 28 mm; laterality = 11.5 mm. DBS refers to deep brain stimulation.

There was no change with DBS off. Multiple sedative-hypnotics were tried, with quetiapine having the best clinical effect. Clinical neuropsychology consultation found no evidence for a psychiatric diagnosis of mania.

Two overnight polysomnograms were performed, 1 at 6 weeks postoperatively during severe insomnia and the other at 16 months postoperatively when subjective symptoms resolved (Table 1).

Disclosure Statement
This was not an industry supported study. Drs. Quigg, Frysinger, Harrison, and Elias have reported no financial conflicts of interest.

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Table 1—Polysomnography Results of 2 Studies Performed at 6 Weeks and 16 Months Postoperatively for Insomnia Following Right Thalamotomy and Left Ventral Intermediate Nucleus Stimulation.

Polysomnographic Variable	6 Weeks[a]	16 Months[a]
Time in Bed, min	559	536
Total Sleep Time, min	384	221
Sleep latency, min	0	86
REM latency, min	72	179
REM episodes, no.	3	2
Awakenings, no.	8	15
Sleep efficiency, %	68	41
Sleep stage, %		
1	15.0	14.5
2	78.3	68.1
3	0.4	5.4
4	0	0
REM	6.3	12.0

[a]Time after the operation.

The earlier study (DBS off with reemergence of mild hemibody tremor and during treatment with quetiapine) demonstrated shortened sleep latency and arousals with 3 prolonged periods of wakefulness. The later study (bipolar DBS on[2] and off medications) demonstrated increased sleep latency, shortened total sleep time, and 8 brief awakenings. Both studies showed markedly decreased stages 3/4 sleep. A sleep log before the later study revealed a habitual bedtime at approximately 8:00 pm and 2 to 3 awakenings. Despite the decline in sleep time, his Epworth Sleepiness Scale score was 4 (normal $\leq$ 10). Clinically, the patient and his wife report resolution of insomnia 8 months postoperatively and no excessive daytime somnolence. Bilateral tremor control remains.

DISCUSSION

In summary, a patient with resting and action tremor presented with insomnia following left thalamic DBS and right thalamotomy. Although initial sleep latency was brief, associated with acute sleep deprivation and possible medication effects, polysomnography in the recovery phase demonstrated chronic defects in sleep initiation and sleep maintenance and lack of slow-wave sleep that persisted despite clinical improvement.

One of the difficulties in this case was the characterization of insomnia, given the lack of reliable actigraphy at our institution at the time of presentation and the potential confounders of medications and movement disorder in the evaluation of polysomnography. The present case resembles a previously reported case in which a parkinsonian patient developed severe insomnia following ablation of bilateral central thalami.[3] The present case suggests that unilateral thalamic ablation is sufficient to generate insomnia, since the patient's sleep symptoms were resistant to DBS adjustments. Within the limits of the data, the worse sleep efficiency and longer sleep latency during the later sleep study (with DBS on) compared with the early study (with DBS off) suggest additive effects of contralateral thalamic DBS with insomnia, supporting the analogy of high-frequency DBS to a "physiologic" lesion. Improvement in the patient's sleep deprivation could also account for these changes. However, we could not further explore these effects because tremor recurrence with the DBS off was not tolerated. The marked dissociation between clinical improvement and PSG findings, specifically, the lack of excessive daytime sleepiness despite awakenings and lack of deep sleep, may stem from his overall successful treatment of tremor or from the reduction in duration of arousals.

Although insomnia following stereotactic thalamic surgery is rare, the present case underscores thalamic function in the maintenance of sleep. Bilateral thalamic lesions[3] and the neuronal loss seen predominately in anteroventral and dorsomedial thalamus in fatal familial insomnia[4] produce severe insomnia. In contrast, some investigations have emphasized the role of the thalamus as a relay for the activating input from the upper mesencephalic reticular system; accordingly, lesions of paramedian thalami in humans produce a chronic "subwakeful" state presumably by blocking ascending signals from the upper mesencephalic reticular system.[5] Intermittent left thalamic hypoperfusion corresponded to somnolent periods in a case report of hypersomnia.[6] These contradictory outcomes are echoed in studies of brain metabolism. The thalami, normally metabolically inactive during non-rapid eye movement sleep, should be overactive during insomnia but, instead, are depressed in subjects with primary insomnia.[7] Altered dynamics of thalamic metabolism and interactions with subthalamic nuclei, hypothalamic nuclei, and the upper mesencephalic reticular system have been proposed to account for these observations.[7]

Although the severity of sleep disturbance in the present case is unusually severe, greater awareness of potential changes in sleep regulation will aid in patient counseling prior to planned stereotactic thalamic surgery. This rare untoward event may become more common as the number of those treated with DBS increases.

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