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## Sleep-Wake Pattern Following Gunshot Suprachiasmatic Damage

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**Background:** The suprachiasmatic nucleus (SCN) plays a critical role in maintaining melatonin and sleep-wake cycles.

**Methods/Patient:** We report a case of 38-year-old woman who, after gunshot wound to the right temple, developed a sleep complaint of multiple nocturnal awakenings and several naps throughout the day.

**Results:** Computerized tomography and magnetic resonance imaging revealed bilateral optic nerve and optic chiasm damage. Diagnostic polysomnography and actigraphy

revealed an irregular sleep wake rhythm.

**Conclusions:** We speculate concurrent damage of the SCN and optic nerves bilaterally resulted in the posttraumatic irregular sleep-wake rhythm.

**Keywords:** Circadian rhythm sleep disorder, irregular sleep wake rhythm, suprachiasmatic nucleus

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### REPORT OF CASE

A 38-year-old woman presented with a history 4 years earlier of a gunshot wound (GSW) to the right temple with exit wound on the left temple leaving her blind. Computerized tomography revealed a bullet tract damaging the optic nerves bilaterally (**Figure 1**). Current magnetic resonance imaging revealed damage to the optic nerves and optic chiasm.

Current sleep complaints consisted of multiple nocturnal awakenings and several naps throughout the day. Her reported bedtime varied from 6 PM to 9 PM, and wake time varied from midnight to 3 AM. She reported sleeping sporadically throughout the day but cannot identify the exact times. She denied snoring or witnessed apnea; and she wakes from sleep unrefreshed. She is single, does not have a bed partner, and is disabled.

Past medical history is significant for depression and headaches. The patient sees a psychiatrist who has ruled out posttraumatic stress disorder. Current medications include acetaminophen, 500 mg as needed, and amitriptyline, 25 mg at night. Prior medications used to consolidate nocturnal sleep were unsuccessful and included clonazepam 0.5 mg at night, melatonin 1 mg at 9 PM and melatonin 9 mg at 9 PM, gabapentin 600 mg at night, and hydroxyzine 25 mg at bedtime.

Physical exam revealed a thin woman in no distress. Oral airway was unremarkable. Pupils were dilated and non-reactive; conjugate extraocular motility was intact in all cardinal directions of gaze. The remainder of her neurological examination was non-contributory.

Limited Epworth Sleepiness Scale score, reflecting the inability to drive or read, was 10/18. Serum basic metabolic panel, complete blood count, liver function panel, prolactin,

thyroid stimulating hormone, follicle stimulating hormone, and luteinizing hormone were all normal.

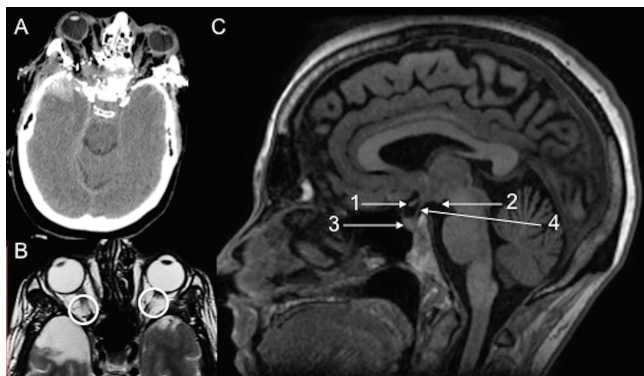
Diagnostic polysomnogram (PSG) data: total sleep time (TST) 325 min; sleep latency 48 min; wake after sleep onset 143 min; N1: 11.7%, N2: 73.9%, N3: 13.1%, REM: 1.3%; sleep efficiency 52%; and TST apnea-hypopnea index 0.3. Two weeks of actigraphy were obtained with the wrist device placed the night of the diagnostic polysomnogram (**Figure 2**). Actigraphy revealed an irregular sleep wake rhythm (ISWR) with an estimated average total sleep time per 24-h period of 8.8 hours.

**Figure 3** represents the PSG hypnogram corresponding to day 1 of actigraphy and demonstrates clearly disrupted sleep that was not well defined by actigraphy alone.

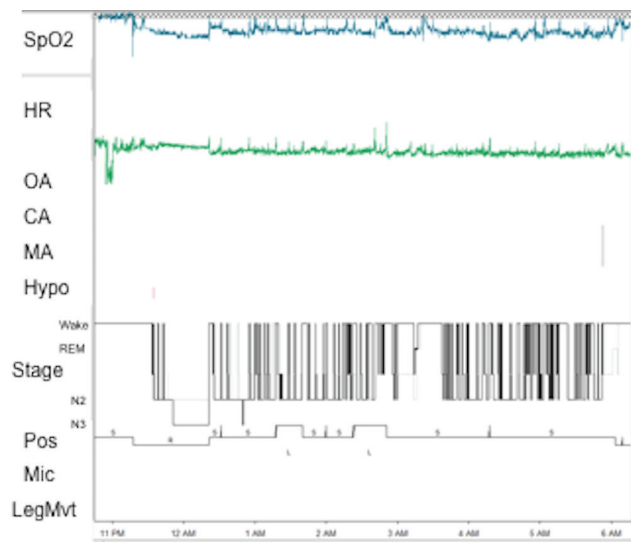
### DISCUSSION

As light is the most potent zeitgeber, blindness has been associated with various sleep disturbances. Circadian rhythm disorders, particularly free-running rhythm, have been reported in 27% of blind patients with reduced light perception.<sup>1</sup>

Light receptors in the retina transmit photic signals to the suprachiasmatic nucleus (SCN) through the retinohypothalamic tract, which travels along the optic nerves; hence, lesions of the optic nerves may result in a free-running circadian rhythm.<sup>2</sup> The SCN lies just above the optic chiasm, ventrolateral to the third ventricle in the anterior hypothalamus. Animal studies have demonstrated that complete ablation of the SCN results in abnormal melatonin cycling and irregular rest/activity cycles.<sup>3,4</sup> In humans, destruction of the SCN has also demonstrated disrupted patterns of body temperature and behavioral function.<sup>5</sup> Destruction of adjacent nuclei, the ventral sub-paraventricular zone, which receives a large number of projections

**Figure 1**—Neuroimaging of the brain.

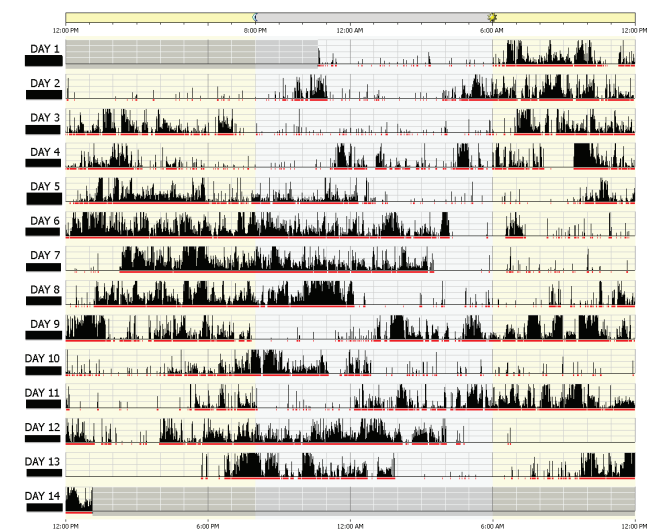
(A) Computerized tomography of the head showing damage of the optic nerves bilaterally following a gunshot wound to the right temple. Note bone fragments along the bullet path across the suprachiasmatic area. (B) Axial T2 weighed magnetic resonance imaging (MRI) of the head showing bilateral optic nerve hyper-intensities consistent with nerve damage (circles). (C) Sagittal T1 weighted MRI of the head. The optic chiasm (arrow 1) forms the anterior boundary of the hypothalamus. The infundibulum (arrow 4) to the pituitary gland (arrow 3), and the mammillary bodies (arrow 2) form the inferior boundary of the hypothalamus. The optic chiasm appears thinned along with the adjacent hypothalamus.

**Figure 3**—Hypnogram showing multiple nocturnal awakenings not well identified by actigraphy alone.

SpO2, pulse oximetry; HR, heart rate; OA, obstructive apneas; CA, central apneas; MA, mixed apneas; HYPO, hypopneas; Pos, sleep position; S, supine sleep position; R, right lateral decubitus sleep position; L, left lateral decubitus sleep position; MIC, microphone; LegMvt, leg movements.

from the SCN, has shown disruption of sleep and activity cycles without affecting body temperature. Damage to the dorsal sub-paraventricular zone, which receives a smaller number of projections from the SCN, has shown to affect body temperature, with a lesser effect on sleep or activity level.<sup>6</sup>

We speculate that the damage of the SCN or adjacent nuclei after optic nerve transection bilaterally resulted in posttraumatic ISWR. The International Classification of Sleep Disorders, second edition (ICSD-2) criteria for diagnosis of ISWR

**Figure 2**—Two-week actigraphy does not show three distinct bouts of sleep as required by current criteria for Irregular Sleep Wake cycle.

disorder include: complaints of insomnia, excessive sleepiness, or both; at least one week of actigraphy or sleep logs demonstrating at least 3 irregular bouts of sleep during a 24-hour period; a normal for age sleep time over a 24-hour period; and exclusion of drugs, medications, mental disorders, neurological conditions, or other medical diagnosis.<sup>7</sup>

The criteria are based on the irregular sleep wake data patterns of elderly patients with Alzheimer disease, which may or may not all qualify for true irregular sleep wake cycle due to degeneration of the SCN. A revision of the criteria may be necessary after new case reports such ours are found in the literature. Our patient does not fit criteria by actigraphy alone, since actigraphy does not show evidence of at least three distinct bouts of sleep. However, concomitant PSG shows multiple sleep-wake transitions that would qualify for ISWR. The absence of multiple awakenings on the actogram could be secondary to low actigraphy sensitivity and is better demonstrated on PSG.

The current practice parameters for evaluation of circadian sleep disorders recommend the use of circadian markers (melatonin secretion) when free-running sleep disorder is suspected in both sighted and unsighted individuals, but there are insufficient data to recommend their use in other circadian disorders (suspected irregular sleep cycle). Melatonin secretion analysis was not performed in our patient.<sup>8</sup>

Treatment of ISWR entails: exposure to bright light during the day; avoidance of bright light in the evening/night; and structured physical/social activity across the 24 hours. Given that our patient has severely damaged optic nerves, normal cognition, and is able to perform her activities of daily living, we utilized treatment approaches typically reserved for blindness associated free-running type circadian rhythm sleep disorder. These included use of 1 mg of melatonin 1 hour before bedtime, and maintenance of rigid sleep time and wake time.

We also recommended a fixed wake/sleep schedule combined with planned daily social activities. Treatment success for this ISWR has been variable. Our patient continues to experience

fragmented sleep all day and was not able to maintain the recommended schedule. Alerting medications were considered, but the patient declined.

We propose that the damage of the SCN or adjacent nuclei in our patient is responsible for the lack of response to typical treatments of circadian rhythm disorders. We will continue to stress the importance of daily social activities. This case demonstrates the importance of an intact SCN in circadian regulation. When not intact, zeitgebers have limited utility.

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## DISCLOSURE STATEMENT

This was not an industry supported study. This case was presented during the SLEEP meeting, Brown Bag Challenging Cases, Baltimore, 2014. The authors have indicated no financial conflicts of interest. The authors report no off-label/investigational drug uses regarding this manuscript.