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require one of the aforementioned two elements in some patients and both in other patients. Our patient demonstrated presence of both factors; therefore, it is difficult to strongly favor one factor over the other. This may partly explain the rarity of this abnormal MRI finding among patients with epilepsy.

Our MRI and EEG data suggest that rapid AED reduction could have caused AVP levels to increase abruptly, producing transient focal ischemia evident by cytotoxic edema. However, we cannot exclude the effect of frequent seizures. Future MRS studies may help to differentiate seizure-related signal abnormalities on MRI from the effect of AEDs.

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Abstract—The authors report the case of a 39-year-old sighted woman who displayed non-24-hour sleep–wake cycles following a car accident. The phase relationship between endogenous circadian markers such as plasma melatonin and 6-sulfatoxymelatonin rhythms and self-selected sleep times was abnormal. A laboratory investigation indicated that she was sensitive to bright light as a circadian synchronizer. MRI and brain CT scans were normal, but microscopic brain damage in the vicinity of the suprachiasmatic nucleus or its output pathways is plausible.

Sleep disruption following traumatic brain injury has been reported in as much as 50% of patients with brain injury.[1] A few cases of delayed or longer-than-24-hour sleep–wake cycles have been observed in sighted patients following traumatic brain injury.[2-5] The origins of these disturbances are unclear. We report the circadian evaluation of sleep–wake disturbances in a patient following head injury.

Case report.   In March 2000, a 39-year-old woman was referred to our sleep clinic by her neurologist for severe and cyclic sleep disturbances. Her medical history was notable for migraines since age 25, managed with valproate 375 mg BID as prophylaxis and oral morphine 5-mg tablets about once per week.

In 1991, she was the seatbelted driver of a car struck from behind at moderate speed by another car. She probably experienced a brief loss of consciousness and had 1 to 2 hours of anterograde amnesia. When assessed in the emergency room, she had headache and could not remember her telephone number or the

date. Her neurologic examination was otherwise normal. She was discharged with a diagnosis of concussion. Neuropsychological testing in the following months showed globally impaired cognitive function, with deficient verbal and nonverbal memory. After 2 years of rehabilitation, tests showed improvement in most spheres, except nonverbal memory. She nevertheless remained unable to return to her professional activities. The patient also reported episodes of altered behavior and amnesia, suggesting partial seizures. Multiple wake and sleep EEG, ophthalmologic examination, and CT and MR scans of the brain were all normal.

Following the accident, the patient had altered consciousness, memory troubles, difficulty concentrating, and chronic fatigue. Two years after the accident, she was unable to maintain stable sleep times and increasingly delayed her bedtime. Attempts to adopt a regular sleep schedule led to nighttime sleep disruption and daytime sleepiness that resulted in a worsening of her headaches. When she followed her natural tendency to live on "longer-than-24-hour days," she experienced some relief from her sleep disruption.

Four years after the accident, the patient had a brief depressive episode with suicidal ideation. Repeated psychiatric evalua-
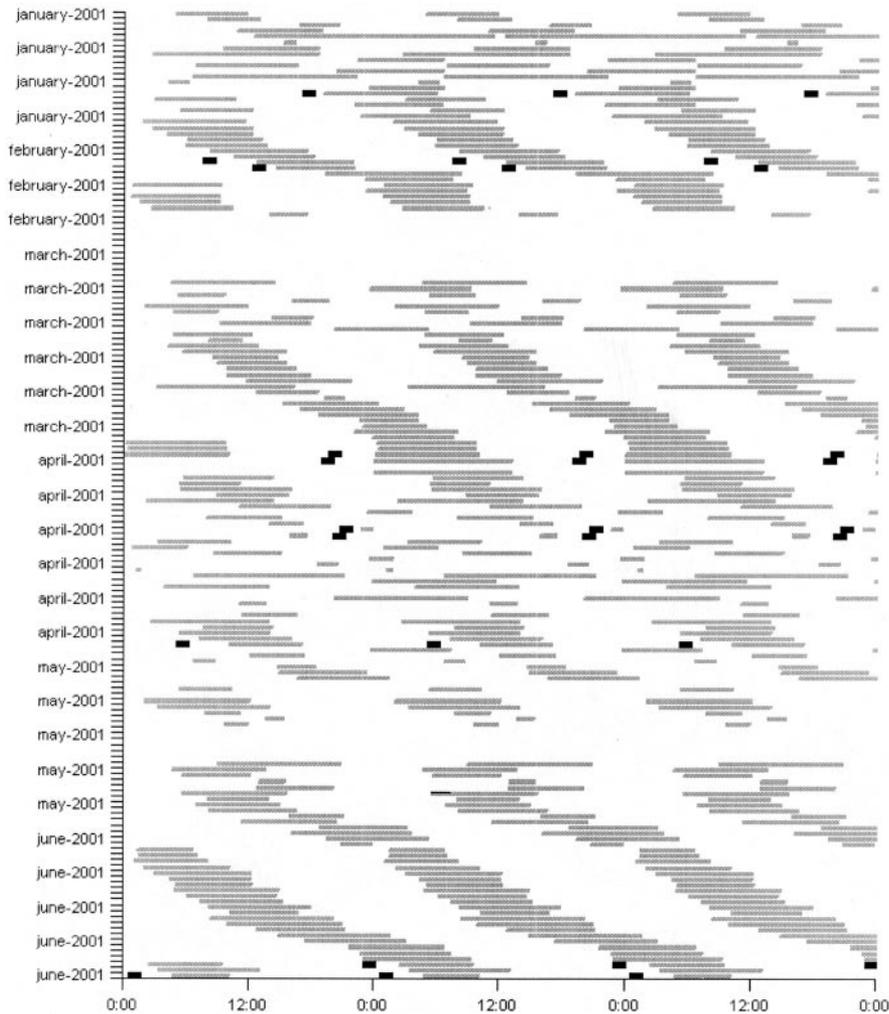
Figure 1. Sleep–wake cycles of our patient. Sleep episodes are shown as gray bars and are triple-plotted for clarity, with successive days appearing both side by side and along the vertical axis. Detectable levels of urinary 6-sulfatoxymelatonin were found where indicated by black squares.

tions suggested a schizoid and borderline personality disorder. At the time of referral for her sleep problems, the patient was cooperative and pleasant.

Methods. An interview conducted by a sleep disorder physician suggested the presence of a circadian rhythm disorder based on her tendency to delay the timing of her sleep episode later from one day to the next. No symptoms suggestive of sleep apneas/ hypopneas or parasomnias were presented. The patient kept a detailed sleep diary for over 6 months, and sleep times were confirmed by wrist actigraphy recording throughout this period (Mini Mitter, Bend, OR). She refused the recording of core body temperature both at home and in the laboratory. To reliably assess circadian phase at home, we collected urine samples on several occasions to measure its content in 6-sulfatoxymelatonin (6-OHMS; Stockgrand, Surrey, UK). Progression of the menstrual cycle was not documented throughout the study, although the patient was still premenopausal. The levels of thyroid-stimulating hormone, complete blood cell count, liver, kidney, and blood lipids were normal.

To determine the patient's sensitivity to bright light, she was admitted for a 3-day investigation in a windowless room equipped with ceiling-mounted banks of cool-white fluorescent fixtures. All sleep episodes took place in total darkness (about 0.03 lux) and were polysomnographically recorded according to a standard method.

Upon admission, the patient remained in very dim ambient light (≤10 lux) until bedtime. Blood samples destined for the assay of melatonin concentration (Stockgrand) were drawn once per hour for 50 consecutive hours. Throughout her stay, she was allowed to choose her sleep times. Four hours after the beginning of her second sleep episode, the patient was awakened for a melatonin suppression test,[6] during which ambient light intensity was

raised to approximately 10,000 lux over a 90-minute period. At the end of the test, she resumed sleep in darkness. Upon awakening, she remained in bright light of about 2,500 lux until she went to sleep for a third and final episode. This schedule of bright light exposure was designed to optimize the chances of inhibiting melatonin secretion—the precise timing of which was initially unknown.

Results. The patient demonstrated an irregular sleep–wake pattern with a tendency to delay bedtimes from one day to the next (figure 1). Peak 6-OHMS urinary excretion was observed at different clock times during the ambulatory period and tended to free-run according to a longer-than-24-hour day.

In the laboratory, the patient slept from 00:01 to 11:04 hours during her first night. Total sleep time was 10:29 hours, sleep efficiency was within normal limits (98%), and REM sleep latency was short (56 minutes). Her bedtimes on subsequent nights were 03:24 and 02:46 hours.

Melatonin secretion was robust under dim light conditions (peak value 137.6 pg/mL, 8.24-hour duration of secretion exceeding midline) but was undetectable during periods of bright light exposure (figure 2). The patient displayed a tendency to sleep in the declining phase of her melatonin secretion curve where the midpoint of peak melatonin concentration occurred 3.9 hours before the start of her sleep episode.

Discussion. This investigation revealed the free-running sleep–wake cycle and the endogenous circadian pacemaker in this patient. Previous investigations have demonstrated that visual pathways and those for circadian entrainment can be dissociated.[6] However,
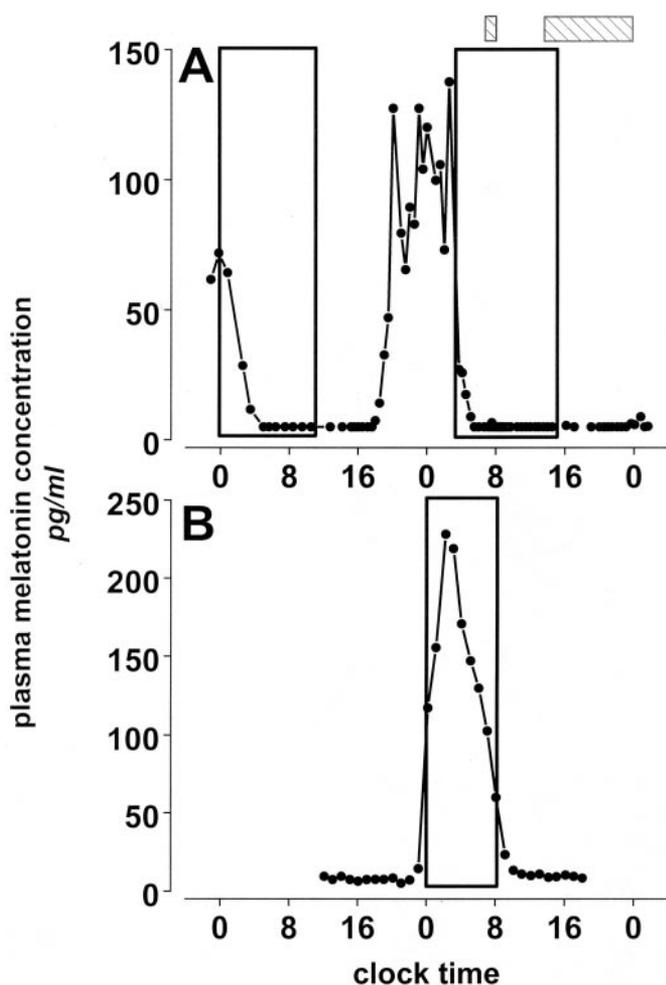
Figure 2. Rhythm of plasma melatonin secretion relative to projected sleep episodes for the patient as determined during a 4-day laboratory observation (A) and for a healthy 22-year-old man as determined under constant dim light conditions (B). Periods of exposure to bright light are indicated with hatched bars, and projected times of sleep are shown as open rectangles. In the patient, the peak occurrence of melatonin secretion occurs during the waking episode (upper panel). In the healthy subject, peak melatonin concentrations occur in the middle of the projected sleep episode.

the absence of melatonin secretion during the melatonin suppression test or the third waking episode under approximately 2,500 lux suggests that this patient remains sensitive to bright light as a circadian synchronizer. Circadian blindness to light would have resulted in detectable and rising levels of melatonin from 18:00 hours on the last day of investigation. However, we cannot exclude a reduced sensitivity to light of lower intensities.[7]

The delay in reporting sleep–wake cycle disturbances raises some concerns regarding the causal relationship with the car accident. Nevertheless, the patient's life was disrupted following her car acci-

dent, and it is conceivable that it took her several years to acknowledge her tendency to delay her sleep schedule from one day to the other. Previous cases of non-24-hour sleep–wake syndromes have been reported following traumatic brain and neck injuries. For instance, delayed sleep phase syndrome (DSPS), a predisposing condition for non-24-hour sleep–wake syndrome, has been described following vehicle accidents with coma[2,3] or head and neck injuries.[4] A series of 16 cases of DSPS following rear-end car collisions and minor brain–neck trauma has also been reported.[5] In all reports, neurologic exams were unremarkable,[2-5] except for one case of mild cerebral atrophy.[3]

The absence of detectable brain lesions on MR and CT scan in our patient does not exclude microscopic brain damage[8] in the vicinity of the suprachiasmatic nucleus (SCN), the master component of circadian rhythms. A case of a 34-year-old woman who developed an irregular sleep–wake pattern following surgery for a tumor encasing the optic tract has been reported.[9]

The tendency displayed by our patient to initiate sleep later in the endogenous curve for melatonin secretion is consistent with earlier studies.[10] This observation raises the possibility that output pathways from the SCN to sleep and waking promoting centers are affected. As suggested from neck injury cases, disruption of the indirect pathways from the SCN to the pineal gland is also possible.[4] We cannot exclude a psychological contribution to our patient's sleep disorder, yet she reported no such sleep difficulties prior to the car accident.

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