Chronic Behavioral Disorders of Human REM Sleep: A New Category of Parasomnia

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Summary: Four men, aged 67-72 years, had 4-month to 6-year histories of injuring themselves or their spouses with aggressive behaviors during sleep, often during attempted dream enactment. A 60-year-old woman had disruptive though nonviolent sleep and dream behaviors. Polysomnography did not detect seizures but did document REM sleep pathology with variable loss of chin atonia, extraordinarily increased limb-twitch activity, and increased REM ocular activity and density. A broad range of REM sleep behaviors was recorded on videotape, including stereotypical hand motions, reaching and searching gestures, punches, kicks, and verified dream movements. Stage 3-4 slow wave sleep was elevated for age in all patients. NREM sleep was devoid of harmful behaviors, although three men had periodic myoclonus. There was no associated psychiatric disorder, whereas serious neurologic disorder was closely associated in four cases: olivo-ponto-cerebellar degeneration, Guillain-Barré syndrome, subarachnoid hemorrhage, and an atypical dementia. Two patients had immediate and lasting sleep behavioral suppression induced by clonazepam, and another patient had the same response with desipramine. All instances of drug discontinuation prompted immediate relapse. In four cases there was associated dream hyperactivity, which resolved with behavioral control. These REM sleep neurobehavioral disorders constitute another category of parasomnia, replicate findings from 21 years ago in cats receiving pontine tegmental lesions, and offer additional perspectives on human behavior, neurophysiology, pharmacology, and dream phenomenology. Key Words: REM sleep—Parasomnia—Behavioral disorders—Neurological disorders—Geriatric disorders—Dreams—Clonazepam—Desipramine.

During a two-year period, we identified five patients with similar behavioral disturbances during REM sleep associated with variable loss of chin and limb electromyographic (EMG) atonia. Four elderly men inflicted injuries on themselves and their spouses while asleep, most notably during attempted dream enactment. A 60-year-old woman shared many of the behaviors demonstrated by these men and had numerous REM-related arousals.

REM sleep is defined electrographically by an activated electroencephalogram.

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(EEG), atonic submental EMG, and phasic REMs (1). The Diagnostic Classification of Sleep and Arousal Disorders (2) does not include a category of parasomnia involving skeletal motor disturbances during REM sleep.

**CLINICAL HISTORIES**

**Patient 1**

A 67-year-old dextral man was referred because of violent behavior during sleep. His previous medical history was remarkable for duodenal ulcers and cholecystectomy but not for a psychiatric disorder. He had slept uneventfully through adolescence in a small room with three brothers. But on his wedding night, his wife was "scared with surprise" over his sleep talking, groaning, tooth grinding, and minor body movements. This persisted without consequence for 41 years until one night, 4 years before referral, when he experienced the first "physically moving dream" several hours after sleep onset; he found himself out of bed attempting to carry out a dream. This episode signaled the onset of an increasingly frequent and progressively severe sleep disorder; he would punch and kick his wife, fall out of bed, stagger about the room, crash into objects, and injure himself. These harmful behaviors, most prominent every 10th night, typically appeared several hours after sleep onset and never within the first hour. There was never any nocturnal urinary or fecal incontinence or tongue biting, and he quickly became alert with each awakening. In search of sound sleep, his wife began to sleep in another room 2 years before referral. They remain happily married, believing that these nocturnal behaviors are out of his control and discordant with his waking personality. An example of a recurring dream consisted of his delivering a speech and emphasizing certain points with his right hand from which he awakened sitting up with right arm outstretched and fingers pointing in a manner consistent with the dream action. What follows are some tape-recorded dream recollections.

"I was on a motorcycle going down the highway when another motorcyclist comes up alongside me and tries to ram me with his motorcycle. Well, I decided I'm going to kick his motorcycle away and at that point my wife woke me up and said, 'What in heavens are you doing to me?,' because I was kicking the hell out of her." In the dream, he saw clearly, heard nothing, and felt fear of being rammed.

"I had a dream where Someone was shooting at me with a rifle and it was in a field that had ridges in it, so I decided to crawl behind a ridge—and I then had a gun too—and I look over the ridge so when he showed up I would shoot back at him and when I came to (i.e., awakened) I was kneeling alongside the bed with my arms extended like I was holding the rifle up and ready to shoot." As in the previous dream, the vision was clear, he heard no sound, and he felt "scared silly."

His most vivid dream was described in this manner: "I was a halfback playing football, and after the quarterback received the ball from the center he lateraled it sideways to me and I'm supposed to go around end and cut back over tackle and—this is very vivid—as I cut back over tackle there is this big 280-pound tackle waiting, so I, according to football rules, was to give him my shoulder and bounce him out of the way, supposedly, and when I came to I was standing in front of our dresser and I had knocked lamps, mirrors, and everything off the dresser, hit my head against the wall and my knee against the dresser." In the dream he fully experienced the sensation of motion while running and had very clear vision, but there was no awareness of sound until he knocked objects off the dresser and awakened to the crash.
Finally, one night he dove into a bedside dresser and cut himself. This prompted medical evaluation of his sleep disorder, which initially entailed an unremarkable psychiatric interview before he was referred to our sleep center. His initial polysomnographic (PSG) evaluation, which included an extensive scalp EEG montage, did not detect ictal activity but did reveal intermittently augmented EMG activity and intermittent complex behaviors during REM sleep. During a 15-s interval occurring 7 min after onset of the first REM period (REMP), he flung his right arm up and out as if he were casting a fishing line. Frequent jerky movements of all extremities and brief vocalizations characterized the second and third REMPs. NREM sleep was without EMG abnormality.

Treatment focused on securing a safer sleeping environment and on suppressing REM sleep, but imipramine, desipramine, and nortriptyline were not tolerated. He was restudied (on 12/21/82) and complex behaviors during REM sleep were again observed. In addition, periodic NREM sleep myoclonic EMG activity was detected and was also found during all subsequent PSG studies. An effort was made (on 12/22/82) to correlate observed sleep behaviors with dream recall. Fig. 1 illustrates how the closest association occurred during a NREM transitional sleep stage. REM sleep behaviors were never inconsistent with reported dream activity.

Alprazolam, 0.5 mg h.s., gradually reduced vigorous sleep behaviors, but after 8 months PSG studies (8/15 and 8/16/83) confirmed the return of symptomatic REM behaviors that persisted in spite of increasing doses of alprazolam. Clonazepam, 0.5 mg h.s., then immediately restored restful sleep for 8 months until it was discontinued 2 weeks prior to follow-up PSG studies (on 5/30 and 5/31/84), which again showed excessive REM sleep limb twitch activity and gross behaviors that were episodically

![FIG. 1. Polygraphic correlates of an attempted dream enactment by patient 1, as recorded on videotape. Forty-seven minutes after onset of the first REMP and 40 min after its offset, phasic REMs (channels 1 and 2) mark the transition from stage 4 (slow wave) sleep into stage 2 (spindle) sleep (A) that has some intermixed electroencephalographic desynchronization (channels 3–6). A behavioral sequence (C) commences with a REM and consists predominantly of right arm shaking and pounding followed by a pause (D), which is terminated by further right arm pounding, then flexion of that arm as the patient turns toward his left side while making an abortive effort to lift himself up from the bed (E). When an examiner appears 20 s later, the patient reports having just dreamed of holding a dog or cat in his right arm to restrain it from jumping away, but when it escaped he turned to his left side in an unsuccessful attempt to capture it. Chin electromyogram (EMG) (channel 7) has tonic suppression and phasic activations, the electrocardiogram (EKG) (channel 8) demonstrates occasional PVCs, and the limb EMG (channel 9) shows persistence of periodic myoclonus (B) preceding dream movements. Respirations (channel 10) show irregularity during muscular activity. These tracings depict a dissociated state for which there is a neurophysiological model (see reference 3).]
violent. When clonazepam was restarted, it again was immediately effective; only three nonviolent episodes occurred during the next 11 months. The current nightly dose is 1.0 mg h.s.

The patient has also complained of occasional “dizziness” restricted to sleep. For example, “In one dream I was trying to get up to reach for something, but it was as if I were inebriated; I could not get up because of my disequilibrium. Then I told myself in the dream, that if I shake my head enough, then the dizziness would go away and then I could get up and reach for what I wanted. When I awakened, I was shaking my head while my body was on the floor and my arms were on the bed as if I were actually reaching for something. The dizziness then immediately stopped.”

The results of several neurological examinations have been unremarkable, apart from the findings of a mild peripheral neuropathy. Brainstem auditory evoked responses (BAERs) were normal on three occasions during a 2-year, 9-month period (from 12/82 to 9/85). Somatosensory evoked responses (SSERs) suggested mild peripheral disturbance without central abnormality on two occasions during the same period. A computed tomographic (CT) scan of the brain was normal. Numerous psychiatric interviews have consistently found a dapper, pleasant, well-adjusted man enjoying retirement. He is considered to have an idiopathic REM sleep disorder.

Patient 2

A 60-year old woman was hospitalized (in 5/84) with a 2-week history of progressive weakness and sensory loss involving all her limbs. She had contracted an upper respiratory infection 1 month prior to admission. Examination disclosed mild dysarthria and a peripheral facial weakness on the left, but no other cranial nerve abnormalities. Diffuse muscular weakness, complete areflexia, and distal sensory loss in all limbs were also found. She could neither stand nor walk without assistance, and was ataxic. A Romberg test gave positive results. A lumbar puncture for cerebrospinal fluid showed a leukocyte count of 1/ml and a protein count of 111 mg/dl, but other laboratory studies, including serology tests, were unrevealing. Acute polyradiculitis (Landry-Guillain-Barré syndrome) was diagnosed. The patient did not require ventilatory support during her hospitalization.

Distinct changes in sleep and dream experience closely paralleled the onset, progression, and resolution of this neurological disorder. Diminished diurnal alertness coincided with frequent nocturnal arousals, often interrupting dreams that had become, in her words, “very active” in two regards. There was a definite increase in the amount and sustained duration of physical activity on the part of the dream characters. Also, she noticed upon awakening from a dream that her limbs appeared to have been moving, although she never fell out of her bed or hurt herself. She had not previously experienced a similar sensation upon awakening.

Medical history included alcoholism, hypertension, and osteoarthritis, but no prior sleep or major psychiatric disorders. Her primary physician unsuccessfully prescribed amitriptyline, 50 mg h.s., in an attempt to treat her complaint of disrupted sleep while she recovered from the polyradiculitis.

A PSG study was performed (on 5/19/84) because obstructive sleep apnea was suspected, but there was minimal oxygen desaturation by ear oximetry, and the apnea index was only 12/h. However, REM sleep was marked by complex movements of the upper extremities, some of which corresponded to dream content. At 6:27 a.m., the
technician believed she was awake and "exercising" in bed, but his speaking to her caused an unexpected arousal from sleep. She was instantly alert and mentioned that she was just dreaming of shoveling snow. In fact, the preceding minutes had been filled with moderately vigorous upper extremity movements that were consistent with her dreamed snow-shoveling activities. Her REM sleep also contained lengthy periods of stereotypical searching and reaching gestures, hand waving, and arm flailing. There were no vocalizations nor affective displays. This woman refused a multiple sleep latency test (MSLT) to evaluate her complaint of diminished diurnal alertness. During the next 3 months she experienced gradual improvement without specific treatment, to the point of full restoration of neurological functioning and return of sound and inactive sleep, customary dreams, and sustained diurnal alertness. She is unavailable for follow-up sleep study.

Patient 3

A 72-year-old, right-handed, retired farmer, without history of psychiatric disorder or aggressive tendencies, developed vigorous and at times dangerous sleep behaviors in conjunction with the onset of a neurological disease 2 years before referral. The sleep and neurological disorders initially progressed in tandem. His wife complained of increasingly "wild dreams," which occurred throughout most nights. During the dreams he would punch and kick her, strike at walls and furniture, thrash about the room with limbs jerking, talk, shout, and engage in other complex behaviors. His vocalizations suggested considerably high levels of physical activity in his dreams. His hands would feel sore after a night of pounding on the walls. When awakened during these nocturnal episodes, which had no diurnal counterpart, he would be alert and conversant; there was never any urinary or fecal incontinence or tongue biting. Nevertheless, before referral he had been treated for nocturnal seizures with diphenylhydantoin and phenobarbital, which were ineffective. There was no history of fatigue. His brother had been diagnosed as having "parkinsonism," which the patient was also initially believed to have.

Neurological examination on referral detected dysarthria, limited vertical gaze, jerky pursuit movements of the eyes, bilateral static and intentional tremor, diffuse but asymmetrical hyperreflexia (L > R), left extensor plantar response, diminished vibratory sense, bilateral dysmetria and dysdiadochokinesia, and ataxic gait. CT brain scan showed cerebellar atrophy. BAERs performed elsewhere revealed prolongation of the I–III interpeak latency on the right side and no reproducible tracing with stimulation of the left ear. Several waking EEGs were normal. Previous digital venous and standard arterial angiographies were normal. Blood chemistry and serology determinations were repeatedly normal. Therefore, the clinical and CT findings were consistent with the diagnosis of olivo-ponto-cerebellar degeneration, and the abnormality of the BAERs also indicated pontine dysfunction.

PSG evaluation (Fig. 2) did not detect seizures but did reveal a prominent abnormality restricted to REM sleep. The patient showed searching and reaching gestures, hand waving, punches, turning in bed, kicks, generalized nonrhythmic twitches and prominent jerking. He also moaned, laughed, snickered, and chanted briefly. The result of an MSLT was normal. Fifteen months later, the family reported that the sleep behaviors had diminished markedly in concert with further neurological deterioration. He still talked aloud nonsensically during sleep.
FIG. 2. Nocturnal polysomnogram during onset of the first REMP in patient 3. This 30-s interval has continual, high-amplitude REMs (channels 1 and 2), which began abruptly 16 s earlier and which persist for another 84.5 s before terminating abruptly. Electroencephalogram (channels 3–5) shows tonic activation. Chin electromyogram (EMG) has very high tone with phasic accentuations. As recorded on videotape, at 2:56:47 a.m. (large arrow) the legs suddenly display running activity while the supine patient is waving the right arm high over his head and vocalizing loudly and strangely. Timing of the left and right anterior tibialis EMG twitching (channels 7 and 8) matches precisely the timing of the observed behaviors. Behavioral and EMG activities cease at 2:56:57 a.m. (small arrow). Regular electrocardiographic (EKG) rate of 78 speaks against a conventional arousal.

Patient 4

A 70-year-old, right-handed, retired farmer was referred 4 months after the sudden onset of violent nocturnal behaviors, which occurred as late as 7 a.m. but never within 1 h of sleep onset. While moaning, he would punch and kick his wife during as many as five distinct episodes within any given night. There were never more than 3 consecutive nights without such activity. Once he flung himself out of bed and incurred a facial injury. On another occasion he attempted to strangle his wife while dreaming of fending off a mauling bear. She was convinced that his dreaming had become more action-filled, especially with running and fighting. There was never nocturnal incontinence or tongue biting. He developed excessive daytime sleepiness and took naps that were not physically restless. His wife previously had observed long-standing sleep moaning and diffuse body jerking, traits he shared with his mother, sister, and son. There was no psychiatric history; his wife commented on his gentle nature.

The onset of progressive memory failure coincided with onset of the sleep disorder. A CT scan showed mild cerebral atrophy. Waking EEG demonstrated no seizure activity. The result of a neurological examination was normal except for anterograde memory deficit. PSG study (Fig. 3) did not detect seizures but did confirm the clinical suspicion of REM sleep behavioral disorder with variable release from EMG atonia. The patient showed intermittent stereotypical searching and reaching gestures, waving of the hands, punches, kicks, moans, and diffuse body jerks of variable intensity. Desipramine, 50 mg h.s., immediately suppressed vigorous sleep behaviors and restored diurnal alertness. Occasional failure to take this medication resulted in same-night relapse. At 12-month follow-up, he still frequently vocalized and had minor limb twitching in his sleep. However, his family had noticed progressive spatial disorientation, even in familiar places. He had also developed increasing difficulty in buttoning clothes and tying shoelaces, and his dancing skills had considerably diminished. Neurological examination revealed normal associated movements. There was diffuse hyperreflexia, including prominent ankle jerks with an upgoing right toe. There was no tremor and only minimal cogwheeling with augmentation. BAERs, CT brain scan, and magnetic resonance imaging (MRI) brain scan were normal. Neuropsychological testing indicated low-average verbal ability, consistent with his eighth-grade education,
FIG. 3. Nocturnal polysomnogram during the second REMP in patient 4. Prominent right arm electromyographic (EMG) twitching (channel 6) corresponds to concurrent waving of that limb, as seen on videotape. High-amplitude REMs are present (channels 1 and 2). Chin EMG has elevated tone with phasic accentuations. Leg EMGs (channel 7 and 8) are atonic for most of this interval and display minimal twitching relative to the arms and chin EMG. Electrocardiogram (EKG) has a tonic rate of 70. Nasal airflow shows typical REM irregularity. Electroencephalographic montage (channels 11–18) detects no seizure activity and shows typical REM sleep tonic activation.

on an abbreviated form of the Wechsler Adult Intelligence Scale—Revised (WAIS–R). In contrast, the performance subtests (picture completion = 7, block design = 3, object assembly = 4, digit symbol = 4) suggested severe visuospatial impairment. Immediate and delayed recall of nonverbal (figural) material was severely impaired. Immediate recall was average on the first prose passage and moderately impaired on the second. Wechsler Memory Scale (WMS) quotient of 95 was within the normal range. Tasks of automatic speech and conceptual tracking elicited numerous errors. Verbal associative fluency was average. Porteus maze test performance was in the low-average range, with an estimated test age of 11.5 years and a quotient of 82. The results suggested generalized brain dysfunction, with perhaps greater involvement of the non-dominant hemisphere as indicated by severe impairments of visuospatial abilities and figural memory. This pattern suggested an atypical dementing process.

Patient 5

A 70-year-old dextral man was seen 6 years after a spontaneous subarachnoid hemorrhage, confirmed by lumbar puncture, triggered the sudden onset of wild sleep behaviors and "active dreams". During this hospitalization, meningismus and an equivocal toe sign were the only neurologic abnormalities. Arteriography failed to disclose the source of bleeding. Recovery of waking neurological functioning was unremarkable, apart from persistent memory impairment and penile impotence with preserved ejaculatory capacity. The altered dreaming also persisted ("chasing or being chased by animals and people"), and vigorous, often violent, dream-enacting behaviors intensified. Fear of injury soon led him to tie a rope around his waist and secure it to the bed; but, he regularly managed to escape and continued to suffer injuries. Violent sleep behaviors initially occurred once weekly but eventually occurred four times weekly, usually beginning 2 h after sleep onset and never within the first hour of sleep. When awakened by a collision or injury, he would be alert. He was aroused more easily by an auditory stimulus than by a tactile stimulus. Once he grabbed his wife's neck with both
hands while dreaming that he had just staggered a deer with a blow to its head and was going to break its neck, which was, in fact, his wife’s neck. Since then, his wife has generally slept apart from him. Nocturnal seizures originally were suspected; but, phenobarbital was ineffective and had been discontinued before our evaluation.

This man’s dreaming had generally been pleasurable with diverse content before the subarachnoid hemorrhage, but afterwards, in association with vastly increased dream motor activity, anger became the predominant emotion, usually preceded by “feeling scared” during a frightening dream situation. During taped interviews, he recalled the most eventful dreams:

“Somebody was after me and I figured my only escape was to jump through a window, so I got up and I jumped... and I hit the wall and the dent is still in there like a soup bowl. Then I fell down on the baseboard heater along the radiator. I evidently jammed a foot under there and split my big toe because of all the sharp ends, and then I hit my mouth on there and split it right down the front and loosened up my teeth. That was one of the worst ones [dreams].” During a similar dream episode he cut his foot and could not wear a shoe for several weeks. Subsequently, on 3 consecutive nights, during typical dreams of being pursued, he jumped from the bed and landed head-first onto the floor; the first night he also cut his left elbow on the dresser, the second night he also gashed his left knee and the third night he also bruised his right knee.

A former tavern owner and alcoholic, he has been abstinent for 28 years and is now a retired real estate agent. There is a history of angina and arthritis. Examination at our center showed him to be pleasant and outgoing, with mildly impaired anterograde memory, bilateral intention tremor, hyperreflexia (L > R) except for diminished ankle jerks, bilateral plantar extensor responses, and decreased vibratory sensation of the feet. His BAERs indicated peripheral hearing loss with normal central conduction; SSERs and MRI brain scan were normal. Blood chemistries, thyroid function tests, and vitamin B12 level were normal.

Seizures were not detected during two PSG studies (11/26 and 11/27/84). Periodic myoclonus was distributed throughout the nocturnal NREM sleep periods. Strain gauges detected negligible nocturnal penile tumescence. On both nights, the patient exhibited frequent REM sleep behaviors, including minor twitches and prominent jerks of all body parts, hand waving, searching and reaching gestures, punches, arm swinging, kicking, angry shouts, moans, chuckles, laughs, and quiet words. His behaviors often suggested heated conversations; he would point a threatening finger and motion with his arms while making angry remarks.

Treatment with desipramine only briefly (3 weeks) suppressed his problematic sleep behaviors and hyperactive dreaming, although the dosage was increased to 250 mg with serum levels in the high therapeutic range. Alprazolam was temporarily prescribed to control the symptoms of a 2-month Adjustment disorder with mixed emotional features [ref (4), code 309.28], but it had no impact on the sleep problem. After desipramine was discontinued, lithium carbonate was not tolerated, but clonazepam produced immediate relief, which has lasted 8 months. Abnormal sleep behavior has reappeared on the nights he has not taken clonazepam. On his current dose of 1.5 mg h.s., he considers his sleep to be as sound as before the subarachnoid hemorrhage.

The neurological findings, BAERs, and SSERs did not change at testing 10 months later. Neuropsychological testing revealed average verbal and perceptual functioning on an abbreviated WAIS. There was a normal memory quotient score of 88 on the
WMS. On a nine-word list learning task he learned all the items in three trials. After a 45-min delay, only 33% of the items were spontaneously recalled. When presented with a longer list containing filler items, he recognized 66% of the items. Performance of motor tasks demonstrated slightly slowed fine manual dexterity skills. The test results argue against prominent neuropsychological dysfunction, although there were moderate long-term and mild short-term memory deficits.

METHODS

Sleep laboratory data

In all patients, polysomnography was performed during their routine sleeping hours. Nocturnal behaviors were continuously recorded on 1/2-in videotape while a technician made direct visual observations that were noted directly on the polysomnogram or on separate paper. A 13-channel Grass Model 78 polygraph or a 19-channel Grass Model 8 electroencephalograph was used to record continuous activities of the EEG, electrooculogram (EOG), EMG (chin and 1–4 limbs), electrocardiogram (ECG), nasal air flow, and respiratory effort.

The standard EEG paper speed was 10 mm/s except for one night’s recording of patient 5, when speeds of 15 mm/s and 30 mm/s were also used. Several EEG montages were used, all of which included the standard electrode placements for sleep recording (C3 and C4).

BAERs

During each recording session, patients were seated in a quiet room. Monaural stimulation was given on each side, using a click signal at 60 dB above threshold for click perception. Rarefaction clicks were used. Stimulus rate was 11.1 clicks/s. Each trial averaged 2,000 responses, and at least two trials were obtained to insure reproducibility. Three channels were acquired: vertex to ipsilateral ear, vertex to contralateral ear, and ipsilateral ear to contralateral ear. Absolute and interpeak latencies of waves from I, III, and V were measured and compared with normal values established by use of identical procedures in 30 normal subjects in the same laboratory.

SSERs

The median nerves were independently stimulated at the wrist at a stimulus rate of 5.1/s using a current sufficient to produce a thumb twitch. In each trial, 1,024 repetitions were obtained; multiple trials assured reproducibility. Three channels were recorded: ipsilateral Erb’s point to FZ, CII cervical vertebra to FZ, and contralateral central parietal scalp to FZ. Absolute and interpeak latencies for N-10 over Erb’s point, N-14 over CII cervical vertebra, and N-20 over the contralateral central parietal scalp were measured and compared with results obtained by use of the same procedures in 20 normal subjects tested in the same laboratory using identical parameters.

MRI brain scan

The technique yielded spin echo images. Pixel size was 1.2 mm. For patient 4 there was mixed T1 and T2 weighting, whereas for patient 5 there was predominantly T2 weighting. Patient 4 had 10-mm axial cuts with repetition time (TR) of 1.9 s and echo time (TE) of 35 and 70 ms. There were also three 10-mm sagittal midline cuts with TR of 0.5 s and TE of 30 ms. Patient 5 had 10-mm axial cuts with TR of 1.9 s and TE of 35 and 70 ms. There were also 5-mm sagittal cuts with TR of 1.5 s and TE of 35 and 70 ms.
RESULTS

Tables 1 and 2 list results derived from the standard sleep-stage scoring system of Rechtschaffen and Kales (1), which was modified to allow REM sleep to be scored without requiring the presence of EMG atonia. Basic sleep architecture was intact. Phasic REMs and characteristic desynchronized EEG (often with saw-toothed waves), were present in all REM epochs for all patients; the variably augmented EMG was the only unusual feature. Although release from the normal atonia of REM sleep was common, it was a fluctuating, complex phenomenon. Patterns of limb twitching, gross movements, level of chin EMG tone, and REMs formed a broad range of combinations. In all of these patients, REM sleep was characterized by jerky movements and at times complex behaviors that were clearly inappropriate to the immediate environment; sometimes they could readily be identified as attempted dream enactments. All the patients demonstrated an extraordinary amount of EMG twitching during REM sleep, which appeared in burst and nonburst forms. There were examples of persistent EMG limb lateralization and preferential upper or lower extremity movements. Potentially harmful sleep behaviors were confined to REM sleep, with the exception described in Fig. 1. All four men punched and kicked, and all five patients shared non-violent stereotypies, as already described. Patient 5 was singular in his display of emotion, usually anger but also some laughter and amusement. There was never an instance where observed REM sleep behavior contradicted subjective dream activity, and there was generally close correspondence. Thus, sleep laboratory evaluation documented intentional behaviors generated during REM sleep dreams.

Tables 1 and 2 also contain REM period ocular activity and density measures (RA and RD) based on the "Pittsburgh method" (5). A consensus between two raters determined the scores. In patients 1, 3, 4, and 5, RA and RD were increased on all study nights.

Concerning other parameters of these patients' sleep, several observations can be made from Tables 1 and 2: (a) pronounced increase in percentage of stage 3–4 sleep in all five patients, when compared with data for age-matched normals (6); (b) increased percentage of REM on both nights in patient 5 and on one night in patient 1; (c) increased REM time on both nights in patient 5; and (d) periodic NREM myoclonus in patients 1, 3, and 5 on all study nights except one.

DISCUSSION

This report documents the existence of complex and clinically consequential behaviors during human REM sleep that resemble REM sleep behaviors observed 21 years ago in cats experimentally subjected to pontine tegmental lesions (7). Diverse nonepileptic neuropathology was associated with this sleep disorder in four cases; pontine involvement was established in patient 3. The data can be considered along at least two dimensions, the behavioral and the experiential (dream and transitional state experience).

Behavioral

In humans, REM sleep becomes recognizable between the 27th and 30th week of gestation (8–10). From the outset and extending through infancy, there are prominent REMs, limb jerks, and simple orofacial behaviors (8,11,12). Other mammals demonstrate comparable early developmental phenomena (13), which may reflect a matura-
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<th>TABLE 1. Electrographic sleep measures (patient 1)*</th>
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<td>Sleep latency (SL = min)</td>
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* Patient 1, male.
TABLE 2. Electrographic sleep measures (patients 2, 3, 4, and 5)*

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<tr>
<td>Time spent asleep (TSA = min)</td>
<td>253.0</td>
<td>323.0</td>
<td>381.5</td>
<td>518.5</td>
<td>548.0</td>
</tr>
<tr>
<td>Sleep efficiency (TSA/TRP = %)</td>
<td>58.9</td>
<td>65.6</td>
<td>88.3</td>
<td>77.4</td>
<td>88.0</td>
</tr>
<tr>
<td>Sleep maintenance (TSA/TRP - SL = %)</td>
<td>64.1</td>
<td>74.7</td>
<td>92.1</td>
<td>79.2</td>
<td>89.2</td>
</tr>
<tr>
<td>Wake after sleep onset (WASO = min)</td>
<td>141.5</td>
<td>109.5</td>
<td>32.5</td>
<td>136.5</td>
<td>66.0</td>
</tr>
<tr>
<td>Arousals</td>
<td>15.0</td>
<td>7.0</td>
<td>5.0</td>
<td>7.0</td>
<td>11.0</td>
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<tr>
<td>Sleep architecture (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>5.7</td>
<td>28.5</td>
<td>8.6</td>
<td>6.1</td>
<td>7.5</td>
</tr>
<tr>
<td>Stage 2</td>
<td>51.4</td>
<td>39.9</td>
<td>44.6</td>
<td>47.2</td>
<td>48.8</td>
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<tr>
<td>Stage 3 and 4</td>
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<td>14.7</td>
<td>26.7</td>
<td>21.5</td>
<td>15.7</td>
</tr>
<tr>
<td>Stage REM</td>
<td>8.9</td>
<td>16.9</td>
<td>20.1</td>
<td>25.2</td>
<td>28.0</td>
</tr>
<tr>
<td>Sleep maintenance (TSA/TRP = %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM sleep periods (no.)</td>
<td>1.0</td>
<td>2.0</td>
<td>5.0</td>
<td>5.0</td>
<td>6.0</td>
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<tr>
<td>REM time (RT = min)</td>
<td>22.5</td>
<td>54.5</td>
<td>76.5</td>
<td>130.5</td>
<td>153.5</td>
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<tr>
<td>REM activity (RA = units)</td>
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<td>216.0</td>
<td>189.0</td>
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<td>274.0</td>
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<td>REM density (RA/RT)</td>
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<td>3.96</td>
<td>2.47</td>
<td></td>
<td>1.78</td>
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<tr>
<td>REM latency (min)</td>
<td>230.5</td>
<td>182.0</td>
<td>40.5</td>
<td>112.0</td>
<td>49.0</td>
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<td>Other</td>
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<td>Periodic NREM Myoclonus</td>
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<td>No</td>
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<td>Medication name</td>
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*Patient 2, female; patients 3, 4, and 5, male.

tional lag in central nervous system (CNS) inhibitory capacity (14–16). During childhood, REM sleep achieves a stable pattern that persists through adulthood, which includes EMG atonia of chin and limbs with infrequent twitches (1,8). The neuronal bases for this atonia, as identified in cats, involve pontine excitation of a medullary center whose inhibitory projections hyperpolarize spinal motoneuron postsynaptic membranes (17). Irregular excitatory surges from central neural structures can briefly overcome motoneuronal inhibition to produce twitches (18). The atonia is adaptive insofar as “it seems logical for the organism to protect itself from the deleterious consequence of undirected and inappropriate movements when it is blind and unconscious” (18).

The clinical histories of patients 1 and 4 suggest longstanding REM sleep prodromes consisting of accentuated twitching, simple behaviors, and vocalizations. A possibly related finding has been documented in young adults with repetitive head movements occurring exclusively during REM sleep (19–21). A familial contribution also may be indicated by the history of patient 4.

The original pontine tegmental lesion studies in cats demonstrated that REM sleep retained its basic characteristics despite the loss of muscle atonia and the appearance of behavioral repertoires, including head raising, signs of rage, and hallucinatory motor activity (7,22). In a replication of the study, REM sleep behaviors appeared as early as the second postlesion day (23). Subsequent work revealed that loss of atonia, though necessary, was not sufficient to produce REM sleep behaviors (24). Lesions at various pontine sites released site-specific stereotypical behaviors, which formed four syndromes: (a) a minimal syndrome consisting of loss of atonia and unorganized head and limb movements; (b) a repertoire of staring, orienting, head raising, and reaching behaviors, which also included attempts at standing; (c) phasic episodes of attack be-
havior alternating with periods of quiet staring or searching movements; and (d) loco-
motion. These results suggest that the pontine tegmentum during REM sleep has re-
sponsibility not only for motoneuron inhibition causing atonia, but also for inhibition of
the putative brainstem generators of motor activity (24,25). A lesion affecting the
former mechanism would result in REM sleep without atonia, whereas a lesion af-
fecting both mechanisms would also release REM behaviors. Chloramphenicol, a pro-
tein synthesis inhibitor, has restored the atonia of REM sleep in cats with experiment-
tally induced REM behavioral release (26).

These experimental data correspond closely with our human data. All five patients
had REM sleep that retained its basic features despite variable EMG activity, and all
had documented REM behaviors consistent with experimental syndromes (a) and (b)
just mentioned. In addition, the four men were documented to have syndrome (c), and
their histories were consistent with syndrome (d) just mentioned.

Our cases represent a new category of REM sleep parasomnias that should incorpo-
rated within the recognized nosology (2). The Japanese literature contains reports of
apparently similar, if not identical, REM sleep behavioral disorders associated with
pontine tumors and spinocerebellar degeneration [references (43–45) in (27)]. The be-
haviors were described as “delirious,” but the state of consciousness upon arousal
was not specified (27). Loss of REM atonia and behavioral release also have been
reported in two patients with olivo-ponto-cerebellar degeneration (28) and in a neuro-
logically intact elderly woman (29). REM sleep with augmented EMG but without
gross motor activity has been reported in patients with parkinsonism and the Shy-
Drager syndrome (30,31). A new syndrome involving thalamic degeneration encom-
passes oneiric behaviors similar to those of our patients (32,33) and serves to re-em-
phasize the importance of forebrain mechanisms in the regulation of REM sleep com-
ponent processes (34). Transient appearance of motor activity during REM sleep has
been documented in the context of delirium tremens and related withdrawal syndromes
(27,35).

Experiential

The association of dreaming with sleep behaviors was reported directly by patients
1, 2, and 5 and was inferred by the spouses of patients 3 and 4. Dream processes
consisted of mental alertness or hyperalertness; vivid perception, particularly in the
visual sphere; frequent motor hyperactivity of the dream characters, including the
dreamer; variable emotional experiences; and complex and sometimes bizarre se-
quences of events, which among the four men often entailed aggressive acts. Arousals
from sleep led to the rapid return of alertness and orientation with appropriate behavior
and social interactions in all patients, and immediate dream recall in patients 1, 2, and
5. These features seem inconsistent with NREM sleep or with delirious or ictal phe-
nomena, but rather suggest the experience of REM sleep. Figure 1 exemplifies how
dissociated REM processes can underlie NREM dreams. The reports by patient 1 sug-
gest sleep and dream vestibular activation, which has been shown to occur during
REM sleep in cats (36,37).

The reported dream hyperactivity may have been another consequence of disinhi-
bited brainstem motor drive, as would be predicted by the “activation-synthesis”
model of dream generation (38,39), which postulates that during the activated state of
REM sleep (40,41), specific brainstem generators activate motor, perceptual, affective,
mnestic, and cognitive neuronal circuits, which feed their information to an integrating
forebrain whose resultant is the dream. Increased activity of motor pattern generators (42) might induce corresponding dream changes. The hyperactive dreaming and released REM behaviors appear to share a similar response to medication, which is also consistent with this hypothesis.

Treatment

The specific mechanisms of action of clonazepam and desipramine in patients 1, 4, and 5, are currently unknown. The benzodiazepine clonazepam has been effective in the control of other motor disorders, such as periodic NREM sleep myoclonus (43–45), neuroleptic-induced somnambulism (46), and motor hyperactivity in bipolar manic states (47). It is also used as an anticonvulsant in the treatment of infantile spasms and myoclonic epilepsy (48). Experimentally, it has been shown to presynaptically block dopamine-mediated stereotypical behavior (49) and also increase serotonin synthesis (50). The tricyclic antidepressant desipramine is known to suppress both phasic and tonic components of REM sleep (51).

In summary, these five patients, four of whom had associated neuropathology, displayed abnormalities of REM sleep that were predicted by animal experiments beginning 21 years ago. The initial clinical diagnoses included seizures, apnea, or psychiatric disturbance. The correct diagnosis was established by means of standard PSG techniques, including a scalp EEG montage, EMG recording from all limbs, and videotape recording of sleep behaviors. Treatment with either clonazepam or desipramine was rapidly effective and well tolerated.

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REFERENCES


