Familial Nocturnal Cramping

John H. Jacobsen, Richard S. Rosenberg, Peter R. Huttenlocher, and Jean-Paul Spire

Sleep Disorders Center, Department of Neurology and the Brain Research Institute, University of Chicago, Chicago, Illinois, U.S.A.

Summary: A familial syndrome of painful nocturnal cramping and jerking in members of three generations is described. All-night polysomnograms demonstrated both myoclonic jerks and sustained muscular activity in three family members, a 4-year-old girl, who presented with frequent episodes of painful awakenings; her 7-year-old brother, who had similar but less severe symptoms; and the 28-year-old mother, who had suffered nocturnal cramping and awakenings for much of her life. To the authors' knowledge, this is the first description of a familial disorder characterized by exclusively nocturnal intermittent cramping and myoclonus of brainstem or spinal origin. Key Words: Myoclonus—Familial disorders—Nocturnal cramping.

Repetitive, stereotyped movements, primarily of the lower extremity, occurring in NREM sleep and followed by arousal, are termed nocturnal myoclonus or periodic movements during sleep (1–3). These movements are never associated with cortical epileptic discharges, but they may be associated with other types of abnormal muscle activity such as that found in the stiff-man (Moersch-Woltman) syndrome (4). We describe the familial occurrence of nocturnal myoclonus accompanied by sustained muscle contractions in members of three generations. The association of nocturnal myoclonus and sustained activity has not been previously described in a single family to our knowledge.

CASE REPORTS

Case 1 (proband)
A 4-year-old black girl had suffered from painful muscle cramping and jerking of the arms, legs, abdomen, and face during sleep since her first few months of life. The patient was the second child of a 25-year-old mother (gravida III, para II, ab I) and weighed 7 lb 4 oz at birth. The mother’s gestation was unremarkable except for the presence of mild maternal hypertension and schizophrenia (vide infra), which were untreated during the pregnancy. There was also an episode of premature labor. The delivery, neonatal course, growth, and development were unremarkable.

The parents reported that the attacks occurred nightly and that at times cramping of the various muscles would be severe enough to awaken the child and produce crying.
The result of physical examination of the patient was normal except for mild hypertrophy of the calf muscles. There was no myotonia.

Case 2
The brother of the proband was 7 years old. Medical history showed that his early development was uneventful and had followed an uneventful pregnancy and delivery. Only after the parents noted the cramping in the proband did they become aware of milder, but otherwise similar, symptoms in the brother. The result of physical examination, including detailed testing of muscle bulk, tone, strength, and reflexes, was unremarkable.

Case 3
The 28-year-old mother of the children just described had suffered painful nocturnal muscle cramping for as long as she could remember. Otherwise, she had been in good health except for a psychiatric disorder diagnosed in 1979 (before the birth of the proband) as schizophrenia and treated since then with a phenothiazine. While taking this medication she functioned as a housewife and had not needed hospitalization for several years. She also noted significant lessening of her nocturnal muscle cramping while taking the phenothiazine. The results of her physical and neurological examinations were normal except for obesity and mild hypertension.

The maternal grandmother of the children was said to have a history of similar nocturnal cramps but was not examined by us (see Fig. 1).

LABORATORY STUDIES
For the proband, the results of routine laboratory studies, including complete blood count and differential; hemoglobin electrophoresis; urinalysis; determination of serum CPK, calcium, and magnesium; and evaluation of kidney and liver function, were normal. A screen of the urine for drugs was negative. The waking electroencephalogram (EEG) was normal. The waking electromyogram (EMG), which included repetitive stimulation of the right abductor digitii minimi at 2 Hz under ischemic conditions in an attempt to elicit tetany, was within normal limits.

All three patients underwent all-night polysomnographic recordings, which began at \(-2300\) h and continued until \(0600\) h. Electrode placement and EEG, EMG, electro-oculographic, and electrocardiographic recordings were performed as described by Rechtschaffen and Kales (5), with additional surface recordings of leg muscle activity. Sleep stages were scored according to the criteria of Rechtschaffen and Kales.

Typical portions of the polysomnographic records are presented in Figs. 2–5. In the initial study of the proband, muscular activity throughout most of sleep was nearly con-
continuous and of such high amplitude that accurate sleep staging and quantitation of myoclonic events was not possible (Fig. 2). In spite of the prevalence of abnormal muscle activity on the record, an experienced polysomnographic technician observed only discrete twitches of the extremities during this study, and no period of intense pain with awakening occurred.

Treatment with clonazepam (0.25 mg at bedtime) produced sustained improvement of symptoms. A polysomnogram after 1 year of treatment showed persistence of intermittent myoclonus and occasional episodes of sustained activity in extremity muscles. In comparison to the nearly continuous muscle activity, sustained EMG activity was recorded for only 5 min of a total of 446 min of sleep in the follow-up study. Peroneal nerve block by injection of procaine at the right fibular head produced abolition of voluntary ankle dorsiflexion. During the block, the sleep EMG record of the tibialis anterior muscle was silent; tonic and phasic activity was eliminated for the entire night (Fig. 3). Sleep architecture was

FIG. 2. Polysomnogram of the proband prior to treatment, showing intermittent bursts of electromyographic (EMG) activity from the left gastrocnemius, occurring every 10 s, and virtually continuous activity from the right gastrocnemius. The bursts of activity from the left gastrocnemius were associated with leg jerks and artifacts in recordings from scalp derivations, but no arousal from NREM sleep as evidenced by an absence of alpha activity. EKG, electrocardiogram; EOG, electro-oculogram.

FIG. 3. Polysomnogram of the proband after treatment and with right peroneal nerve block. Note continued activity in the left tibialis anterior muscle but complete abolition of activity in the right tibialis anterior. This portion of the recording was obtained during stage 3 sleep. Abbreviations as in Fig. 2.
entirely normal with a sleep latency of 24 min, REM latency of 67.5 min, and a sleep efficiency of 96%.

Polysomnograms of the mother and brother, who were unmedicated, were also abnormal with 36.7 and 64.1 myoclonic events per hour, respectively. Furthermore, runs of sustained muscle activity, each lasting several seconds, were noted in each record (Figs. 4 and 5). However, sleep stages were normal in their duration and distribution across the night. Abnormal muscle activity was invariably most striking during sleep stages 1 and 2. Activity during REM sleep could not be distinguished from the physiologic REM-associated phasic EMG activity.

DISCUSSION

Members of this family displayed two abnormal muscular activities during sleep: (a) intermittent small jerks occurring periodically and (b) episodes of sustained contraction.

FIG. 4. Polysomnogram of the 7-year-old brother during stage 2 sleep. Note prolonged burst of electromyographic activity from the right quadriceps and gastrocnemius, as well as fragmentary activity from these muscles after the burst. As with the proband, no arousal is evident, and alpha activity is absent. Abbreviations as in Fig. 2.

FIG. 5. Polysomnogram of the 28-year-old mother during stage 2 sleep. Bursts of electromyographic (EMG) activity are evident in recordings from the chin and, to a lesser degree, the right rectus femoris and gastrocnemius. Abbreviations as in Fig. 2.
The relationship between the two phenomena is unclear. In the initial recording of the proband, intermittent activity at times increased in frequency and developed into sustained activity. Perhaps the two phenomena reflected the same event occurring at different levels of severity.

According to the criteria of the Association of Sleep Disorders Centers (2), a clinical diagnosis of nocturnal myoclonus is reserved for those patients whose movements are "consistently followed by partial arousal or awakening." Unfortunately, the criteria for identifying a movement event have not been clearly established. Most would agree, however, that so-called "nocturnal myoclonus" is not truly myoclonic, and that the term "periodic movements in sleep" is more accurate. The movements tend to involve extensive muscle groups, both extensors and flexors; have a duration of 0.5-5 s; and are separated from other similar movements by an interval from 20 to 40 s duration (3). The intervals are very rarely < 5 s (6). Periodic movements during sleep may be causally related to complaints of insomnia but are also associated with narcolepsy, sleep apnea, and a variety of other sleep disturbances (3).

Montplaisir et al. (7) recently reported a family with restless legs syndrome in which three of nine affected members also had nocturnal myoclonus of the periodicity and duration described above. The family described here does not have typical nocturnal myoclonus because the interevent intervals were often < 5 s (even < 1 s), and because the continuous movements were usually not associated with arousal, at least during the time of hospital observation.

 Syndromes of continuous muscular activity can be divided into those thought to be of central nervous system origin and those appearing to arise peripherally. The abnormal muscular activity in our patient is deemed to be of central origin for the following reasons: (a) it was abolished by peripheral nerve block; (b) electromyographic and clinical examinations revealed normal results, without suggestion of peripheral neuropathy or radiculopathy; (c) the activity was present only during sleep, suggesting that its generation was under central control.

The absence of activity during wakefulness as reported here is unusual, inasmuch as most movement disorders are attenuated by sleep (8). Animal studies have demonstrated decreased excitability of lower motor neurons during sleep (9).

Several other syndromes of continuous motor activity thought to be of central origin have been described. These include the stiff-man syndrome, described by Moersch and Woltman (4), that is characterized by persistent stiffness of muscles and by tonic EMG activity at rest, but with normal-appearing motor units. Muscular discharges disappear during neuromuscular block, following peripheral nerve block or spinal or general anesthesia, and, most importantly, in sleep (10,11). Nonetheless, associations between stiff-man syndrome, nocturnal myoclonus, and epilepsy have been noted (4,12). The stiff-man syndrome is usually sporadic, with onset in adulthood, but a hereditary disorder with onset in infancy and with similar clinical features has been described (13,14). Stiff-man syndromes differ from the disorder described here in that contraction of muscles occurs primarily during waking. However, cases of waking myoclonus associated with muscular rigidity (15,16) have been reported, with myoclonus persisting during sleep in one patient (16).

Hyperexplexia (17,18), a hereditary disorder characterized by exaggerated startle responses and generalized muscular rigidity, associated on occasion with nocturnal myoclonus, bears a superficial resemblance to our cases, but again the abnormal muscular activity is more prominent during wakefulness. Another type of muscle activity during sleep was reported recently by Lugaresi and Cirignotta (19). These authors describe in-
termittent dystonic-ballistic movements in five patients, with protracted, stereotypic, opisthotonic contraction and motor activity resembling seizures. In contrast, overt activity was absent in the cases reported here.

Two infants born to a mother taking phenothiazine medication manifested tremors, abnormal posturing, and hypertonia that persisted as long as 10 months after birth, but the abnormalities disappeared during sleep (20). The mother in our study had been taking phenothiazines for years; however, the negative toxic screen in the proband, the presence of abnormal muscle activity only during sleep, and the length of time since birth argue against any role for phenothiazines in the pathogenesis of the disorder we describe. Moreover, the mother had symptoms before she began taking medication, and the brother, who had similar symptoms, was born before the mother began taking phenothiazines. The mother was not taking phenothiazines during the gestation of the proband.

To our knowledge, our three cases constitute the first report of a familial disorder characterized by exclusively nocturnal (or, more accurately, sleep-associated) intermittent muscle cramping and myoclonus of brainstem or spinal origin. Muscle disorders during sleep may have a spectrum of severity; perhaps the fragmentary myoclonus described by Broughton and Tolentino (21) represents a mild form of abnormal muscle activity during sleep, and the disorder we describe represents an exaggerated form of the same syndrome. Until more is known of the pathogenesis of the above-mentioned syndromes, attempts should be made to delineate disorders of continuous and periodic muscular activity, myoclonic jerks, and dystonic movements during sleep. Continuous and periodic muscle activity responded to clonazepam therapy, whereas the patients with dystonic movements responded only to carbamazepine (19). Therefore, classification through polysomnography may lead to specific therapeutic approaches.

Acknowledgment: The authors wish to thank Allan Rechtschaffen and Barry Arnason for their critical review of the manuscript.

REFERENCES


