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Original Article

# Peripheral nerve function in patients with excessive fragmentary myoclonus during sleep

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ABSTRACT

*Objectives:* Excessive fragmentary myoclonus is a frequent incidental finding in patients undergoing polysomnography for other reasons. The aim of this study was to evaluate whether electrophysiological examination in patients with excessive fragmentary myoclonus during sleep according to American Academy of Sleep Medicine (AASM) criteria shows findings of peripheral nerve dysfunction.
*Methods:* Ninety-eight of 100 patients with excessive fragmentary myoclonus detected as an incidental finding during routine polysomnography underwent electrophysiological workup. Motor nerve conduction studies of the right peroneal and tibial nerves, F-wave recordings of the tibial nerve, antidromic sensory nerve conduction studies of the left sural nerve and needle electromyography of the right tibialis anterior muscle were performed and classified as normal, peripheral neuropathy, lumbar 5 (L5) nerve root lesion, or benign fasciculations.
*Results:* Fifty percent (49 out of 98) presented with electrophysiological abnormalities, most frequently polyneuropathy (32 out of 49, 65.3%), followed by L5 nerve root lesions (13 out of 49, 26.5%) and benign fasciculations (4 out of 49, 8.2%). Patients with electrophysiological abnormalities were older than those without.
*Conclusions:* The high prevalence of abnormal neurophysiological findings in patients with excessive fragmentary myoclonus during polysomnography suggests that excessive fragmentary myoclonus during sleep according to AASM criteria is not primarily a sleep-related phenomenon, but only persists during sleep and points to peripheral nerve pathology at least in part of the cases. Patients with incidental EFM during polysomnography should undergo electrophysiological workup for peripheral nerve pathology.


## 1. Introduction

Fragmentary myoclonus (FM) is an incidental finding in patients undergoing polysomnography (PSG) for other reasons, and its clinical relevance is still unclear.

FM during sleep was first described as a pathological phenomenon by Broughton and Tolentino in 1984 [1] in a single patient with excessive sleepiness who presented "marked amounts of brief, multifocal and aperiodic myoclonus during NR sleep." Myoclonic activity was defined as bursts of muscle activity recorded by surface (or needle) electromyogram (EMG) from the tibialis anterior muscle. Two years later, Broughton et al. [2] published a series of 38 cases with "excessive fragmentary myoclonus" (EFM) which they *ad hoc* defined as "EMG-activity consisting of brief usually less than 150 msec hypersynchronous potentials exceeding 50 μV and sometimes over 200 μV in amplitude", recorded during at least 20 consecutive minutes of stage 2, 3 or 4 sleep, with a rate of at least 5/min" [2].

Montagna et al. [3] in 1988 reported on seven healthy subjects with "physiological hypnic myoclonus" (PHM), based on the 1932 definition by De Lisi [4] as arrhythmic and asynchronous muscle twitches during light sleep. The EMG activity underlying these twitches had a duration of less than 100 ms, and Montagna observed that the potentials also extended into wakefulness and involved asynchronously not only the tibialis anterior muscles, but also face and upper limbs, often resembling fasciculation potentials, based on their shape, duration and discharge characteristics [3].

To better characterize EFM, Lins et al. in 1993 [5] presented a study in a series of 11 men with excessive amounts of FM and suggested an EFM index, in order to quantify FM and thus providing a measure for statistical analysis. The EFM Index was based on the occurrence of one or more FM potentials during 3-s miniepochs; they reported the presence of EFM during all sleep stages, but wakefulness was not analyzed. Our own group [6] investigated the

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occurrence of fragmentary myoclonus in a series of 62 consecutive sleep laboratory patients and found that FM was present in every single patient, but with a very large variation and with an index ranging from 4 to 371 per hour. The FM index (FMI) was higher during rapid eye movement (REM) sleep (median 55/h), followed by similar indices during wakefulness (median 43.3/h) and was lower in deep sleep stages (median 31.9/h), suggesting that FM is not restricted to sleep but is also present during relaxed wakefulness, as previously observed by Montagna et al. [3]. Although in that study EFM was not assessed according to the Broughton criteria, it was observed that in some patients rates were excessively high [6]. In addition, FMI increased with the apnea–hypopnea index (AHI) and with the oxygen desaturation index (ODI) [6]. In another study, our group reported that EFM meeting the Broughton [2] and American Academy of Sleep Medicine (AASM) [7] criteria was present in 9% of 100 healthy subjects, whereas non-excessive fragmentary myoclonus was seen in every single subject of the same study [8].

The ad hoc criteria defined by Broughton et al. in 1985 [2] were incorporated into the International Classification of Sleep Disorders (ICSD-2) in 2005 [9] and EFM was categorized among the isolated symptoms, normal variants and unresolved issues. In the latest International Classification of Sleep Disorders (ICSD-3) [10], EFM was transferred to the category Movement Disorders of Sleep, still as an isolated symptom or normal variant.

Based on our previous observations that FM is probably not only sleep-related but also persists in wakefulness [6,8], we designed the present study to evaluate whether EFM is associated with peripheral nerve lesions.

## 2. Subjects and methods

### 2.1. Patient recruitment

One-hundred patients with an incidental finding of EFM during polysomnography were recruited from the Sleep Laboratory at the Department of Neurology, Innsbruck Medical University and referred for EMG/NCV studies to the Laboratory for Neuromuscular Diseases. Only patients who underwent EDX workup at the same institute were used in this analysis. For the purpose of this study, we categorized the final diagnoses into the main categories of the ICSD-3 [10]: insomnia, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake disorders, parasomnias, and sleep-related movement disorders. A written informed consent was obtained from all patients for PSG and EMG, and all procedures were performed in agreement with the Helsinki Declaration. The study protocol was approved by the local ethical committee.

### 2.2. Polysomnographic recordings

Polysomnographic recordings were performed according to the standard AASM scoring criteria [7] and included frontal, central, and occipital electroencephalographic derivations (19 recordings, carried out before 2007, only included C3-A2 and C4-A1), two-channel electro-oculography, at least mental, submental, and both tibialis anterior muscles surface EMG, electrocardiogram, oro-nasal airflow by thermocouple, blood oxygen saturation by pulse oximetry, thoracic and abdominal breathing effort by strain gauge, and snoring by laryngeal microphone. The bipolar tibialis anterior surface electromyographic electrodes were placed 2–3 cm apart longitudinally and symmetrically around the middle of the muscle. The tibialis anterior EMG potentials were recorded with low pass filters set at 50 Hz and high pass filters set at 300 Hz. The sampling rate was 1000 Hz. Sensitivity was set to 100 μV/cm and adjusted as needed for visual analysis.

### 2.3. Sleep and fragmentary myoclonus analysis

For sleep stage scoring, 30-s epochs were visually scored according to the Rechtschaffen and Kales criteria [11] for PSG conducted before 2007, and according to AASM criteria [7] for PSG performed after 2007. The AHI was defined as the number of apneas and hypopneas per hour of sleep, while the ODI was defined as the number of oxygen desaturation falls (≥4%) per hour of sleep. Periodic limb movements during sleep (PLMS) were recorded and calculated according to standard criteria [7].

Fragmentary myoclonus was scored according to the AASM criteria [7]. As described above, according to these criteria EFM is identified visually when at least 5 EMG potentials per minute meeting criteria are recorded during at least 20 min of NREM sleep [7,12].

### 2.4. Electrodiagnostic studies

Complete nerve conduction studies and needle EMG were performed in 98 out of 100 patients, according to standard procedures. Motor nerve conduction studies of the right peroneal and tibial nerves, F-wave recordings of the tibial nerve and antidromic sensory nerve conduction studies of the left sural nerves were performed. When abnormal results were obtained, more extensive bilateral studies were carried out. All patients underwent quantitative EMG of the right tibialis anterior muscle. The results of the electrodiagnostic (EDX) studies were classified as normal, peripheral neuropathy, L5 nerve root lesion, or benign fasciculations (including cramp-fasciculation syndrome). Two patients had to be excluded because their EDX studies were incomplete.

### 2.5. Statistical analysis

Data were tested for normal distribution using the Shapiro–Wilk test. Descriptive statistics are given as numbers (percentages) as well as means ± standard deviations, as data are normally distributed. For comparison between groups, the Student's *t*-test was used for continuous variables and the Chi-square test or Fisher Exact test for the analysis of categorical data, depending on the sample size. Differences were considered to be significant at $p < 0.05$. For the computation of the statistical tests, the freely available online tools at http://vassarstats.net/ were used.

## 3. Results

As complete EDX studies were lacking in two male patients, 98 patients (87 men, 11 women) with a mean age of 61.1 ± 10.1 years were included in the final analysis.

A total of 49 patients (50%, 43 men and 6 women) had abnormal EDX test results; polyneuropathy accounted for the majority (65.3%), followed by L5 nerve root lesion (26.5%) and by benign fasciculations (8.2%), Fig. 1 shows the number of EFM patients with or without EDX abnormalities.

The patients with EDX abnormalities were older (mean age 64.3 ± 9.4 years) than those without (mean age 57.9 ± 9.9 years, $p = 0.002$), whereas gender distribution was similar in the two groups. Fig. 2 shows the number of sleep disorder categories diagnosed in EFM patients with or without EDX abnormalities. A total of 26.5% of all patients had a single main sleep disorder category while in the remaining patients, two, three, or four different sleep disorders were diagnosed; however, this was similar among patients with or without EDX abnormalities and essentially reflects the features of the overall patient population referred to our sleep laboratory. The frequency of the different sleep disorders was similar in both patient groups, with or without EDX abnormalities (Table 1). Among patients with a sleep-related movement disorder as one of more