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A retrospective study of the clinical and electrophysiological characteristics of 32 patients with orthostatic myoclonus

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ABSTRACT

Objectives: To review the electrophysiological and clinical characteristics of 32 patients with orthostatic myoclonus (OM), a relatively newly identified movement disorder, and compare these characteristics to those of primary orthostatic tremor (OT) patients and patients with similar gait and balance complaints without either hyperkinesia diagnosed during the same 30-month period.
Methods: The database of the Mayo Clinic Florida Movement Disorders Electrophysiology Laboratory (MDEL) was searched for all patients referred for possible OM or OT from 6/2010 to 12/2012. All available clinical records and archived surface electromyographical data for these patients were reviewed and analyzed.
Results: 32 patients with OM (mean age 74 years), 8 with primary OT (mean age 71), and 55 with neither orthostatic hyperkinesia (NOH) (mean age 68) were identified. All OT patients and 84% each of OM and NOH patients complained of involuntary leg movements while standing, e.g., "shaking," "trembling," or "jerking." All OM and OT patients experienced symptomatic and electrophysiological abatement or attenuation of their leg hyperkinesias by leaning forward onto an object while standing.
Conclusions: OM has some similarities to OT, including causing "shaky legs" subjectively in standing older patients. Novel data from this work include that, as in OT, OM essentially abates when patients remove their weight from their legs. This shared isometric phenomenon may reflect that OT and OM are on a pathophysiological continuum. Further, many patients who complain of their legs "shaking" while standing may have neither OT nor OM. Surface electromyography may be a useful adjunct in extrapolating patients complaining of "shaky legs."

1. Introduction

Orthostatic myoclonus (OM) is a recently recognized hyperkinesia that may exacerbate gait instability [1,2]. Like orthostatic tremor (OT), OM is primarily noted in patients over 65 years of age in leg muscles while standing, may produce "shaky legs," and is diagnosed definitively with surface electromyography (SEMG) [1–3]. However, unlike "primary" OT patients, those with OM (and "OT-plus") have abnormal gaits [1,3–5]. Most reported OM patients, as well as those with OT-plus, have had some parkinsonian gait and balance characteristics (e.g., stride reduction and/or freezing of gait, postural instability on "pull" testing, etc.), although their clinical diagnoses have been variable [1,2,4,5].

Since the original two reports on OM describing 18 patients [1,2], no others have been published. This article is a retrospective study of observations garnered over two-and-a-half years of assessing 95 patients for possible OT or OM clinically and with SEMG. Analysis of this cohort sheds light on similarities and disparities between OM, primary OT, and neither orthostatic hyperkinesia (NOH), prompting some provocative questions regarding gait and balance dysfunction in older patients, and potentially offering insights into gait and balance pathophysiology.

2. Methods

The author searched the Mayo Clinic Florida Movement Disorders Electrophysiology Laboratory's (MDEL's) database for all patients referred for possible OT or OM from 6/2010 to 12/2012, and each patient's chart was reviewed. OM was identified using the electrophysiological criteria established by Matsumoto and colleagues. These include semi-rhythmical bursts of motor activity with durations less than 100 ms that occur consistently over several leg muscles simultaneously during standing and are not present during sitting or a "marked increase of myoclonic burst frequency in leg muscles upon standing" [1]. OT, like other true tremors, has a

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consistent frequency, i.e., is rhythmical, and was diagnosed based on the guidelines published by the Movement Disorders Society [4,5].

Surface 8-channel EMG recordings were made with 1.5 m lead CareFusion (Middleton, WI) disposable, adhesive disk electrodes that were applied, then taped to the skin 2–4 cm apart over arm and leg muscle bellies after the overlying skin had been lightly abraded with rubbing alcohol and, if necessary, shaved. Signals were amplified and filtered at a bandpass of 30 Hz–3 kHz using a Nicolet Viking (Madison, WI) machine. Twenty divisions per screen were present, and the sweep speed was 50 or 100 milliseconds (ms), with the gain set typically at 100–200 μV (uV). Surface EMG (SEMG) waveforms were visualized and heard continuously throughout the recordings. The auditory signature of OT is similar to the sound of a helicopter's rotating blades [4] (video 1). In isolation, myoclonic bursts sound as fasciculations do on needle electromyography, and when occurring semi-rhythmically in multiple muscles, they resemble the sound of popcorn heating (video 2). Both OM and OT sound very different from non-specific tonic and semi-rhythmical activity lasting hundreds of milliseconds. Each study lasted a minimum of 15 min. The standard montage used consisted of the following muscles: unilateral triceps, wrist extensors (WEs), abductor digiti minimi (ADM), vastus lateralis (VL), and bilateral tibialis anteriors (TAs) and medial gastrocnemii (MGs). In each case, activity was recorded with the patient sitting comfortably on the edge of an examination table with their arms in their lap and their legs dangling above the floor. They were then asked to position themselves with their shoulders, arms, wrists, and knees extended, and their feet dorsiflexed, simultaneously. The patients then were instructed to perform finger-nose testing with the limb attached to recording electrodes. With the patients' hands at rest and extended, the examiner tapped on their phalanges to assess for stimulus-sensitive myoclonus. Prior to the recordings, the same maneuvers were examined to aid in choosing the upper extremity to record from, i.e., if jerks and/or tremulous activity were more predominant on one side, then those limbs were selected as the primary recording side. Finally, recordings were made with the patient standing for at least 5 min and then leaning forward onto a chair or walker while continuing to stand. Patients were queried whether they felt involuntary leg movements, and if so, whether these were only apparent while standing, and if these changed when they leaned onto the object. Multiple representative SEMG tracings were printed and saved with each report. Myoclonic bursts were identified per muscle per page and tabulated. Synchronous bursts were defined as two or more bursts occurring in separate muscles within 15 ms of one another [1]. Averages of synchrony and frequency were calculated from each patient's recordings.

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.parkreldis.2014.05.006.

A Mayo Clinic staff neurologist evaluated each patient. Provisional neurological diagnoses for each patient's gait disorder were made based on current published diagnostic criteria (see Supplemental Tables 1 and 2) [6–22]. None of the subjects has undergone a brain autopsy; all are still alive. If the diagnostic certainty was less than probable, a question mark in parenthesis was listed after the proposed diagnosis (Supplemental Tables 1 and 2). "Higher level gait disorders" (HLGDs) merit particular explication as there are various designations in the literature of "lower body parkinsonism," "vascular parkinsonism," "cautious gait of the elderly," HLGDs, etc., [13,19,22], which are often ambiguous. Here, following Nutt [23], HLGD refers to a gait syndrome characterized by varying degrees of hypokinesia (legs >> arms), including potentially freezing of gait (FOG), as well as ataxia and postural instability that is not associated with limb bradykinesia, ataxia, or rigidity on seated or supine testing. The gait ataxia may only manifest on tandem-walking. If neuroimaging of a patient with an HLGD was unremarkable (e.g., did not clearly show extensive white matter disease, frontal lobe atrophy, hydrocephalus, etc., which are known etiologies of this gait disorder), then the diagnosis, as well as the gait, are classified as "HLGD" (Supplemental Tables 1 and 2).

Medications known to cause myoclonus [8] were tabulated for each patient to ascertain whether these might have contaminated the SEMG results. With rare exceptions, these medications were initiated before the patients were evaluated at Mayo Clinic Florida.

The study was approved by the Mayo Clinic Institutional Review Board (IRB).

3. Results

The author clinically examined 30/32 (94%) of the OM patients; 6/8 with OT; 51/55 (93%) with NOH; and performed all of the SEMGs. The data from each cohort are summarized in Supplemental Tables 1–3. Regarding OM, a variety of electrophysiological patterns was evident. Approximately 70% of OM bursts occurred synchronously, with the bilateral TAs being the most commonly affected muscles. Sometimes, synchrony between homologous muscles and a unilateral antagonist was also present. Synchrony between the bilateral TAs and MGs was rare. Also, unilateral, intermittent, semi-rhythmical bursts of motor activity alternating between muscle antagonists at approximately 7 Hz or less, were observed in 53% of patients (present in 21% of the total tracings overall), reminiscent of the firing pattern typical of OT [3] (see Fig. 1). The OM frequency range was 4–11 Hz in 88% of patients. The median frequency was 7 Hz, but as Matsumoto et al. found, there was great variability in the frequency of myoclonus between lower limb muscles, whether ipsilateral or homologous to each other, as well as in the same muscle over time. Stimulus-sensitive myoclonus was present in only two OM patients. One of these has an ipsilateral 4 Hz rest hand tremor, likely secondary to Parkinson Disease (PD), and the other had normal cortical somatosensory evoked potentials (SEPs) and no long latency reflexes (LLRs) at rest during median nerve stimulation [6]. Overall, three OM subjects (14, 16, 27) have had repeat SEMGs, separated by over 1.5 years. OM was evident on all studies.

All OT patients had tremor frequencies between 12 and 17 Hz, with very consistent synchrony between homologous muscles and the typical alternating firing pattern between muscle antagonists. The tremor frequency in each muscle was virtually identical (i.e., strongly coherent), as has been reported in OT [3]. No OT-plus patients were identified.

All OT patients and 84% each of the OM and NOH patients reported involuntary leg movements only while standing, usually describing these as "shaky," "trembly," or "jerky." Complaints of their legs feeling like they would "give-out" or "will not hold me up" were described by 28% of OM patients, almost half of whom have suffered idiopathic drop attacks. One OT and NOH patient each complained that their legs would "give-out," although no drop attacks have been noted in either of these cohorts. All OT and OM patients experienced either utter cessation of their leg hyperkinesias while standing and leaning forward onto an object, or a marked attenuation thereof (see Fig. 2); however, whereas 100% of the OT patients then developed the same hyperkinesia in their arms during this maneuver (video 3), only 13% of the OM patients did (video 4).

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.parkreldis.2014.05.006.

In comparing diagnoses between the OM and NOH patients, 19% of the OM patients had PD, whereas only 7% of the NOH patients did. A parkinsonism-plus syndrome was present in 27% of the NOH group and 16% of the OM group. Thus, each group had about one-third of patients with either PD or a parkinsonism-plus syndrome. Also, about one-third in each group had microvascular encephalopathy (MVE) (34% of OM and 25% of NOH patients, respectively). A functional gait disorder was at least probable in 16% of NOH patients [20,21]. Finally, the use of medications overall known to potentially cause myoclonus was similar between the OM and NOH cohorts. A full list of the medications taken by the patients in this study can be found in Supplementary Table 2.

4. Discussion

Over 30 months, 32 patients were diagnosed with OM in the Mayo Clinic Florida MDEL, and 8 were diagnosed with "primary" OT. As noted by other investigators, both conditions are uncommon before the fifth decade of life. [1,4,5] OM may be more prevalent than OT, which is considered "rare" [3]; however, whether OM is actually four times as common as OT undoubtedly will require much larger, prospective, longitudinal studies to ascertain. However, it is possible that OM is more prevalent than OT and may be at least as common in men. Also, unlike "primary" OT, OM typically co-exists with an abnormal gait and impaired postural reflexes [1–4]. Four of the OM patients have suffered drop attacks, and none of the OT or NOH patients has, raising the possibility that OM may entail negative, as well as positive myoclonus. Except in the case of asterixis, identifying negative myoclonus on SEMG may prove difficult (Caviness J, personal communication). Nonetheless,

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