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ORIGINAL COMMUNICATION

Proprioceptive muscle tendon stimulation reduces symptoms in primary orthostatic tremor

M. Wuehr[1] · C. Schlick[1] · K. Möhwald[1,2] · R. Schniepp[1,2]

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Abstract

Introduction Primary orthostatic tremor (OT) is characterized by high-frequency lower limb muscle contractions and a disabling sense of unsteadiness while standing. To date, therapeutic options for OT are limited. Here, we examined the effects of proprioceptive leg muscle stimulation via muscle tendon vibration (MTV) on tremor and balance control in patients with primary OT.

Methods Tremor in nine patients with primary OT was examined during four conditions: standing (1), standing with MTV on the bilateral soleus muscles (2), lying (3), and lying with MTV (4). Tremor characteristics were assessed by frequency domain analysis of surface EMG recordings from four leg muscles. Body sway was analyzed using posturographic recordings.

Results During standing, all patients showed a coherent high-frequency tremor in leg muscles and body sway that was absent during lying ($p<0.001$). MTV during standing did not reset tremor frequency, but resulted in a decreased tremor intensity ($p<0.001$; mean reduction: $32.5 \pm 7.1\%$) and body sway ($p=0.032$; mean reduction: $37.2 \pm 6.8\%$). MTV did not affect muscle activity during lying. Four patients further reported a noticeable relief from unsteadiness during stimulation.

Conclusion Proprioceptive stimulation did not reset tremor frequency consistent with the presumed central origin of OT. However, continuous MTV influenced the emergence of OT symptoms resulting in reduced tremor intensity, improved posture, and a relief from unsteadiness in half of the examined patients. These findings indicate that MTV either directly interferes with the peripheral manifestation of the central oscillatory pattern or prevents proprioceptive afferent feedback from becoming extensively synchronized at the tremor frequency.

Keywords Orthostatic tremor · Muscle tendon vibration · Proprioception · Tremor · Body sway · Unsteadiness

Introduction

Primary orthostatic tremor (OT) is a rare condition of unknown prevalence, characterized by a high-frequency pattern of coherent muscle contractions (13–18 Hz) in the lower limbs and trunk while standing [1]. The tremor is linked to the main presenting symptom of subjective unsteadiness and dizziness during standing that typically relieves during sitting and lying or when patients start to ambulate.

The pathophysiological mechanisms underlying primary OT are not completely understood. However, the strong coherence between high-frequency activations of widely separated muscles suggests that the latter are a peripheral manifestation of a central oscillator. Correspondingly, a central oscillatory ponto-cerebello-thalamo-cortical network has recently been identified in patients with OT [2, 3]. This network appears to be active during symptomatic (i.e., standing) as well as non-symptomatic states (i.e., lying). During standing, isometric muscle contraction is believed to entrain the central oscillatory pattern in the respective anti-gravity muscles. Continuous tremor in anti-gravity muscles is in turn thought to negatively interfere with proprioceptive afferent feedback required for adequate balance regulation with the result of subjective unsteadiness and objectively impaired stance performance. Both phenomena typically develop over seconds in patients with OT while standing [4].

✉ M. Wuehr
Max.Wuehr@med.uni-muenchen.de

1 German Center for Vertigo and Balance Disorders, University Hospital, LMU Munich, Marchioninistrasse 15, 81377 Munich, Germany

2 Department of Neurology, University Hospital, LMU Munich, Munich, Germany

The aim of this study was to examine whether the course of symptoms emergence in patients with OT during standing might be positively influenced by a continuous proprioceptive stimulation of afflicted muscles. We, therefore, tested the effects of a continuous low-intensity muscle tendon vibration (MTV) on the bilateral soleus muscles on tremor frequency and intensity as well as balance performance and subjective unsteadiness in patients with OT.

Methods

Standard protocol approvals, registrations, and patients consent

The study protocol has been approved by the Ethics Committee of the University of Munich and was registered (DRKS00012907). All procedures were in accordance with the Helsinki declaration and patients gave their written informed consent.

Subjects

Nine patients with primary OT participated in the study (patient characteristics are presented in Table 1). Definite diagnosis was made by surface EMG-recording exhibiting a coherent tremor between homologous leg muscles within a frequency range of 13–18 Hz. Patients underwent a standardized neurological examination to exclude additional signs indicative of a secondary OT (i.e., hypokinesia, rigidity, dystonia, and failure of gait initiation). Age-associated signs of a reduced vibration sense of the feet were frequently observed. However, none of the patients presented with a clinically manifest peripheral neuropathy.

Procedures

Tremor intensity and postural performance (only stance conditions) were evaluated during four conditions (each 60 s duration): standing vs. standing with MTV and lying supine vs. lying with MTV. Recordings during MTV conditions were started 30 s after stimulation onset. After the recordings patients were asked whether they felt any noticeable change in subjective unsteadiness during MTV stimulation.

Muscle tendon vibration was applied bilaterally with two cylindrical vibrators (8.8 cm × 3.2 cm, 180 g) containing a small DC motor (Buehler, type 1.13.055.221, Germany), that were attached on the soleus muscle tendon by elastic bands. Stimulation consisted in a continuous moderate vibration (50 Hz, 1 mm) [5]. Surface EMG activity was recorded with Ag/AgCl electrodes simultaneously from the tibialis anterior, gastrocnemius, biceps femoris, and vastus medialis muscles of the dominant leg side using a Zebris DAB-Bluetooth device (Zebris Medical, Germany) at 1000 Hz. EMG signals were amplified, bandpass-filtered at 10–100 Hz, and full-wave rectified. Body sway was recorded on pressure-sensitive posturographic platform FDM-T (Zebris Medical, Germany) at 100 Hz.

Data analysis

Tremor intensity and coherence between every combination of recorded muscle pairs were analyzed by spectral analysis using finite fast Fourier transformation with a block size set to 2 s resulting in a frequency resolution of 0.5 Hz [6]. Body sway was analyzed by spectral analysis on the time series along *z*-axis of the posturographic measurements (N) and by calculating the mean position (mm), sway area (mm^2), path

Table 1 Patient characteristics including neurological findings and medication

Patient	Sex	Age (years)	Tremor frequency (Hz)	Duration (years)	Medication	Neurological findings
1	m	62	14.5	1	No	1, 4
2	f	55	14	5	Gabapentin 1200 mg/day	1
3	m	75	17.5	10	No	1, 2, 4
4	m	75	14	14	Clonazepam 1 mg/day	1, 2, 3, 4
5	f	56	17	5	No	1
6	f	75	16.5	6	No	1, 2, 3, 4
7	f	66	14	13	No	1, 2, 4
8	m	75	13.5	4	Gabapentin 600 mg/day	1, 4
9	m	76	15	3	Levodopa/benserazid 300/75 mg/day	1

Neurological findings: 1 = postural instability, 2 = dysmetria, dysdiadochokinesia or intention tremor upper limbs (uni- or bilateral), 3 = dysmetria lower limbs (uni- or bilateral), and 4 = diminished ankle reflexes and/or reduced vibration sense

f female, *m* male

(mm), and root mean square (RMS, mm) of the recorded center-of-pressure (CoP) trajectories [2].

Statistical analysis

Data are reported as mean ± SEM. MTV effects on tremor intensity and coherence were analyzed by repeated-measures analysis of variance and Bonferroni post hoc analysis with condition (standing vs. lying), stimulation (MTV vs. no MTV), and muscle type as factors. Because posturographic measures were not normally distributed, MTV effects on body sway were analyzed using a Wilcoxon matched-pairs signed-rank test. Results were considered significant at $p < 0.05$.

Results

During upright standing, all patients showed a coherent high-frequency tremor in all examined leg muscles and in *z*-axis body sway (mean tremor frequency: 15.1 Hz; range 13.5–17.5 Hz) that was absent during lying ($p < 0.001$). MTV did not reset tremor frequency but effectively reduced tremor intensity equally in all muscles by in average 32.5 ± 7.1% ($p < 0.001$). This was accompanied by a moderately reduced inter-muscular tremor coherence (mean reduction: 5.6 ± 1.7%, $p < 0.001$) (Fig. 1a–d). MTV effects on posture resulted in reduced high-frequency body sway along *z*-axis (mean reduction: 37.2 ± 6.8%; $p = 0.032$)

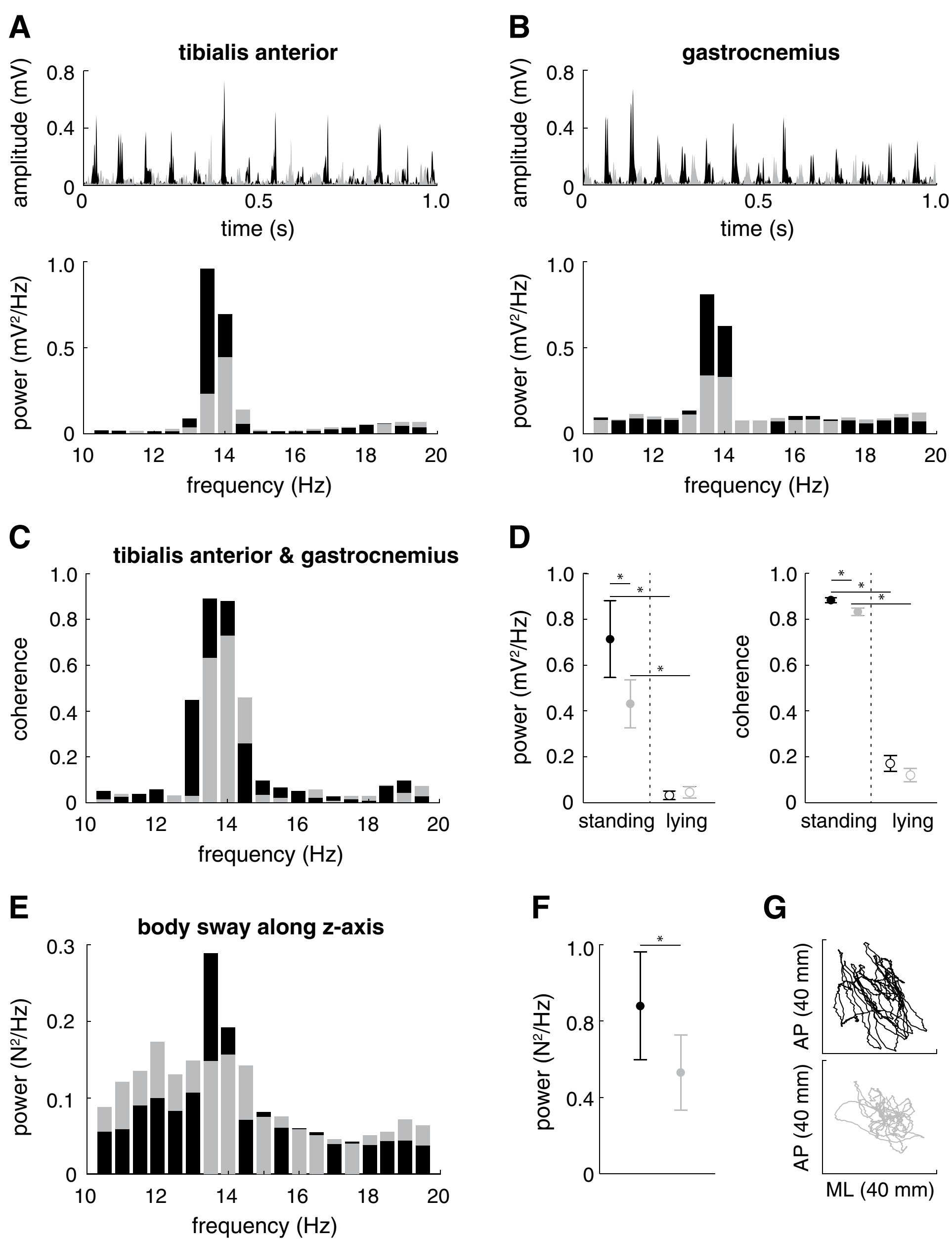

Fig. 1 Effects of proprioceptive stimulation on tremor characteristics and body sway. Rectified EMG traces and power spectra of the tibialis anterior (**a**) and gastrocnemius muscle (**b**) as well as coherence between both muscles (**c**) during normal standing (black) and standing with muscle tendon vibration (MTV) on the bilateral soleus muscle (gray). **d** Group effects of MTV on tremor intensity and inter-muscular coherence during standing as well as during lying. **e** Representative power spectrum of body sway along *z*-axis during normal standing (black) and standing with muscle tendon vibration (MTV) on the bilateral soleus muscle (gray). **f** Group effects of MTV on high-frequency body sway. **g** Corresponding center-of-pressure trajectories in anterior–posterior (AP) and medio-lateral plane (ML). Asterisk indicates a significant difference

and moderately improved balance indicated by smaller outcomes for area (mean reduction: 30.8 ± 10.0%; $p = 0.011$) and RMS (mean reduction: 10.6 ± 5.3%; $p = 0.038$) of body sway (Fig. 1e–g). Finally, we observed a moderate backward shift of the mean CoP position (− 24.2 ± 16.2 mm, $p = 0.015$) in response to the illusionary forward body tilt, which is known to be provoked by MTV on the soleus muscles [5, 7]. Four patients reported a subjectively felt improvement of unsteadiness during MTV and no patient indicated increase of unsteadiness due to stimulation. The presence of reduced vibration sense did not correlate with MTV effects on tremor intensity or posture.

Discussion

The present findings indicate that continuous low-intensity modulation of proprioceptive feedback has a positive moderating influence on the course of symptoms emergence in patients with OT while standing. In consistence with the previous examinations on the influence of peripheral stimulation in OT [1, 8], continuous MTV did not reset tremor frequency and only showed minor effects on inter-muscular tremor coherence underpinning the presumed central origin of OT. However, the observed reduction of tremor intensity indicates that continuous proprioceptive stimulation may mitigate the peripheral manifestation of the centrally generated oscillatory pattern during standing. In line with this, we further found that MTV induced improvements in body balance and subjective unsteadiness of patients with OT, whereas, in the healthy elderly vibratory leg muscle stimulation rather tends to destabilize posture [9].

OT could manifest peripherally via a direct projection of central oscillatory sources to spinal motoneurons. However, the observation that motoneurons can be activated voluntarily without exhibiting the tremor pattern (e.g., lifting one leg from the floor), while tremor burst persist in homologous muscles of the other limb, makes a direct connection unlikely [1]. The central oscillatory pattern could alternatively be relayed via spinal interneurons, since tremor bursts occur during muscle contraction under load, i.e., during activation of Golgi tendon organ (GTO) afferents that directly project to Ib interneurons [8]. GTO afferents as well as muscle spindle afferents are known to be strongly modulated by MTV applied on muscles under load [10], which would give a plausible site of action for a direct influence of MTV on peripheral tremor manifestation.

Alternatively, MTV might have a more indirect deescalating influence on symptoms emergence in OT. Accordingly, it has been suggested that after tremor onset while standing, proprioceptive feedback from the periphery becomes increasingly synchronized at the tremor frequency [3, 4]. This tremor-locking of proprioceptive afferents would disrupt normal peripheral feedback regulation of posture and give rise to an increased co-contraction of anti-gravity musculature leading to a vicious cycle of escalating subjective and objective postural unsteadiness [4]. The continuous engagement of proprioceptive afferents via MTV could to some extend prevent the tremor-locking of peripheral feedback and thereby deescalate the symptoms occurrence in OT. In this regard, the mode of action of MTV could be similar to that of continuous lower limb movements during gait that consistently relieve clinical symptoms in patients with OT, although the high-frequency leg tremor persists during ambulation [1].

Many patients with OT insufficiently respond to currently available pharmacological treatment options [11, 12]. Alternative interventions such as deep brain stimulation of the thalamus [13, 14] or spinal cord stimulation [15] showed positive effects in single patients that, however, need to be confirmed in future controlled clinical trials. In this respect, the present findings may open new avenues for a non-invasive therapeutic intervention via low-intensity modulation of proprioceptive feedback in patients with OT.

Author contributions Conceived and designed the study: MW, CS, and RS. Performed the study: MW, CS, KM, and RS. Performed statistical analysis: MW. Wrote the paper: MW. Critical revision of the manuscript: CS, KM, and RS.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing interests.

Ethical standard All experimental procedures were approved by the appropriate Ethics Committee.

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