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Single Case – General Neurology

No Efficacy with Noninvasive Brain Stimulation for Painful Legs and Moving Toes: A Case Report

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Keywords
Painful legs and moving toes · Brain stimulation · Repetitive transcranial magnetic stimulation

Abstract
Introduction: Painful legs and moving toes (PLMT) is a rare neurological disorder characterized by neuropathic pain and involuntary movements in the lower limbs. The pathophysiological mechanisms are unclear, but central mechanisms might be involved, suggesting that noninvasive brain stimulation might be helpful. Thus far, no reports have been published on noninvasive brain stimulation to treat PLMT. ***Case Presentation:*** A 70-year-old female had a 1-year history of PLMT. After several unsuccessful medical attempts, the patient received repetitive transcranial magnetic stimulation and transcranial direct current stimulation to alleviate the pain and involuntary movements with no benefit. ***Conclusion:*** This is the first report on noninvasive brain stimulation in a PLMT patient. Although ineffective in our patient, noninvasive brain stimulation should be further studied in this often difficult to treat and debilitating syndrome.

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Introduction

Painful legs and moving toes (PLMT) is a rare debilitating neurological syndrome, characterized by neuropathic pain and involuntary movement in the lower limbs, originally described in 1971 [1]. The neurobiological mechanisms are not yet understood, and there are no published treatment trials. Current evidence for treatments is based on anecdotal case

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reports and series that are likely associated with publication bias favoring positive findings. For example, gabapentin, pregabalin, clonazepam, pramipexole, and botulinum toxin injections have shown some benefit in PLMT [2]. Brain imaging has shown that central mechanisms may contribute to the symptoms [3], which suggests that brain stimulation treatment might be useful, but there are no reports of noninvasive brain stimulation to treat PLMT. Here, we describe a patient who received noninvasive brain stimulation with multiple different treatment protocols. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536467).

Case Presentation

A 70-year-old female with a history of atrial fibrillation, hypercholesterolemia, and migraine with aura was referred to the neurology outpatient clinic due to lower extremity pain. Her medical history included a lower back surgery due to spondylolisthesis 19 years earlier (laminectomy LIV-V and spondylodesis LIV-V/LV-SI) with postoperative right LV-SI nerve root damage and motor weakness.

The patient reported 1-year history of neuropathic pain bilaterally in the heels and lateral parts of the feet that had gradually progressed proximally up to the shins. In addition, the patient had noticed new-onset involuntary movements of the toes, which she described as cramps and twitching.

On clinical examination, there was mild weakness in the distal lower extremity motor strength together with incomplete right peroneal paresis, partial distal lower extremity sensory loss, bilateral loss of the Achilles reflex, and the gait was affected by the right-sided peroneal paresis. There was a continuous involuntary movement bilaterally in her toes at rest (online suppl. video). These movements could be stopped with a gentle touch on the toes or by asking the patient to focus on stopping the movement. Otherwise, her neurological examination was unremarkable.

Before the onset of the involuntary toe movements, the patient had undergone lumbar spine MRI, which was unremarkable, and ENMG showing old bilateral LV and right SI nerve root damages. Cervical and thoracic spine MRI and laboratory examinations were unremarkable. PLMT was diagnosed based on the clinical phenomenology.

Several medications failed to alleviate the symptoms and were discontinued due to lack of efficacy. The inefficacious medications included NSAIDs, paracetamol, paracetamol+codeine, oxycodone, tizanidine, amitriptyline, gabapentin, tramadol, lamotrigine, and levodopa. The patient developed anxiety and depression because of her disabling symptoms, which were partly alleviated with oxazepam and escitalopram. Mild benefit was obtained with clonazepam and pramipexole, but both were discontinued due to side effects. Finally, a combination of gabapentin (600 mg three times per day) and baclofen (15 mg three times per day) provided partial benefit for pain but not for the involuntary movements. At this point, the patient declined from botulinum toxin injections due to fear of side effects.

The patient received repetitive transcranial magnetic stimulation (rTMS) treatment to several targets, including the primary motor cortex (bilateral lower limb M1 representation, 10 Hz), supplementary motor area (bilateral SMA, 1 Hz), right secondary somatosensory area (S2, 10 Hz), and left dorsolateral prefrontal cortex (DLPFC) (10 Hz). No significant benefit was achieved for either pain or movement disorder. In addition, the symptoms did not respond to transcranial direct current stimulation (tDCS) either. tDCS was carried out with the cathode

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over the bilateral SMA and the anode over the left dorsolateral prefrontal cortex (2 mA, 20 min per session, 15 sessions in 3 weeks). Dorsal column stimulator was declined because of the anticoagulant therapy.

Discussion

In this case, noninvasive brain stimulation (rTMS and tDCS) did not provide symptomatic benefit despite the use of multiple different targets that have previously been used for neuropathic pain [4], mood disorders [4], and hyperkinetic movement disorders, such as dystonia [5]. Despite being ineffective in our patient, noninvasive brain stimulation could still be a worthwhile avenue to explore for treatment of PLMT. These techniques have shown promise in several neurological disorders and are increasingly used clinically [4]. In movement disorders, however, only Parkinson's disease has reached level B (probable efficacy) according to the most recent evidence-based guidelines on the therapeutic use of rTMS [4]. In PLMT, there are no published studies or case reports of noninvasive brain stimulation, but low-frequency rTMS to the premotor cortex showed some benefit in a patient with cervical dystonia and possible painless legs and moving toes syndrome [6], which is considered a rarer variant of PLMT. These observations can facilitate the search for efficacious targets for PLMT in the future. We also hope that our case report will encourage publishing negative findings to provide balanced information to the literature. This is particularly important in rare conditions, such as PLMT, where available information of treatment efficacies is mostly based on case reports and series.

Statement of Ethics

The authors confirm that the approval of an institutional review board was not required for this work. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images and videos.

Conflict of Interest Statement

Dr. Brück reports conference travel support from Teva, AbbVie, NordicInfu Care, Lundbeck, Pfizer, and the Finnish Neurological Society; and lecturer honoraria from Teva and AbbVie. Dr. Pullinen has received grants from the Finnish Parkinson Foundation, Maire Taponen Foundation, and the Finnish Medical Foundation, and conference travel support from the Finnish Neurological Society and Orion. Dr. Joutsa reports research grants from the Finnish Medical Foundation, Sigrid Juselius Foundation, Finnish Foundation for Alcohol Studies, University of Turku, and Turku University Hospital; conference travel support from AbbVie, Abbott and Insightec; consulting for Summaryx and Adamant Health; and lecturer honoraria from Lundbeck and Novartis. Other authors have no conflicts of interest to declare.

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Author Contributions

A.B.: organization, execution, writing the first draft, and review and critique; J.P., J.N., and S.L.: execution and review and critique; and J.J.: conception, organization, execution, writing the first draft, and review and critique.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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