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Letters to the Editor Related to Published Articles

Reply: Painful Legs and Moving Toes: Clinical and Electrophysiological Observations

I read with great interest the article by Alvarez et al.[1] In their review, they confirmed that Painful Legs and Moving Toes (PLMT's) etiology is diverse although the majority of patients had evidence of peripheral nerve involvement or radiculopathy. However, in some patients, namely in patients with Wilson's disease[2] and myelitis,[3] a structural central nervous system lesion is evoked to be associated with the development of PLMT. We reported a patient with Hashimoto's disease[4] who developed slight dystonia and bradykinesia and presented PLMT. The patient had any electrophysiological signs of neuropathy or any clinical sign indicative of a root or nerve disorder. MRI brain scan showed several small subcortical white matter fronto-parietal lesions, without diffusion restriction. Discrete and diffuse high signal in periventricular white matter was visible in T2-weighted images. These aspects are frequently found in Hashimoto's encephalopathy.[5] We also believe that at least in some cases PLMT has a central origin and is composed of a variety of dystonic movements. In our reported case,[4] we think PLMT was associated with Hashimoto's encephalopathy.

João Guimarães, MD*
British Hospital XXI
Lisboa, Portugal
**E-mail: joaoguimaraes.neuro@gmail.com*

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Painful Legs and Moving Toes Following a Traumatic Medial Plantar Nerve Injury

Video 

Painful legs and moving toes (PLMT) is a rare syndrome, which is characterized by involuntary movements of the toes and pain in the legs.[1] Peripheral nerve injury results in sensory and motor loss in relation to the extend of the axonal degeneration distal to the site of injury and subsequent denervation and reorganization of peripheral and central connections, which lead to significant alterations and in peripheral connectivity and reflex organization.[2]

A 40-year-old male patient presented with shaking of the right toes. Patient had a partial rupture of the right Achilles tendon 3 years ago following a direct blunt trauma to the medial and posterior side of the ankle and treated with a short leg cast for 3 months. He noticed the shaking of the right toes after removing the cast. He had dysesthesia and pain in the sole of the right foot extending from the heel to the toes after the trauma. Sensory symptoms gradually improved and disappeared within 2 months. He was diagnosed with dystonia and treated with baclophen. There was no sign of improvement.

Upon neurological examination, there was mild hypoesthesia in the right medial plantar nerve distribution. A rhythmic, continuous, and complex flexion/extension, adduction/abduction, fanning, and clawing of the right toes with slow frequency was noted. Involuntary movements were present at rest and disappeared during sleep and when the foot was touched by the examiner (Video 1).

Nerve conduction studies of bilateral peroneal, posterior tibial, lateral plantar, sural, and left medial plantar nerves were normal. Sensory nerve conduction study of the right medial plantar nerve revealed decreased amplitude of the sensory nerve action potentials (decreased by 65.2% when compared with the right side;[3] Table 1). Surface EMGs were recorded from flexor digitorum brevis muscle. Movements had a synchronous pattern with a frequency of 3 Hz, burst duration of 190–210 m/sec, and mean amplitude of 236 μV (Fig. 1).

Patient was commenced on Propranolol 20 mg daily and was increased up to 40 mg. Movements disappeared completely by 40 mg propranolol. There was no sign of involuntary activity in the control examination at the first month (Video 2).

Additional Supporting Information may be found in the online version of this article.

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TABLE 1. *The results of medial and lateral plantar sensory nerve conduction studies*

	Medial plantar nerve		Lateral plantar nerve	
	NCV (m/sec) (NL: 28.0)	Amp (μV) (NL:2.8)	NCV (μV) (m/sec) (NL:22.9)	Amp (μV) (NL: 1.0)
Right	38.4	4.6	36.4	3.1
Left	37.6	1.6	35.2	2.8

NCV, nerve conduction velocity; m/sec, meter per second; NL, normal limit; Amp, amplitude; μV, microvolt.

In this case, there are two possibilities which may injure the medial plantar nerve. One of them is the direct blunt trauma and the latter is prolonged compression by the cast. We believe that the time interval of 3 months until the removal of the cast was sufficient for the recovery of mild and partial affection of a peripheral nerve. Therefore, we think that the lesion was probably related with the direct trauma or compression due to the haemorrhagia following the trauma.

A few cases were reported, suggesting a relationship between focal peripheral nerve lesions and moving toes, which showed myokymic discharges on EMG examination.[4,5] We think that this may also be related with the increased excitability and impaired excitation of the motor neuron. It was demonstrated that peripheral nerve injuries and subsequent reinnervation result in alterations of the central connectivity and the peripheral circuitry.[2] Another case with tarsal tunnel syndrome was reported, which also showed myokymic discharges and an absent lateral plantar nerve response on electrophysiological examination.[4] The different feature of our case was the absence of the pain after the first few months. Additionally, treatment options are relatively limited in PLMT and medications such as gabapentin, which also have analgesic effects, are usually preferred. We think that propranolol may be used especially in cases without pain.

It was shown that the effects of the peripheral nerve lesion and subsequent reinnervation are far reaching and may lead to impaired excitability in the spinal cord.[2,6] Also, cortical hand representations are highly abnormal following reinnervation, where larger and often multiply represented receptive fields have a disordered and fractured somatotopic arrangement.[7]

In conclusion, peripheral nerve injuries may rarely present with involuntary movements, and this may be related with the abnormal reorganization of the reinnervated axons and the abnormal central connectivity. The incidence of the movement disorders and the underlying pathology following the peripheral nerve injuries should be further investigated. Propranolol may be a choice for the treatment.

Legends to the Video

Segment 1. Complex flexion/extension, abduction/adduction movements in the toes before the treatment.

Segment 2. No sign of involuntary movements at the first month of the treatment with propranolol.

Author Roles: Zinnuroglu M: Patient assessment and writing of the first draft and review and critique of the manuscript; Ozkayran T: Writing of the first draft and review and critique of the manuscript.

Murat Zinnuroglu, MD*
Department of Physical Medicine and Rehabilitation
Gazi University
Ankara, Turkey
Department of Physical Medicine and Rehabilitation
Bursa Military Hospital
Bursa, Turkey
**E-mail: muratz@gmail.com*

Tufan Ozkayran, MD
Department of Neurology
Bursa Military Hospital
Bursa, Turkey

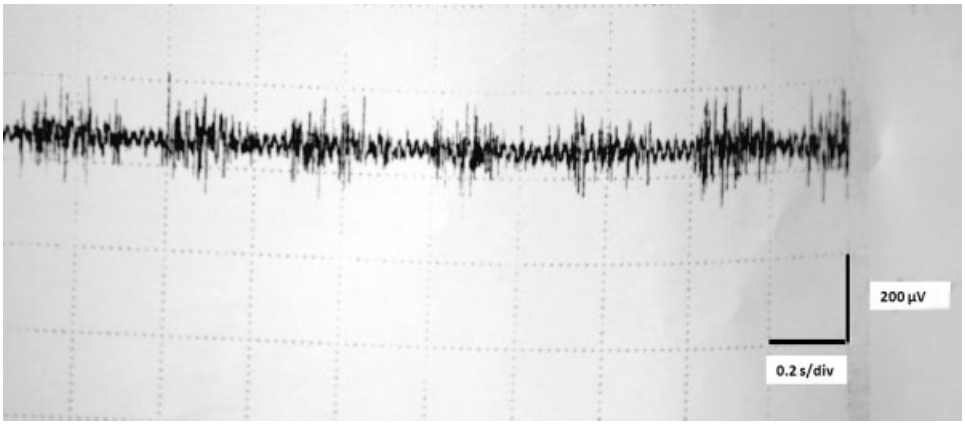

FIG. 1. Surface EMG record from the flexor digitorum brevis muscle.

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Quality of Life Score Is Primarily Affected by the Mental Rather than the Physical Component in Patients with Restless Legs Syndrome

We read with interest the article by Nomura et al.[1] concluding that the prevalence of restless legs syndrome (RLS) in the rural population is lower than that reported for Caucasian population.[1] The study presents further evidence of disturbed quality of life (QoL) and poor sleep in patients with RLS. Interestingly, it was reported that in patients with primary RLS, there were no evidence of reduced physical related QoL parameters, although mental related ones were significantly affected.

Our group has an interest in RLS of uremic etiology, investigating means of improving functional capacity and QoL in hemodialysis (HD) patients with the syndrome.[2] From baseline data in a study underway assessing the effectiveness of exercise training in HD patients with RLS, we made similar observations regarding the QoL to those reported from Nomura et al.[1] More specifically, our preliminary data are derived from 78 stable HD patients (58 male, 20 female, 53.94 $\pm$ 16.74 years), divided into two groups according to their RLS status using the International RLS (IRLS) study group criteria[3]: the RLS group (n = 30, 20 male, 53.0 $\pm$ 19.0 years) and the non-RLS group (n = 48, 38 male, 55.1 $\pm$ 13.2 years). We examined the impact of RLS in patients' with physical-related QoL and functional capacity. QoL was assessed by the SF-36 questionnaire, and functional capacity was evaluated by using the North Staffordshire Royal Infirmary test, whereas RLS severity was assessed by the International RLS study group rating scale.[4]

Even though Nomura's study deals with primary and our study with uremic RLS, we also observed the total QoL score and mental health component were both significantly compromised in the RLS group compared to the non-RLS group. In agreement with Nomura's study, our SF-36 physical health dimension and functional capacity score did not differ between the RLS and non-RLS groups. In addition, significant negative correlations ($P < 0.05$) were observed between the IRLS score on one hand and the SF-36 total score ($r = -0.463$), the SF-36 role physical scale ($r = -0.519$), the SF-36 general health ($r = -401$), and the SF-36 physical health dimension ($r = -0.523$) on the other.

The differences in total QoL score when comparing RLS and non-RLS patients could be explained by the significantly diminished mental-related scales score that both our and Nomura's patients experienced, compared with their free RLS counterparts.

Even though primary and secondary RLS do not seem to share the same etiology, both studies conclude that RLS did not seem to have any detrimental effect on the physical and functional capacity of the patients. These findings seem logical because limp movements and in general various types of physical activities that temporarily ameliorate RLS symptoms result in more physical activity; however, because this type of activity is a necessity rather a personal choice, the situation can in turn make RLS patients mentally distressed.

Nomura et al. have reported a low-RLS prevalence in a rural population (1.8%) compared to general adult population of Japan (4.01%)[5], in agreement with another study by Hadjigeorgiou et al,[6] contacted in a similar mixture of population in central Greece that reported a low-prevalence of RLS (3.9%) compared to other Caucasian populations. The fact that high levels of physical activity are usually observed in rural population because the nature of their occupations could also help toward preserving functionality.

In conclusion, similar to primary RLS as shown by Nomura et al, uremic etiology RLS appears not to have any detrimental effect on physical QoL or functional capacity. It is important, however, to note that in rural RLS patients, the increased everyday activity could mask any potential effect of the syndrome to the physical related QoL, and therefore, further research is needed engaging other types of populations.

Christoforos D. Giannaki, BSc, MSc*
Giorgos K. Sakkas, PhD
Department of Nephrology
School of Medicine, University of Thessaly
Larissa, Greece
Institute for Human Performance and Rehabilitation CE.RE.TE.TH
Trikala, Greece
**E-mail: giannaki@med.uth.gr*

Georgios M. Hadjigeorgiou, MD, PhD
Department of Neurology
School of Medicine, University of Thessaly
Larissa, Greece
Institute of Biomedical Research and Technology, CE.RE.TE.TH
Larissa, Greece

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Vassilios Liakopoulos, MD, PhD
Department of Nephrology
School of Medicine, University of Thessaly
Larissa, Greece
Institute of Biomedical Research and Technology, CE.RE.TE.TH
Larissa, Greece

Georgios Anifandis, PhD
Department of Nephrology
School of Medicine, University of Thessaly
Larissa, Greece

Christina Karatzaferi, PhD
Yiannis Koutedakis, PhD
Department of Sport Science
University of Thessaly
Trikala, Greece
Institute for Human Performance and Rehabilitation CE.RE.TE.TH
Trikala, Greece

Ioannis Stefanidis, MD, PhD
Department of Nephrology
School of Medicine, University of Thessaly
Larissa, Greece
Institute of Biomedical Research and Technology, CE.RE.TE.TH
Larissa, Greece

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Reply: QOL Score is Primarily Affected by the Mental Rather than the Physical Components in Patients with RLS

We congratulate Dr. Stefanidis and his coworkers for their beautiful and important study. They found significantly diminished mental-related scores in uremic patients with restless legs syndrome (RLS) compared with patients without RLS.[1] This supports and expands our previous findings.[2] The findings that RLS goes along with diminished mental-related scores are consistent both in patients with primary and secondary RLS. Another study in dialysis patients showed that most of the domains of the SF-36 were affected in RLS (except physical function).[3] Our study supports that RLS itself tends to affect mental aspects independent of primary or secondary forms. In fact, the association of RLS with poor mental health has been noted in several epidemiological survey studies.[4] We hypothesize that deteriorated mental aspects in RLS could relate to cognitive impairment. Although patients with RLS performed worse than normal controls on the prefrontal cognitive impairment,[5] the cognitive deficits in RLS did not result from the chronic sleep disruption.[6] Recently, an association between RLS and neuroticism has been additionally implicated.[7] Further investigation about this issue in RLS is needed.

Author Roles: Takashi Nomura: Conception, organization, and execution of research project, design and execution of statistical analysis, writing of the first draft of manuscript and editing/review of final manuscript. Masayoshi Kusumi: Execution of research project, review and critique of statistical analysis, review and critique of final manuscript. Yusuke Uemura: execution of research project, execution of statistical analysis, review and critique of final manuscript. Kenji Nakashima: Conception and organization of research project, review and critique of statistical analysis, editing and review of final manuscript. Yuichi Inoue: Conception and Organization of research project, review and critique of statistical analysis, editing and review of final manuscript.

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Takashi Nomura, MD, PhD*
Masayoshi Kusumi, MD, PhD
Yusuke Uemura, MD
Kenji Nakashima, MD, PhD
Department of Neurology
Department of Brain and Neurosciences
Faculty of Medicine, Tottori University
Yonago, Japan
**E-mail: ntnomura@med.tottori-u.ac.jp*

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Yuichi Inoue, MD, PhD
Japan Somnology Center
Neuropsychiatric Research Institute, Shibuya-ku
Tokyo, Japan

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Reply: Plasma Cholesterol and Parkinson's disease: Is the Puzzle only Apparent?

Our first publication in *Movement Disorders*[1] reporting an "association" between lower cholesterol and Parkinson's disease (PD) noted the limitations of case-control analysis. It cautioned the readers that "*we could not make a causal inference between LDL-C and/or statin use and risk of PD*.[1]" To reduce the possibility of reserve causality, we subsequently studied a prospective cohort[2] and found a similar association. Similar findings were also reported in two other prospective cohorts.[3,4] Interestingly, Scigliano and colleagues themselves found "*the association of untreated IPD with reduced vascular diseases risk(s)*" including higher cholesterol.[5] There has been one inconsistent report[6] in which the cases were identified from a National Insurance Register that entitles patients to medication free of charge.

Therefore, the overall evidence to date favors an association between higher cholesterol and lower PD occurrence. The three prospective cohorts cited earlier[2-4] have generated some useful insight on PD etiology. Rigorous diagnostic criteria[7] were applied in the Honolulu Asia Aging Study, and of 25 cases that had autopsy, PD was confirmed pathologically in 21. Further, the age of onset in any study population is bounded by its age distribution. The average age at cholesterol assay in the Honolulu cohort was 77 years old,[2] thus, it is not surprising that the onset of incident cases was also higher in this cohort. Given the consistency of this association across prospective studies, it seems to us that more, not less, research should be conducted to understand the nature of this finding and its medical ramifications, if any. Thus, we disagree with Scigliano et al.'s notion that future studies should simply be abandoned. It is both inconsistent with the weight of available evidence, and contrary to the scientific method.

Xuemei Huang*
Department of Neurology
Penn State University College of Medicine
**E-mail: xuemei@psu.edu*

Honglei Chen
Department of Epidemiology
National Institute of Environmental Health Sciences

Helen Petrovitch
Pacific Health Research Institute

Richard Mailman
Department of Pharmacology
Penn State University College of Medicine

Webster Ross
Pacific Health Research Institute

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