Rajan Roopa (Orcid ID: 0000-0003-4987-7252) Vishnu Venugopalan Y (Orcid ID: 0000-0002-3654-8137) Latorre Anna (Orcid ID: 0000-0001-7103-5209) Bhatia Kailash P (Orcid ID: 0000-0001-8185-286X)

TITLE

Reply to: Pregabalin responsive tongue and arm tremor after Guillain Barré Syndrome

AUTHORS

Roopa Rajan¹ MD, DM; Vishnu Venugopalan Y¹ MD, DM; Anna Latorre² MD, PhD; Kailash P Bhatia² MD, FRCP

1 Department of Neurology, All India Institute of Medical Sciences, New Delhi

2 Sobell Department of Motor Neuroscience and Movement Disorders, University College London (UCL) Institute of Neurology, London, United Kingdom

Corresponding author: Dr. Roopa Rajan, Room 708, 7th Floor, Neurosciences Center, AIIMS, New Delhi. rooparajan@aiims.edu

Word count (Text): 361

Running title: Neuropathic tremor in Guillain-Barrè Syndrome

Key words: Neuropathic tremor, Guillain-Barrè Syndrome, tremor analysis, dystonic tremor, pregabalin

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/mdc3.13891

We thank Nóbrega et al for their interest in our article "Neuropathic tremor in Guillain Barre Syndrome".[1] In their letter, Nóbrega et al highlight an important treatment option for neuropathic tremor following Guillain Barre Syndrome.[2] The clinical course and characteristics of tremor in their report are strikingly similar to our series of patients with neuropathic tremor after Guillain Barre Syndrome- being a fine, fast and jerky tremor predominantly in the upper limb.[1] While majority of our patients had dystonic posturing in the upper limb, the patient reported by Nóbrega et al, had prominent tongue tremor.

Out of the five patients in our series, one patient reported subjective benefit on tremor with propranolol and one did not respond. In other patients, tremor was not functionally disabling to warrant medical treatment. None of our patients received pregabalin. Prior studies have reported mixed results while using pregabalin in neuropathic tremor. Individual patients with Guillain Barre Syndrome or chronic inflammatory demyelinating neuropathy were reported to have good benefit on tremor with pregabalin.[3,4] However, in a cohort of 44 patients with neuropathic tremor associated with chronic inflammatory demyelinating neuropathy, pregabalin was used in two patients without benefit; whereas tremor improved with treatment of underlying neuropathy in some.[5]

From a pathophysiological viewpoint, these observations support the hypothesis for a central oscillator at the cerebellar level in neuropathic tremor, particularly that associated with inflammatory neuropathies. GABA is an important neurotransmitter, specifically involved in maintaining hyperpolarization and low firing rates in the cerebellar granule cells, which is key to maintaining high signal-to-noise ratio while processing sensory information in the cerebellum. [6] Pregabalin, a GABA structural analogue, inhibits voltage gated calcium channels mimicking the downstream actions of GABA on its receptors and likely increases the efficiency of sensory processing in the cerebellum in the context of neuropathic tremor.

From a clinical perspective, these reports add to the therapeutic options in neuropathic tremorspropranolol, pregabalin and gabapentin may be initial medications to be trialled, based on anecdotal experience. Of note, many patients may not have functionally disabling tremor and treatment may not be warranted. Further longitudinal, prospective studies are required to understand the natural history and therapeutic response in this unique disorder.

AUTHOR ROLES

1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Roopa Rajan: 1A, 1B, 1C, 3A

Venugopalan Y Vishnu: 1B,3B

Anna Latorre: 1B, 3B

Kailash P Bhatia: 1A, 1B, 1C, 3B

FUNDING SOURCES AND CONFLICT OF INTEREST

There is no funding to specific to this manuscript. The authors declare that there are no conflicts of interest relevant to this work.

FINANCIAL DISCLOSURES FOR THE PREVIOUS 12 MONTHS

The authors report that there are no additional disclosures to report.

ETHICAL COMPLIANCE STATEMENT

The authors confirm that the approval of an institutional review board and patient consent were not required for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

References

- [1] Rajan R, Anandapadmanabhan R, Vishnoi A, Vishnu VY, Latorre A, Agarwal H, et al. Neuropathic Tremor in Guillain-Barré Syndrome. Mov Disord Clin Pract 2023. https://doi.org/10.1002/MDC3.13807.
- [2] Nóbrega, Paulo; Vasconcelos, Thais; Paiva, Anderson; Lima, Pedro Lucas; Braga-Neto, Pedro; Guimaraes, Thiago; Krueger M. Pregabalin responsive tongue and arm tremor after Guillain Barre Syndrome. Mov Disord Clin Pract 2023;in press.
- [3] Coltamai L, Magezi DA, Croquelois A. Pregabalin in the treatment of neuropathic tremor following a motor axonal form of Guillain-Barré syndrome. Mov Disord 2010;25:517–9. https://doi.org/10.1002/MDS.22961.
- [4] Alonso-Navarro H, Fernández-Díaz A, Martín-Prieto M, Ruiz-Ezquerro JJ, López-Alburquerque T, Jiménez-Jiménez FJ. Tremor associated with chronic inflammatory demyelinating peripheral neuropathy: Treatment with pregabalin. Clin Neuropharmacol 2008;31:241–4. https://doi.org/10.1097/WNF.0b013e3181585b71.
- [5] Saifee TA, Schwingenschuh P, Reilly MM, Lunn MPT, Katschnig P, Kassavetis P, et al. Tremor in inflammatory neuropathies. J Neurol Neurosurg Psychiatry 2013;84:1282–7. https://doi.org/10.1136/JNNP-2012-303013.
- [6] Chadderton P, Margie TW, Häusser M. Integration of quanta in cerebellar granule cells during sensory processing. Nat 2004 4286985 2004;428:856–60. https://doi.org/10.1038/nature02442.