Revista de Neurología

Rev. Neurol. **2026**; 81(11): 58763
https://doi.org/10.31083/RN58763

Letter to the Editor

Response to the Letter to the Editor—Re: "Beyond Phenotype: An Anatomical-Compartment Framework for Peripheral Neuropathy"

Tomoo Yuba[1], Ali Dabbagh[2], A. Sassan Sabouri[3,4,5,*]

[1]Department of Anesthesiology and Intensive Care, Osaka University Hospital, 565-0871 Osaka, Japan
[2]Anesthesiology Research Center, Department of Anesthesiology, Faculty of Medicine, Shahid Beheshti Medical Science University, 4739 Tehran, Iran
[3]Department of Anesthesiology, Harvard Medical School, Boston, MA 02115, USA
[4]Department of Anesthesiology, Mass General Brigham, Boston, MA 02114, USA
[5]Department of Anesthesiology, Shahid Beheshti Medical Science University, 4739 Tehran, Iran
*Correspondence: asabouri@mgh.harvard.edu (A. Sassan Sabouri)
Academic Editor: Eduardo Gutiérrez Rivas
Submitted: 9 October 2026 Accepted: 26 October 2026 Published: 17 November 2026

Dear Editor,

We thank Cerasuolo and Barahona Rodriguez for their thoughtful and constructive comments regarding our review, "Peripheral Neuropathy: A Phenotype-Driven Review for Diagnosis and Management". We appreciate their proposal to make anatomical-compartment localization a more explicit component of the diagnostic framework.

We agree that anatomical localization represents an important dimension in the evaluation of peripheral neuropathy. In our original framework, we had considered anatomical localization in several sections, although we did not explicitly incorporate it as a separate step within the diagnostic pathway. For example, sensory neuronopathy was linked to pathology involving the dorsal root ganglion rather than a conventional distal "dying-back" axonopathy; autoimmune nodopathies were discussed in relation to nodal and paranodal structures; ischemic and vasculitic neuropathies were linked to injury involving the vasa nervorum; and focal entrapment neuropathies were approached as anatomically localized disorders [1,2,3,4,5].

In this view, Cerasuolo and Rodriguez's proposal can be a useful refinement of the phenotype-first approach. A practical diagnostic pathway could begin with the clinical phenotype, proceed to anatomical localization, then consider the underlying pathophysiologic mechanism, and finally guide the selection of targeted diagnostic testing.

In this model, the phenotype still remains the initial bedside entry point, defining how the disorder presents, while anatomical localization helps determine where the pathological process resides. Mechanistic interpretation can then guide the selection of the most appropriate confirmatory tests, including electrodiagnostic studies, ultrasound, magnetic resonance neurography, skin biopsy, autonomic testing, and antibody assessment [1]. This approach is closely aligned with the proposed extension of our framework and may add another level of diagnostic precision without diminishing the practical value of phenotype-based clinical recognition.

A related concept is neuroanatomical plausibility, which is highly relevant to the clinical diagnosis of neuropathic pain. Contemporary grading systems for neuropathic pain require that the pain distribution be neuroanatomically plausible in relation to the suspected lesion or disease affecting the somatosensory system [6]. This concept further illustrates how phenotype and anatomical localization are interdependent in clinical reasoning. At the same time, the degree of anatomical resolution achievable in practice depends on the diagnostic tools available. In some patients, localization may be limited to a peripheral nerve or nerve root, whereas advanced techniques such as high-resolution nerve ultrasound, magnetic resonance neurography, specialized electrodiagnostics, or molecular and antibody testing may permit more refined localization [1].

We therefore agree that explicitly emphasizing anatomical localization can further strengthen the phenotype-driven approach. Rather than representing a separate or competing framework, the anatomical-compartment perspective can provide an additional level of precision and improve the transition from clinical presentation to mechanism-based testing and management.

We thank the authors for highlighting this valuable perspective and for extending the discussion initiated by our review.

Author Contributions

TY contributed to the conceptualization and writing of the original manuscript draft. AD contributed to the conceptualization and critical review of the manuscript. AS contributed to the conceptualization, critical review, and revision of the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Copyright: © 2026 The Author(s). Published by IMR Press.
This is an open access article under the CC BY 4.0 license.

Publisher's Note: IMR Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Yuba T, Dabbagh A, Sabouri AS. Peripheral Neuropathy: A Phenotype-Driven Review for Diagnosis and Management. Revista De Neurologia. 2026; 81: 48384. https://doi.org/10.31083/RN48384

[2] Sheikh SI, Amato AA. The dorsal root ganglion under attack: the acquired sensory ganglionopathies. Practical Neurology. 2010; 10: 326–334. https://doi.org/10.1136/jnnp.2010.230532

[3] Eshed-Eisenbach Y, Brophy PJ, Peles E. Nodes of Ranvier in health and disease. Journal of the Peripheral Nervous System. 2023; 28: S3–S11. https://doi.org/10.1111/jns.12568

[4] Ubogu EE. Biology of the human blood-nerve barrier in health and disease. Experimental Neurology. 2020; 328: 113272. https://doi.org/10.1016/j.expneurol.2020.113272

[5] Schmid AB, Fundaun J, Tampin B. Entrapment neuropathies: a contemporary approach to pathophysiology, clinical assessment, and management. Pain Reports. 2020; 5: e829. https://doi.org/10.1097/PR9.0000000000000829

[6] Finnerup NB, Haroutounian S, Kamerman P, Baron R, Bennett DLH, Bouhassira D, et al. Neuropathic pain: an updated grading system for research and clinical practice. Pain. 2016; 157: 1599–1606. https://doi.org/10.1097/j.pain.0000000000000492