

## Neuropathic Pain Following SARS-CoV-2 Infection

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### LETTER TO THE EDITOR

We read with interest Shil *et al.*'s review article on central and peripheral neuropathic pain following SARS-CoV-2 infection [Shil, R.S.K. *et al.*, 2023]. Causes of neuropathic pain identified included compression neuropathy (e.g. history of proning in COVID-19 patients for treatment of ARDS in ICU), axonal sensorimotor critical illness neuropathy (e.g. in severe COVID-19 requiring hospitalization or ICU), drug-related (e.g. neurotoxic drugs used for acute COVID-19 illness such as daptomycin, linezolid, lopinavir, ritonavir, hydroxychloroquine, cisatracurium, clindamycin, glucocorticoids), stroke (e.g. thalamic pain secondary to stroke), or pain secondary to inflammation (e.g., transverse myelitis, Gullian Barre Syndrome) [Shil, R.S.K. *et al.*, 2023]. It was suggested that certain pre-existing condition such as diabetes, hypothyroidism, uraemia, B12/B1 deficiency, malignancy, paraneoplastic syndromes, paraproteins, myeloma, secondary amyloidosis, hepatitis, HIV, syphilis, leprosy, Lyme disease, chronic inflammatory demyelinating polyneuropathy (CIDP), vasculitis-like granulomatosis with polyangiitis, mononeuritis multiplex, sarcoidosis, SLE, Sjogren's syndrome, rheumatoid arthritis, degenerative disc disease, trauma, or hereditary disease (acute intermittent porphyria, hereditary sensory-motor neuropathy, Fabry's disease) may favour the development of SAR-CoV-2-related neuropathic pain [Shil, R.S.K. *et al.*, 2023]. The study is impressive, but several points require discussion.

We disagree with the notion that central nervous system (CNS) disease, such as stroke or transverse myelitis, causes neuropathic pain [Shil, R.S.K. *et al.*, 2023]. Although some authors differentiate central from peripheral neuropathic pain, it has to be stressed that the term "neuropathic" stems from neuropathy. Since there is no neuropathy of the central nervous system but only of cranial and peripheral nerves, the term "central neuropathic pain" is misleading and should be avoided. The confusion may originate from the fact that the

second axon of bipolar cells, which make up A-delta and C-fibres constitute the spinothalamic tract. Anyhow, CNS disease causing pain should not have been included in a review about neuropathic pain.

A category of neuropathic after SARS-CoV-2 infection not considered in the review is pain due to critically ill neuropathy. Since severe SARS-CoV-2 infection often require treatment on an intensive care unit (ICU) with long long-term artificial ventilation, critically ill neuropathy may develop in at least some of these patients [Mitsikostas, D.D. *et al.*, 2022]. Critically ill neuropathy in these patients may not only be primarily due to the infection but secondarily due to nutrition, secondary infections including sepsis, and specific neurotoxic medications administered during ICU stay.

Another cause of neuropathic patient following a SARS-CoV-2 infection not considered in the review is compartment syndrome. Compartment syndrome associated with SARS-CoV-2 infection may result from different pathophysiological mechanisms, such as compression palsy due to special bedding on the ICU.

Not mentioned in the review was that trigeminal neuralgia can be the sole manifestation of neurological involvement in SARS-CoV-2 infection [Molina-Gil, J. *et al.*, 2021].

To sum up, the excellent study has limitations that should be addressed before final conclusions are drawn. Clarifying the weaknesses would strengthen the conclusions and improve the study.

### DECLARATIONS

**Completing interests:** the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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