



Reply to “Intensification of an Essential Tremor by SARS-CoV-2”

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Accepted: 21 April 2022

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Dear Editor,

We read with interest the comment by Dr. Finsterer on our recent work entitled “Worsening of Essential Tremor After SARS-CoV-2 Infection” [1]. We are glad to open a meaningful discussion, which would allow us to further explain and discuss some important issues which were not included in the original paper in the interest of brevity.

The first point raised by Dr. Finsterer concerns the neuroimaging findings in our patients. The first MRI, performed in 2017 at the age of 60 as part of the diagnostic work-up, had shown left pontine small lacunas. To determine the etiology of these lesions, the patient had performed a complete cardiovascular screening, which excluded classical risk factors such as large-artery atherosclerosis, atrial fibrillation, paradoxical embolization, diabetes, hypertension, infections, hyperlipidemia, autoimmune diseases, prothrombotic factors, and other uncommon causes of stroke [2]. The patient was not a smoker. He had no history of acute or paroxysmal neurological manifestations. His anamnestic history only included anemia and an anxious depressive syndrome, and no other disease aside from tremor was detected. As already stated in the original article, the MRI performed after SARS-CoV-2 infection did not depict any appreciable modifications, indicating that the left pontine small lacunas were unchanged [1]. Again, the absence of any other neurological symptom or sign except for tremor, which was still confirmed at the moment of tremor worsening and at the subsequent neurological evaluations, together with the lack any other general health concern, guided us in determining that the use of contrast medium was not indicated in the two MRI. The above factors, along with a temporal factor (we

had the opportunity to visit the patient and record his tremor more than two months after the negatification of the nasopharyngeal swabs), guided our decision to avoid any invasive procedures, including lumbar puncture for the analysis of the cerebrospinal fluid, and any risky therapy, such as immunosuppressant treatment, which was taken in light of a risk-benefit consideration. To date, objective tremor features remained unchanged, although the patient reported a subjective improvement in tremor. Tremor treatment (propranolol 40 mg/daily) has not been modified.

Regarding the tremor relief with alcohol, which is a typical feature of essential tremor, no history of alcohol abuse or regular drinking was present in our patient. The extensive battery of laboratory exams performed at the time of evaluation excluded hepatic functional alterations or any other causes of tremor worsening.

Concerning the statement on inflammatory involvement of the cerebellum and brainstem during SARS-CoV-2 infection, we referred to the interesting post-mortem case series presented by Matschke et colleagues [3] whose results may help us in better interpreting our case report. Matschke et al. assessed the neuropathological features of 43 patients who died of SARS-CoV-2 and found that the “activation of microglia and infiltration by cytotoxic T lymphocytes was most pronounced in the brainstem and cerebellum, and meningeal cytotoxic T lymphocyte infiltration was seen in 34 (79%) patients” [3]. We acknowledge, however, that immune encephalitis following a SARS-CoV-2 infection can occur in all cerebral locations.

In conclusion, despite the clear temporal relationship between SARS-CoV-2 infection and tremor worsening, we are aware that our observation is not sufficient to firmly establish a causal link between SARS-COV-2 infection and essential tremor worsening. We believe that our case may be useful to raise awareness in the medical and scientific community of a possible relationship between SARS-COV-2 infection and essential tremor worsening that will inevitably need to be further investigated and confirmed in large case series.

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Acknowledgements The authors wish to thank Melissa Kerr (melissa.kerr@uniroma1.it) from the Department of Human Neurosciences, Sapienza University of Rome, for help in the English-language editing of the manuscript.

Author Contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Massimiliano Passaretti, Giulia Paparella, Alessandro De Biase, Luca Angelini, Antonio Cannavacciuolo, and Donato Colella. The first draft of the manuscript was written by Massimiliano Passaretti and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

Ethical Compliance Statement The authors confirm that the approval of an institutional review board was not required for this work. A written informed consent of the patient was obtained for the publication of his data. The authors have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Conflicts of Interest The authors declare that there are no funding sources or conflicts of competing interests relevant to this work.

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