Dear Editor,

In 2019, acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the causative agent of a cluster of respiratory infections, later named coronavirus disease 2019 (COVID-19) [1]. Various reports documented that patients with movement disorders, including Parkinson’s disease, experienced a worsening of their symptoms, e.g., tremor, bradykinesia, and gait disturbances, after severe COVID-19 [2–6], although definite conclusions on the COVID-19 impact could not be made in most cases [2–6]. In essential tremor (ET), the possible consequences of SARS-CoV-2 infection are uninvestigated. Here we discuss the case of an ET patient whose symptoms worsened after asymptomatic SARS-CoV-2 infection.

A 60-year-old right-handed man diagnosed with ET in 2015 complained of significant tremor worsening in July 2021. The patient’s symptoms had started at the age of 17 years with action tremor of the upper limbs, which was slightly predominant on the left side and responsive to alcohol administration. The patient had no rest tremor. He reported a family history of tremor on the maternal side (both grandparents and three mother’s siblings). In 2015, he started propranolol 40 mg daily. A brain magnetic resonance imaging (MRI) performed in June 2017 documented millimetric left pons lacunes. From 2015 to 2021, no changes in tremor severity were documented and no therapy modification was needed. The patient was enrolled in a longitudinal research study on ET progression, for which he underwent comprehensive clinical and kinematic assessments in June 2015 (T1) and December 2020 (T2), with movement (Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS), Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPSRD)), psychiatric (Brief Psychiatric Rating Scale (BPRS); Clinical Global Impression (CGI); Hamilton Anxiety Rating Scale (HAM-A); Hamilton Depression Rating Scale (HAM-D)), and cognitive functions (Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE)) evaluated by standardized scales. The assessment also included kinematic analysis of upper limb tremor as detailed in [7]. Briefly, kinematic recordings were performed using an optoelectronic system (SMART motion system, BTS Engineering, Italy) consisting of three infrared cameras (sampling rate of 120 Hz) and reflective markers of negligible weight taped to the subject’s arms and trunk [7]. Upper limb postural tremor of was recorded: (i) with the arms outstretched in front of the chest (posture 1), and (ii) with the arms flexed at the elbows, i.e., lateral “wing beating” posture (posture 2). Upper limb kinetic tremor was recorded during a “pointing task,” in which the subject was asked to repetitively move his index finger from their nose to a reflective target fixed on a heavy support approximately 15 cm above the table at sternal height and at approximately 2/3 arm distance. Rest tremor of the upper limbs was recorded while the patient sat comfortably on a chair facing the cameras, with his arms laying on a desk in front of him. Tremor analysis was performed using dedicated software (SMART Analyzer, BTS Engineering, Italy) [7]. Written informed consent was obtained.

In April 2021, the patient was diagnosed with asymptomatic SARS-CoV-2 infection, confirmed by four consecutive polymerase-chain-reaction nasopharyngeal swab test, during a 28-day period. Three weeks later, he noticed tremor worsening that persisted over time. In July 2021 (T3), an aggravation of postural and kinetic upper limb tremor was clinically present (Fig. 1). No other neurological signs were observed. Psychiatric and cognitive functions did not change as compared to previous evaluations. Brain MRI and laboratory exams did not depict any appreciable changes. The patient underwent a further kinematic assessment, which documented an increase in postural tremor amplitude as
that has also been reported after SARS-CoV-2 infection. Disorders after viral infection is a well-established finding or cognitive status changes since clinical scores remained unchanged. It was unlikely to be due to infection-related psychiatric and/or cognitive status changes, including Purkinje cell loss and axonal swelling. In ET patients, brain pathology depicts several cerebellar changes, including Purkinje cell loss and axonal swelling. Dysfunction in Purkinje cell GABAergic output to the dentate nucleus leading to increased cerebello-thalamic connectivity has also been demonstrated. Altogether, we may hypothesize that the tremor worsening in our patient resulted from further virus-induced immune-mediated cerebellar circuit dysfunction. We did not title, however, serum auto-antibodies responsible for tremor autoimmune conditions (i.e., anti-DPPX, anti-GFAP, anti-mGLUR1).

In conclusion, this is the first study demonstrating that SARS-CoV-2 infection may cause tremor worsening in ET. Our careful pre-infection assessment showed a clear temporal relationship between infection and tremor worsening, which probably reflects a causal link. Tremor worsening in our case was likely due to virus-induced immune-mediated functional alterations in cerebellar networks. More observations are needed to better determine the relation between SARS-CoV-2 and ET in clinical practice.

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Declaration

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.

Competing Interests The authors declare no competing interests.
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