

# Disputes & Debates: Editors' Choice

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## Editors' Note: Incidence of Epilepsy and Seizures Over the First 6 Months After a COVID-19 Diagnosis: A Retrospective Cohort Study

In "Incidence of Epilepsy and Seizures Over the First 6 Months After a COVID-19 Diagnosis: A Retrospective Cohort Study," Taquet et al. reviewed electronic health records and identified 2 cohorts of 152,754 people with coronavirus disease 2019 (COVID-19) or influenza and found a higher incidence of seizures and epilepsy in people with COVID-19 (hazard ratio 1.55 [1.39–1.74] and 1.87 [1.54–2.28], respectively, compared with influenza). Brenner postulated that this may be related to the effect of severe acute respiratory syndrome coronavirus 2 spike protein on release of synaptic vesicle protein 2A, a binding site for levetiracetam on neurons. Lin et al. noted that it is important to recognize the limitations of this study, including (1) potential survival bias in studying nonhospitalized patients, (2) the effect of vaccinations, and (3) the lack of data on seizure or epilepsy severity.

Ariane Lewis, MD, and Steven Galetta, MD  
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## Reader Response: Incidence of Epilepsy and Seizures Over the First 6 Months After a COVID-19 Diagnosis: A Retrospective Cohort Study

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The increased incidence of epilepsy in coronavirus disease 2019 (COVID-19) survivors is of interest.<sup>1</sup> Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein reduces perforin release from CD8+T lymphocytes<sup>2</sup> similar to that of levetiracetam on CD8+T lymphocytes.<sup>3</sup>

Patients treated with levetiracetam for epilepsy have an increased incidence of respiratory tract infections, likely related to reduced immunity from inhibited perforin release mediated by synaptic vesicle protein 2A (SV2A) on CD8+T lymphocytes,<sup>3</sup> the same SV2A present on neurons in the brain through which levetiracetam acts.<sup>4</sup>

SARS-CoV-2 spike protein may affect SV2A, which is a specific binding site for the antiepileptic, levetiracetam, causing an increased incidence of epilepsy in COVID-19 survivors.

1. Taquet M, Devinsky O, Cross JH, Harrison PJ, Sen A. Incidence of epilepsy and seizures over the first 6 months after a COVID-19 diagnosis: a retrospective cohort study. *Neurology*. 2023;100(8):e790-e799. doi:10.1212/WNL.0000000000201595
2. Huang CF, Hsieh SM, Pan SC, Huang YS, Chang SC. Dose-related aberrant inhibition of intracellular perforin expression by S1 subunit of spike glycoprotein that contains receptor-binding domain from SARS-CoV-2. *Microorganisms*. 2021;9(6):1303.
3. Li G, Nowak M, Bauer S, et al. Levetiracetam but not valproate inhibits function of CD8+ T lymphocytes. *Seizure*. 2013;22(6):462-466. doi:10.1016/j.seizure.2013.03.006
4. Ohno Y, Tokudome K. Therapeutic role of synaptic vesicle glycoprotein 2A (SV2A) in modulating epileptogenesis. *CNS Neurol Disord Drug Targets*. 2017;16(4):463-471. doi:10.2174/1871527316666170404115027

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# Reader Response: Incidence of Epilepsy and Seizures Over the First 6 Months After a COVID-19 Diagnosis: A Retrospective Cohort Study

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We read with great interest the study by Taquet et al.<sup>1</sup> on the incidence of epilepsy and seizures over the first 6 months after a COVID-19 diagnosis. This valuable contribution revealed the difference of incidence of epilepsy and seizure between patients with COVID-19 and those with influenza. However, the possible confounder bias hidden in the design should be discussed.

First, the cohorts included all patients diagnosed with COVID-19 or influenza between January 20, 2020, and May 31, 2021, and were still alive at the end of follow-up (August 24, 2021). This may cause survival bias. The results of greater hazard ratio of epilepsy after COVID-19 compared with influenza in nonhospitalized people should be interpreted with caution because the most severe patients were excluded.

Second, the vaccination against SARS-CoV-2 might influence the likelihood of developing seizures, but whether the participants received influenza vaccine should also be considered.

Third, we did not know the severity or course of epilepsy and seizure after COVID-19 and influenza diagnosis from this study.

The authors make a great contribution to evaluating the incidence of seizure and epilepsy after COVID-19 diagnosis. We suggest further discussion on limitations.

1. Taquet M, Devinsky O, Cross JH, Harrison PJ, Sen A. Incidence of epilepsy and seizures over the first 6 months after a COVID-19 diagnosis: a retrospective cohort study. *Neurology*. 2023;100(8):e790-e799.

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## CORRECTION

### PARK2, PINK1, and DJ1 in Patients With Early-Onset Parkinson's Disease in Four European Countries

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In the original author list, there was an error. Cezary Zekanowski was not an author or abstract participant. The AAN scientific programming team regrets the error.

#### Reference

1. Milanowski L, Lindemann J, Barcikowska M, et al. PARK2, PINK1, and DJ1 in patients with early-onset Parkinson's disease in four European countries. (2506) *Neurology*. 2020;94(15 Supplement):2506.

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## **PARK2, PINK1, and DJ1 in Patients With Early-Onset Parkinson's Disease in Four European Countries**

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