



# COVID-19 EEG Studies: The Other Coronavirus Spikes We Need to Worry About

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## Report of Electroencephalographic Finding on Critically Ill Patients With COVID-19

Vespignani H, Colas D, Lavin BS, et al. *Ann Neurol.* 2020. <https://onlinelibrary.wiley.com/doi/full/10.1002/ana.25814>

In March 2020, we treated a cohort of 26 critically ill hospitalized SARS-CoV-2 infected patients who received EEGs to assess unexplained altered mental status, loss of consciousness, or poor arousal and responsiveness. Of the 26 patients studied, 5 patients had EEGs that showed periodic discharges (PD) consisting of high amplitude frontal monomorphic delta waves with absence of epileptic activity. These findings may suggest CNS injury potentially related to COVID-19 in these patients.

## EEG Findings in Acutely Ill Patients Investigated for SARS-CoV-2/COVID-19: A Small Case Series Preliminary Report

Galanopoulou AS, Ferastraoaru V, Correa DJ, et al. *Epilepsia Open.* 2020;5(2):314-324. <https://doi.org/10.1002/epi4.12399>

**Objective:** Acute encephalopathy may occur in COVID-19-infected patients. We investigated whether medically indicated EEGs performed in acutely ill patients under investigation (PUIs) for COVID-19 report epileptiform abnormalities and whether these are more prevalent in COVID-19 positive than negative patients. **Methods:** In this retrospective case series, adult COVID-19 inpatient PUIs underwent EEGs for acute encephalopathy and/or seizure-like events. PUIs had 8-channel headband EEGs (Ceribell; 20 COVID-19 positive, 6 COVID-19 negative); 2 more COVID-19 patients had routine EEGs. Overall, 26 Ceribell EEGs, 4 routine, and 7 continuous EEG studies were reviewed. EEGs were interpreted by board-certified clinical neurophysiologists ( $n = 16$ ). EEG findings were correlated with demographic data, clinical presentation and history, and medication usage. Fisher exact test was used. **Results:** We included 28 COVID-19 PUIs (30-83 years old), of whom 22 tested positive (63.6% males) and 6 tested negative (33.3% male). The most common indications for EEG, among COVID-19-positive versus COVID-19-negative patients, respectively, were new onset encephalopathy (68.2% vs 33.3%) and seizure-like events (14/22, 63.6%; 2/6, 33.3%), even among patients without prior history of seizures (11/17, 64.7%; 2/6, 33.3%). Sporadic epileptiform discharges (EDs) were present in 40.9% of COVID-19-positive and 16.7% of COVID-19-negative patients; frontal sharp waves were reported in 8/9 (88.9%) of COVID-19-positive patients with EDs and in 1/1 of COVID-19-negative patient with EDs. No electrographic seizures were captured, but 19/22 COVID-19-positive and 6/6 COVID-19-negative patients were given anti-seizure medications and/or sedatives before the EEG. **Significance:** This is the first preliminary report of EDs in the EEG of acutely ill COVID-19-positive patients with encephalopathy or suspected clinical seizures. EDs are relatively common in this cohort and typically appear as frontal sharp waves. Further studies are needed to confirm these findings and evaluate the potential direct or indirect effects of COVID-19 on activating epileptic activity.

## Electroencephalogram (EEG) in COVID-19: A systematic Retrospective Study

Petrescu AM, Taussig D, Bouilleret V. *Neurophysiol Clin.* 2020;50(3):155-165. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7315937/>

**Objectives:** Although rare, neurological manifestations in SARS-CoV-2 infection are increasingly being reported. We conducted a retrospective systematic study to describe the electroencephalography (EEG) characteristics in this disease, looking for specific patterns. **Methods:** EEGs performed in patients with positive PCR for SARS-CoV-2 between March 25, 2020 and May 06, 2020 in the University Hospital of Bicetre were independently reviewed by 2 experienced neurologists. We used the American Clinical Neurophysiology Society's terminology for the description of abnormal patterns. EEGs were classified into 5 categories, from normal to critically altered. Interobserver reliability was calculated using Cohen kappa coefficient. Medical records were reviewed to extract demographics, clinical, imaging, and biological data. **Results:** Forty EEGs were reviewed in 36



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COVID-19 patients, 18 in intensive care units (ICU) and 22 in medicine units. The main indications were confusion or fluctuating alertness for 23 (57.5%) and delayed awakening after stopping sedation in ICU in 6 (15%). EEGs were normal to mildly altered in 23 (57.5%) contrary to the 42.5% where EEG alterations were moderate in 4 (10%), severe in 8 (20%), and critical in 5 (12.5%). Generalized periodic discharges (GPDs), multifocal periodic discharges (MPDs), or rhythmic delta activity (RDA) were found in 13 recordings (32.5%). EEG alterations were not stereotyped or specific. They could be related to an underlying morbid status, except for 3 ICU patients with unexplained encephalopathic features. Conclusion: In this first systematic analysis of COVID-19 patients who underwent EEG, over half of them presented a normal recording pattern. EEG alterations were not different from those encountered in other pathological conditions.

## Commentary

By now it is well-known that neurological manifestations occur in ~35% of COVID-19 patients, and potentially in a majority of patients with more severe infections.<sup>1-3</sup> Results of electroencephalogram (EEG) in these patients are of particular interest: (1) How frequently is epileptiform activity seen in this patient population, and are the underlying risks for epileptiform activity different from other critically ill patients? (2) Are there novel EEG features specific to COVID-19? (3) Is the EEG informative in guiding the understanding of the pathophysiology of the frequently observed altered mental status, or prognosis, in COVID-19?

We are now starting to see the early COVID-19 EEG studies in the literature. Obtaining EEG in a safe manner to limit exposure will necessarily limit the number of patients in these studies.<sup>4</sup> Thus, early studies likely represent highly select groups of patients in whom suspicion of seizures was likely substantial. The range of prevalence of electrographic seizures in the intensive care unit (ICU) ranges between ~10% to 45%,<sup>5,6</sup> with the largest series estimating ~15%.<sup>7</sup> The prevalence of electrographic seizures in sepsis is ~15%,<sup>8</sup> although it is lower in patients with sepsis without evidence of acute central nervous system disease.<sup>9</sup> These statistics can serve as a useful baseline.

The following 3 papers are peer-reviewed studies that systematically assessed EEGs in patients with COVID-19, as of July 26, 2020. That the study authors, clinicians engaged in the momentous task of treating these patients in high prevalence hospitals, were able to quickly disseminate this information is a noteworthy and commendable achievement.

The first, published in the *Annals of Neurology* (Vespignani et al<sup>10</sup>) is an observational study performed across multiple ICU departments in Paris during a 2 week period in March 2020. Electroencephalograms were done with a limited 9-electrode (plus reference) device for 30 minutes. They noted that 19 of 26 had “diffuse and nonspecific theta and alpha wave activity” which likely refers to nonspecific slowing. Two patients had isoelectric EEGs. A total of 5 patients were reported to have periodic discharges. Examining the snapshots of the EEGs, 4 of these were labeled as generalized rhythmic delta activity by the authors (which would technically not be periodic) and one of them as lateralized periodic discharges. In my review, 4 of those 5 did have periodic activity. All of them were critically ill, and 3 of them died before completion of the study. The authors suggest that the findings in these 5 patients could be indicative of brain


injury, either related to COVID-19 directly or concurrent illness. The presented examples in the manuscript do not necessarily appear to me to differ significantly from patterns seen in other critically ill patients. In fact, what seems unusual and reassuring is that only 1 of 26 patients had focal discharges, and no patient had electrographic seizures.

The second study, published in *Epilepsia Open*, originates from Albert Einstein College of Medicine, one of the epicenters of the COVID-19 pandemic in New York City during a 6-week period in March to April 2020 (Galanopoulou et al<sup>11</sup>). Electroencephalograms, utilizing either a 10-electrode device or full montage EEGs, were obtained from acutely ill patients who were under investigation for COVID-19. A total of 28 patients were included, most of whom would eventually test positive for COVID-19 (22 patients). The EEG readers were aware of the results of at least some of the COVID testing a priori, potentially introducing both selection and confirmation bias. As expected, all EEGs had abnormal background slowing. Although the high prevalence of COVID-19 did not allow for a more statistically favorable split in this study (thus resulting in mostly nonsignificant results), there were some provocative findings: COVID-positive patients had more seizure-like events (motor events or confusion) prompting the EEG request (63% vs 33%), new encephalopathy (68% vs 33%), sporadic epileptiform discharges (41% vs 17%), and rhythmic/periodic discharges (18% vs 0%). A significantly greater proportion of COVID-negative patients (83% vs 24%) were found to have some other infection other than COVID. This study suggests that perhaps COVID-positive patients differ from a similar COVID-negative cohort. Again, as in the previous study, no electrographic seizures were recorded.


The third study, a single institution retrospective review from France (Petrescu et al<sup>12</sup>), reports 40 consecutive routine EEGs from 36 patients who tested positive for COVID, after excluding brain death studies and asymptomatic patients, half of the patients from the ICU. Electroencephalograms were normal or nearly normal in a little more than half of the recordings (57.5%). Patients with more severe abnormalities on EEG were associated with concurrent neurological disorders, including posterior reversible encephalopathy syndrome, malignancy, or dementia. Periodic discharges were seen in 8 patients, but it was felt that *none* of the patients had epileptiform activity.

Collectively, these studies appear to suggest that encephalitis and cortical irritability may not be major features of central

nervous system manifestations of COVID-19, supporting findings that the virus or its specific encephalitic manifestations are not typically found in brain tissue.<sup>13</sup> Initial reports from China that there was no evidence of increased risk of symptomatic seizures from COVID-19 are reassuring.<sup>14</sup> This is, after all, still a primarily non-neurological disease. There are notable limitations to these early studies. The sample sizes are tiny, and studies obtained are by and large short routine EEGs, which are unlikely to record an electrographic seizure. Studies with sample sizes an order of magnitude larger, with continuously recorded EEG studies, and with recorded longer-term clinical outcomes are required for more reasonable assessments of the full spectrum of EEG abnormalities and their consequences; a multicenter consortium may be a reasonable way to address this.<sup>15</sup> There are already several case reports of seizures in the setting of COVID-19 as well as preprints of continuous EEG studies detailing potentially greater risk of epileptiform activity. Thus, full “damage reports” are still pending, and many questions remain unanswered.

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## References

1. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 2020;77(6):1-9.
2. Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med.* 2020;382(23):2268-2270.
3. Karadas O, Ozturk B, Sonkaya AR. A prospective clinical study of detailed neurological manifestations in patients with COVID-19. *Neurol Sci.* 2020;41(8):1991-1995.
4. Gelisse P, Rossetti AO, Genton P, Crespel A, Kaplan PW. How to carry out and interpret EEG recordings in COVID-19 patients in ICU? *Clin Neurophysiol.* 2020;131(8):2023-2031.
5. Oddo M, Carrera E, Claassen J, Mayer SA, Hirsch LJ. Continuous electroencephalography in the medical intensive care unit. *Crit Care Med.* 2009;37(6):2051-2056.
6. Berisavac II, Padjen VV, Ercegovic MD, et al. Focal epileptic seizures, electroencephalography and outcome of sepsis associated encephalopathy—A pilot study. *Clin Neurol Neurosurg.* 2016;148:60-66.
7. Rodriguez Ruiz AA, Vlachy J, Lee JW, et al. Association of periodic and rhythmic electroencephalographic patterns with seizures in critically ill patients. *JAMA Neurology.* 2017;74(2):181-188.
8. Azabou E, Magalhaes E, Braconnier A, et al. Early standard electroencephalogram abnormalities predict mortality in septic intensive care unit patients. *PLoS One.* 2015;10(10):e0139969.
9. Nielsen RM, Urdanibia-Centelles O, Vedel-Larsen E, et al. Continuous EEG monitoring in a consecutive patient cohort with sepsis and delirium. *Neurocrit Care.* 2020;32(1):121-130.
10. Vespignani H, Colas D, Lavin BS, et al. Report of electroencephalographic finding on critically ill patients with COVID-19. *Ann Neurol.* 2020;88(3):626-630.
11. Galanopoulou AS, Ferastraoar V, Correa DJ, et al. EEG findings in acutely ill patients investigated for SARS-CoV-2/COVID-19: a small case series preliminary report. *Epilepsia Open.* 2020;5(2):314-324.
12. Petrescu AM, Taussig D, Bouilleret V. Electroencephalogram (EEG) in COVID-19: a systematic retrospective study. *Neurophysiol Clin.* 2020;50(3):155-165.
13. Solomon IH, Normandin E, Bhattacharyya S, et al. Neuro-pathological features of Covid-19. *N Engl J Med.* 2020;383:989-992.
14. Lu L, Xiong W, Liu D, et al. New onset acute symptomatic seizure and risk factors in coronavirus disease 2019: a retrospective multicenter study. *Epilepsia.* 2020;61(6):e49-e53.
15. Frontera J, Mainali S, Fink EL, et al. Global consortium study of neurological dysfunction in COVID-19 (GCS-NEURO-COVID): study design and rationale. *Neurocrit Care.* 2020;33(1):25-34.