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Research Article

EEG Characteristics in Hospitalized Patients with Acute COVID-19 Symptoms

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Abstract

The COVID-19 epidemic has revealed significant neurological manifestations including de novo seizures in patients who do not have a prior history of epilepsy or clear epilepsy risk factors. Our center is located in Arizona, which in the early part of January 2021 had more cases per capita than any other place in the world. We performed a retrospective review to observe the Electroencephalogram (EEG) patterns of hospitalized adult patients with COVID-19 between March 2020 and February 2021. The most common EEG abnormality was diffuse background slowing, which was seen in 63.6% of patients (n=63/99), compare to 15.1% of focal background slowing. Epileptiform discharges were seen in 11.1% of patients and seizures were found in 5.1% of patients, as newly diagnosed seizures. When combining all focal abnormalities, the most common location for these abnormalities was in the frontal regions 36.4% (n=8/22). This correlates with a hypothesis that the possible route of entry of the virus into the central nervous system is via the olfactory bulb and may explain why many post-COVID patients later develop executive function deficit. The utility of an EEG may help allow us better insight into how and where the COVID infection affects our central nervous system.

Keywords: COVID-19; Encephalopathy; EEG; New onset seizure; Frontal lobe

Introduction

During the COVID-19, various neurological complications have been described in the acute infectious phase and post-infectious phase. Headaches and anosmia are the more common neurological symptoms and may also be presenting symptoms of the infection prior to fever or any other constitutional symptoms. Neurological disturbances may occur irrespective of the severity of the COVID-19 infection. De novo seizures in patients without a prior history of epilepsy or clear epilepsy risk factors have been described with COVID-19 infection, and may be a presenting symptom in some patients [8]. Though the neurological manifestations are commonly observed clinically, how exactly the central nervous system is affected in unclear. Neurodiagnostic tests may provide insights in understanding how the COVID-19 virus affects the nervous system. Our center in Phoenix, Arizona was in the epicenter of the pandemic in early 2021 during which time we had more cases per capita than any other place in the world [2]. We performed a retrospective observation study of the hospitalized patients of our center to describe EEG findings to see any characteristics can be identified among COVID-10 patients. Within our cohort, we evaluated incidence of seizures, pattern of EEG abnormalities, and localization of abnormal discharges.

Material and Methods

This study is a single center, retrospective review of adult hospitalized patients at the Banner University Medical Center in Phoenix between March 2020 in February 2021. The study was approved by the Institutional Review Board. We reviewed every inpatient with acute diagnosis of COVID-19 based on COVID-19 RNA PCR via nasopharyngeal swab who also had EEG testing during the same hospitalization. Patients that had both continuous and routine EEGs during the same hospitalization were combined to prevent duplication or overestimation of the findings. Patients under the

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age of 18, patients not tested for COVID-19, or the results were not available within the electronic medical record were excluded. We obtained information including demographic data, indications for the EEG, type of EEG obtained (routine or continuous), imaging findings, use of anesthetics during the recording, history of cardiac arrest leading to or during admission, and comorbid neurological conditions. In respect to the EEG, we obtained data on the presence of seizures, epileptiform discharges, abnormal slowing, interictal discharges, and their localization. EEGs were obtained from 21 electrodes utilizing the 10-20 international electrode system and reviewed by board-certified epileptologists. The data was analyzed by simple percentage calculation.

Results

Demographics

We identified 99 patients who were COVID-19 positive and had EEG testing during the same hospitalization. This accounts for 8.2% of all patients who had inpatient EEGs during this time period (n=99/1213). Details of patient demographics are listed in Table 1. The median age was 63 (range 19-88) with 56.6% being over 60. 10 patients (10.1%, n=10/99) of our cohort had prior history of epilepsy. Fifteen patients had cardiac arrest directly prior to their admission or during their hospital admission. Thirteen patients had acute strokes evident on imaging (13.1%). Other acute imaging abnormalities were noted in 28.3% of patients. More than half of the EEGs (57.6%) were obtained in ICU and many of them (51.5%) were on the ventilatory when the EEG was obtained. Anesthetics agents are used in 38.4% when the EEG was obtained. Nearly two thirds of patients (63.7%) had EEG ordered to evaluate encephalopathy and 33.3% for seizure-like activity. Remaining 3% cases were to guide prognosis.

Table 1: Demographics of the hospitalized patients with COVID-19 who had EEGs

Total Patients	N=99
Gender	Female, 47
Age	Median 63 (18-88)
	Age >60 = 56.6% (n=56)
Prior History of Epilepsy	10.1% (n=10)
Cardiac Arrest on Admission	15.1% (n=15)
Acute Imaging Abnormalities	28.3% (n=28)
ICU Admission	57.6% (n=57)
Use of Anesthetics	38.4% (n=38)
Mechanical Ventilation	51.5% (n=51)

EEG Findings

The most common EEG finding was diffuse background slowing (77.7%) followed by focal slowing (15.1%) and suppressed or burst suppressed pattern (6.2%). Interictal epileptiform discharges were seen in 11.1% (n=11/99) of patients with focal epileptiform discharges in 9 of 11 patients. Only 3 patients with epileptiform discharges had prior diagnosis of epilepsy (27.2%, n=3/11). For the location of epileptiform discharges, frontal region origin was most common (Figure 1). Generalized discharges were seen in 2 patients with one patient having history of cardiac arrest and the other patient having a history of juvenile myoclonic epilepsy. Seizures were captured in 5 patients, and 4 patients never had a history of seizures in the past: One patient with myoclonic status epilepticus after cardiac arrest, one with acute right parieto-occipital stroke with dural vein thrombosis, one patient had a remote encephalomalacia in the left medial frontal region from prior meningioma resectioning, and the last one was without any imaging abnormalities. 91 of the patients had neuroimaging with either CT or MRI. 45% of these imaging tests had normal findings (n=41/91). Even though 21 patients had acute focal neuroradiologic findings, only 5 had correlated EEG abnormalities within the same region.

When EEG was obtained with suspected seizures (n=33), 4 cases (12.1%, n=4/33) indeed showed ictal pattern compared to 1.6% when seizures was not suspected (p=0.087).

Discussion

The utility of EEG and evaluating hospitalized patients with COVID-19 has been previously described in a meta-analysis where had been used for evaluating encephalopathy, characterizing seizure-like events, and neuro prognostication following cardiac arrest [1]. EEG findings in COVID-19 patients has been displayed focal abnormalities including focal slowing and interictal discharges seen most prominent in the frontal lobe [1, 9, 10]. This possibly correlates with a hypothesis that the COVID-19 virus enters nasal and oral mucosa via ACE-2 receptors and subsequently spreads into the central nervous system via afferent nerves transynaptically [11]. This spread is preferential to olfactory bulb and orbitofrontal regions of the brain.

Our single center retrospective study in one of the largest metropolitan cities in the United States, showed similar EEG findings among patients with COVID-19 to the previously reported meta-analysis. Our study revealed higher percentage of bilateral and diffuse EEG abnormalities possibly due to the severity of COVID-19 symptoms among our population. The background slowing is partly impacted by the fact that many patients received IV anesthetics or other sedating medications at the time the EEG was obtained.

Focal abnormalities including epileptiform discharges and slowing were seen more frequently in the frontal region compared to other locations in our cohort. As noted in Figure 1, 36.4% of focal slowing and epileptiform findings are seen in the frontal region. Figure 2 displays how frontal abnormalities are seen more common-

ly compared typical abnormalities seen in patients' with epilepsy. One theory of how COVID-19 may enter the central nervous system is through transsynaptic transmission via retrograde manner from the olfactory mucosa to the olfactory bulb which would preferentially affect the orbitofrontal region [3, 11]. Radiological data has also shown an association with frontal lobe abnormalities as well. One patient with 4 days anosmia who had COVID-19 had an MRI showing FLAIR changes during the within the olfactory bulb and the right gyrus rectus [7]. There is also a case report with persistent anosmia 6 weeks after being diagnosed with COVID-19 who had hypometabolism in the orbitofrontal region on an FDG-PET scan [4]. One infected patient with status epilepticus arising from the frontal region was noted to have cortical and subcortical FLAIR changes within the orbitofrontal region [6]. In a case series of hospitalized COVID-19 patients in Paris who had encephalopathy, PET scans had been obtained in the acute phase as well as at 1 and 6 months after COVID-19 onset [5]. A pattern of gyrus rectus hypometabolism was seen in all patients during the acute phase. Although he clear evidence of COVID-19 entry into the CNS via the olfactory bulb to affect the orbitofrontal region has not been fully established, the radiological and electrographic data suggest that the frontal lobes are possibly affected as a result of the direct viral infection.

Prior studies had not systematically reviewed if the EEG finding correlated with the acute imaging abnormality. When reviewing the EEG and the neuroradiological imaging, we only found that only 23% of patients had radiological abnormalities correlated with the localization of EEG abnormalities. Even for those patient who had frontal lobe abnormalities on EEG, only 13% had radiological evidence of frontal lobe abnormalities. This may support the prior hypothesis that EEG abnormality seen in the frontal region may be a biomarker of the COVID-19 virus affecting the CNS which may not be evident on radiological images or physical exam 3.

We found that clinical suspicion is highly important to detect electrographic seizures in COVID-19 patients, which may significantly impact the treatment and further monitoring, especially considering the fact that many of these patients did not have prior history of seizure.

The main limitation of the study was that it was not a prospective study. Due to our smaller sample size, we did not subcategorize epileptiform findings into periodic discharges or rhythmic delta activity. In addition, our cohort may be different severity of symptoms than the national cohort of patients who have COVID-19. Our group of epileptologist did not consistently use the standardized ACNS terminology for reporting EEGs, which makes somewhat challenging to compare to other studies. The utility of finding electrographic frontal lobe abnormality as a biomarker not only in the acute phase of COVID-19 infection but also for the long-COVID symptoms should be further explored. It appears EEG may be more sensitive that imaging studies when evaluate frontal lobe dysfunction. Our plan is to follow those patients with frontal lobe abnormalities in EEG to see whether they are more likely to develop persisted frontal lobe dysfunction even after recovery from acute COVID-19 symptoms. We speculate that frontal lobe involvement is the reason patients with Post-Acute COVID-19 Syndrome (PACS) tend to have persisted executive function deficit long after recovery from respiratory symptoms.

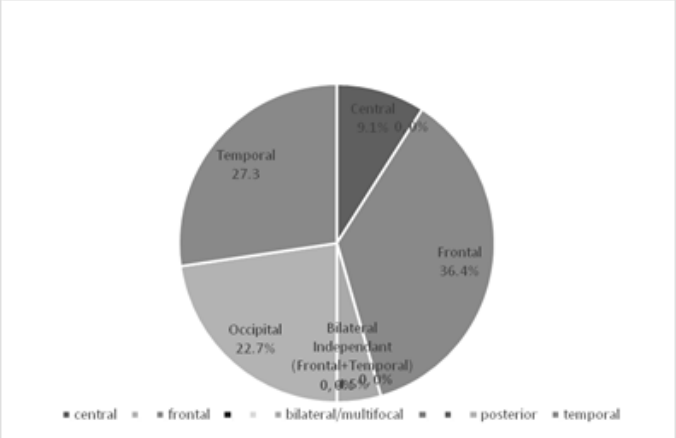

Figure 1: Location of focal EEG abnormality in hospitalized patients with COVID 19.

This pie chart shows topological representation of focal abnormalities (focal epileptiform discharge and slowing) in hospitalized patients with COVID-19.

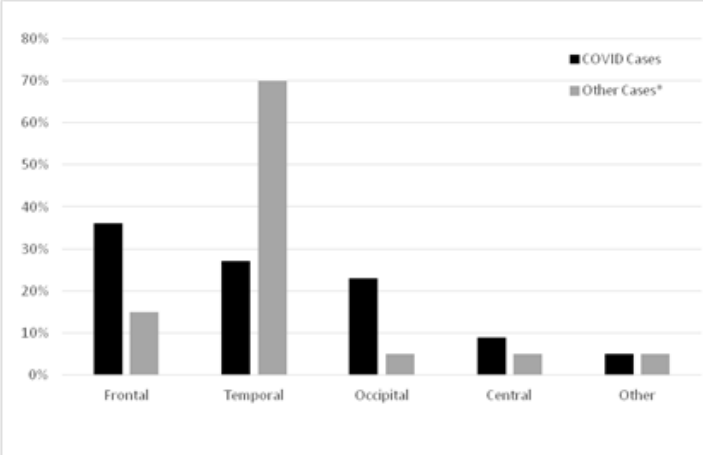

Figure 2: Focal EEG abnormality in COVID-19 patients compared to non-COVID-19 epilepsy patients reported in the EEG lab

This bar graph represents the location of EEG abnormality in hospitalized patients with COVID 19 compared to the EEG abnormality findings in the typical epilepsy population.

Conclusion

Our signal center retrospective review of the EEG findings of hospitalized patients with COVID-19 revealed similar findings seen in prior studies. New onset seizures were seen in patients even when clear radiological or clinical risk factors were not identified. The most common focal EEG abnormalities seen were in the frontal regions which represent a region, which may represent focal frontal lobe dysfunction in COVID-19 as it affects the central nervous sys-

tem. This introduces the possible utility of EEG in the long COVID patients with suspected central nervous system dysfunction along with a multimodality neurological work up alongside imaging, neuropsychological testing, and serological testing.

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