Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

COVID-19 associated encephalopathy: Is there a specific EEG pattern?

We report the history of two patients with coronavirus infectious disease 2019 (COVID-19) whose electroencephalograms (EEG) found a unique pattern, never described up to now.

Patient #1. A 37-year-old man without any previous medical history rapidly displayed a combination of myalgias, headaches, fever and diarrhea. Three days later, he complained of dyspnea, chest pain and displayed incoherent speech. He presented to the emergency room with fever up to 38.2 °C, polypnea 39/min and pulse oxymetry in room air (RA) was 95%. Neurological examination showed neck stiffness, and no confusion. Two nasopharyngeal swabs for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were negative and chest computed tomography (CT)-scan did find neither any lung parenchymal abnormalities nor pulmonary embolism, but SARS-CoV-2 IgM and IgG serology was positive. Troponin increase, echocardiography and myocardial biopsy led to diagnosis of acute myocarditis due to COVID-19. All other biological assays in blood and cerebrospinal fluid for etiological investigation of myocarditis and encephalitis were negative. Because of refractory cardiogenic shock, he was referred to the ICU of Bichat-Claude Bernard hospital (Paris, France) where he rapidly required cardiac assistance. The veno-arterial extracorporeal membrane oxygenation (ECMO) was started in the first 24-hours of arrival. No cardiorespiratory arrest (CRA) was experienced during the procedure neither during his whole stay in the ICU. Continuous long duration EEG was performed for neurological evaluation three days after arrival, under a regimen of sedative drugs composed of propofol 200 mg/h + sufentanyl 15 μg/h. EEG recording was performed with System Plus Evolution, Micromed (Modigliano Veneto, Italy) and eight scalp electrodes positioned according to the standard 10–20 international system montage. EEG revealed continuous, slightly asymmetric, monomorphic, diphasic, delta slow waves with diffuse projection but greater amplitude over both frontal areas and with a periodic organization with a short period around 1–2 s (Fig. 1A). These slow waves did show any reactivity to neither auditory nor nociceptive stimulation. Continuous long duration EEG was repeated one week later under combination of propofol 200 mg/h + sufentanyl 5 μg/h and was similar. Brain magnetic resonance imaging (MRI) with perfusion sequences performed the same day was consistent with hypoxic encephalopathy. A 20-min standard EEG was then performed off-sedation after 15 days in the ICU and found intermittent occurrence of the pattern described above. The patient was eventually extubated 27 days after admission in ICU. At hospital discharge, he displayed only a mild left sensorimotor deficit secondary to right middle cerebral artery infarction without any cognitive symptoms.

Patient #2. A 42-year-old man was admitted to the Bichat-Claude Bernard hospital for acute respiratory failure. His past medical history was marked by arterial hypertension, one episode of acute pulmonary edema, chronic renal failure secondary to suspected nephroangiosclerosis and sleep apnea syndrome. He progressively displayed a combination of fever, chills, hiccup and cough, and then diarrhea and shortness of breath. At hospital admission, he complained of dyspnea with polypnea 22/min, pulse oxymetry was 96% RA and temperature was 39.2 °C. Neurological examination was normal. COVID-19 diagnosis was based on (i) a positive nasopharyngeal swab for SARS-CoV-2 and (ii) a typical thoracic CT-scan. Initial care consisted on nasal oxygen therapy. His respiratory status rapidly worsened leading to transfer to the ICU where he required mechanical ventilation. Similarly to the first case, no CRA occurred during his stay in the ICU before EEG recordings. Sedative drugs (propofol 50 mg/h and sufentanyl 15 μg/h) were interrupted three weeks later when respiratory failure improved. The first 20-minutes standard EEG was performed 24 hours after interruption of sedative drugs because of absence of awakening, with the same technical specifications described above. EEG revealed a strictly similar pattern compared to patient #1 with continuous, symmetric, monomorphic, diphasic (or even triphasic), delta slow waves with diffuse projection but greater amplitude over both frontal areas. These slow waves had a periodic organization with a short period around 1–2 s and did show any reactivity to neither auditive nor nociceptive stimulation (Fig. 1B). Another standard EEG performed still off-sedations one week later was similar with still absence of any reactivity. Withdrawal of care was decided because of persistent coma three weeks after interruption of sedatives and the patient died.

EEG reports are still scarce among literature dedicated to COVID-19 patients and found normal or nonspecific results (Filatov et al. 2020; Morassi et al., 2020; Pilotto et al., 2020). Flamand *et al.* recently reported the case of an 80-year-old woman with COVID-19 whose EEG successively found frontal status epilepticus, then alterations compatible with toxic/metabolic encephalopathy and finally periodic triphasic activity with short periods of 1–1.5 s (Flamand et al., 2020). Reactivity to stimulation was not mentioned in that report. Among the eight patients who underwent EEG reported by Helms *et al.*, only nonspecific changes were detected but one patient had diffuse bifrontal slowing (Helms et al. 2020). Morphology, periodicity and reactivity of this bifrontal slowing were not mentioned. The EEG from the patients we presented did not display any usual pattern found in ICU patients, such as those seen in post-anoxic, toxic or metabolic encephalopathies and had not been described before. Underlying mechanisms of these EEG abnormalities are unknown and perhaps multifactorial. Several hypotheses may be suggested, such as direct viral affection of the brain, demyelination and inflammatory lesions secondary to cytokine storm as a post-viral autoimmune process,

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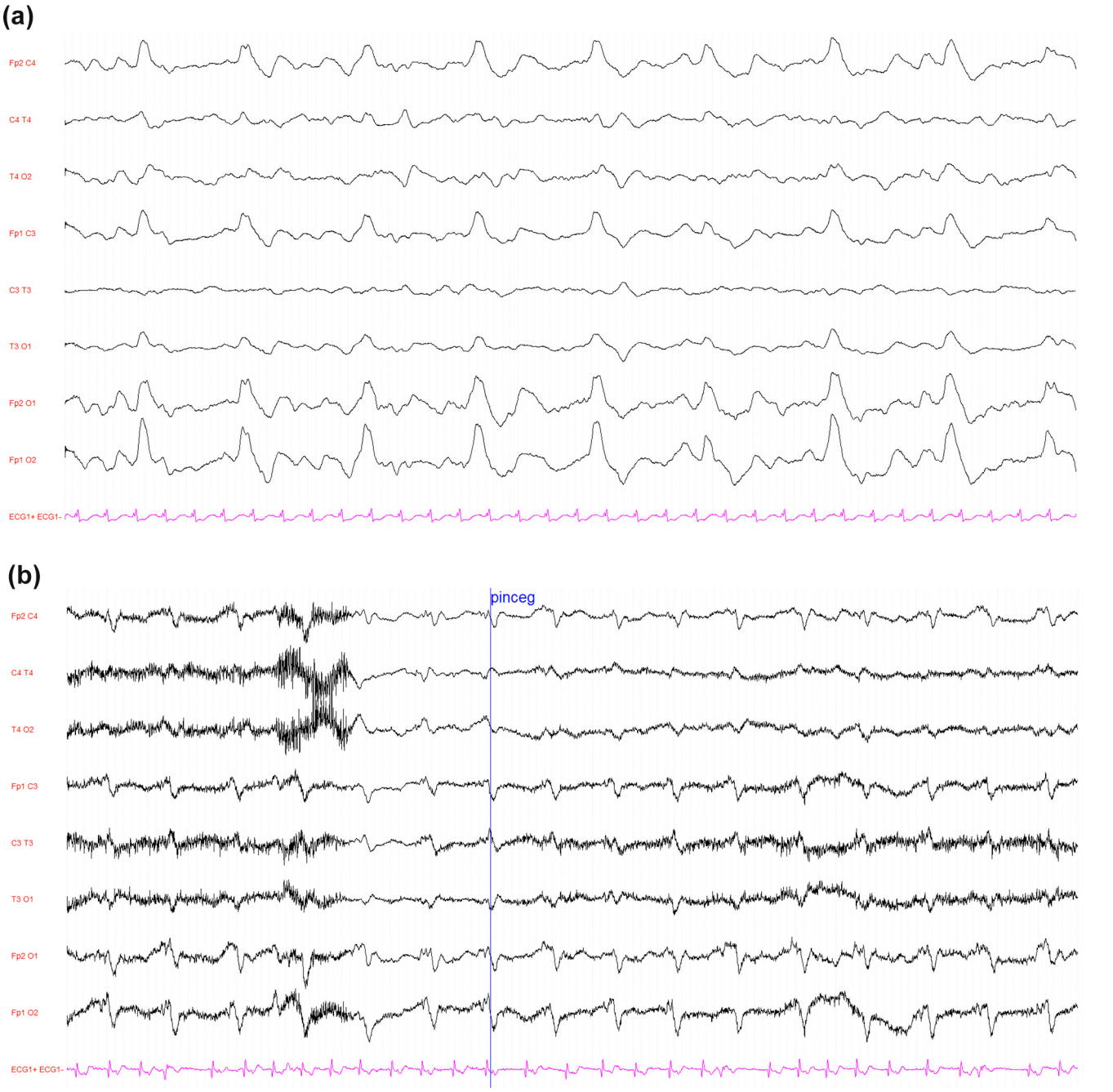

Fig. 1. A. Patient #1, first EEG recording with 8 scalp electrodes, bipolar montage, filter settings at 0.53–70 Hz and 50 Hz notch filter, amplitude 70 μV/cm, epoch of 25 s. Note the continuous periodic monomorphic diphasic delta slow waves over both frontal areas. **B.** Patient #2, first EEG recording with 8 scalp electrodes, bipolar montage, filter settings at 0.53–30 Hz and 50 Hz notch filter, amplitude 30 μV/cm, epoch of 25 s. Note the absence of reactivity to nociceptive left stimulation ('pinceg') of the periodic monomorphic delta slow waves.

hypoxic neuronal injuries and/or side effects of pharmacological treatment used in ICU. The unusual EEG pattern however pleads against the last two hypotheses. To our knowledge, our report is the first to describe strikingly similar EEG patterns in two patients with COVID-19, i.e., non-reactive bifrontal monomorphic diphasic periodic delta slow waves, irrespective of sedative drugs. Opposite outcomes despite similar EEG patterns of the two present patients suggest that these EEG figures are not predictive for neurological prognosis but may represent a signature of SARS-CoV-2 infection. EEG should be more broadly performed in any patients with COVID-19 displaying neurological symptoms. Other EEG investigations are absolutely needed from other neurophysiological teams for patients with COVID-19 to evaluate whether the pattern we described is found in other similar patients.

Authors contributions

GV analyzed EEG and wrote the manuscript. ART, PJ, AG and RS gave their clinician expertise and revised the manuscript. MPO suggested and revised the manuscript.

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Declaration of Competing Interest

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