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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Post-COVID 19 neurological syndrome: Are we facing a neuropsychiatric phenotype?

José David Rubiano-Buitrago [a], Angie Faizuly Rahiran-Ramírez [b], Diana Marcela Peña-Vargas [c], Leidy Angelica Paez-Rincon [d], Ivan David Lozada-Martinez [e,f,*]

[a] School of Medicine, Universidad Nacional, Bogotá, Colombia
[b] School of Medicine, Fundación Universitaria San Martin, Bogotá, Colombia
[c] School of Medicine, Fundación Universitaria Juan N Corpas, Bogotá, Colombia
[d] School of Medicine, Universidad Autónoma de Bucaramanga, Bucaramanga, Colombia
[e] Colombian Clinical Research Group in Neurocritical Care, School of Medicine, University of Cartagena, Cartagena, Colombia
[f] Global Neurosurgery Committee, World Federation of Neurosurgical Societies, Colombia

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Dear Editor,

The management and degree of severity of neurological manifestations during the active phase of COVID-19 and beyond is currently a challenge. Especially because of the indirect impact that the pandemic has had on the mental health of the general population. This makes it difficult to differentially diagnose neuropsychiatric or psychiatric complications in those who develop the moderate or severe phenotype of COVID-19, and these symptoms persist for some time afterwards. Recently, a study was published where the authors conducted a short-term follow-up of a group of patients with COVID-19, to evaluate their physical and psychological sequelae [1]. Although it was observed that 30.4% of these patients maintained residual respiratory dysfunction, it is noteworthy that more than 20% of the patients developed neuropsychiatric manifestations such as anxiety, insomnia and post-traumatic stress syndrome, with reported impairment in quality of life [1]. However, we consider it necessary to mention that these neuropsychiatric manifestations may correspond to a phenotype of post-COVID 19 neurological syndrome, which has been recently described.

Although there is still much to be discovered about COVID-19, many authors have expressed interest in understanding the post-COVID-19 viral syndrome [2]. Although this is an unspecific concept that can encompass a large number of organs and structures [2], one of the most complex pathophysiological processes to understand at present is the neurological involvement during acute disease and long after the resolution of this phase [3]. The post-COVID 19 neurological syndrome is a set of neurological manifestations that can occur in the short- and medium-term, either de novo or by exacerbation of a neurological history [3]. Kempuraj et al [4] propose that neuroinflammation due to COVID-19 triggers mast cell activation at the brain level, causing the release of proinflammatory mediators such as PGD2, IL-1β, IL-6, LTC4, CCL2 and TNF-α, among many others; producing disruption of the blood–brain barrier, endothelial injury, local alteration of coagulation, cellular damage, microvascular damage, neurodegeneration and cell death, thus generating cognitive dysfunction, stroke, status epilepticus, and neuropsychiatric manifestations depending on the affected brain area [4]. Under this description, it has been proposed that the long-term prognosis of patients with a history of stroke, Alzheimer's disease or other types of dementia may worsen substantially [5].

Recent studies have found that those patients with severe COVID-19 phenotype who need in-hospital care have a higher inci-

* Corresponding author at: Colombian Clinical Research Group in Neurocritical Care, School of Medicine, University of Cartagena, Cartagena, Colombia.
E-mail address: ilozadam@unicartagena.edu.co (I.D. Lozada-Martinez).

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dence of neuropsychiatric disorders (HR: 1.58, 1.50–1.67) [6]. One of the factors related to this phenomenon may be that investigated by Bruce et al [7], who demonstrated that in COVID-19 patients managed with prolonged sedation, strokes affecting neurological integrity may go unnoticed [7]. Ortega-Sierra et al [8] discussed these results, mentioning that it is necessary to examine in a personalized way the cases according to sociodemographic data, neurological antecedents, severity of COVID-19, multiorgan involvement and neurological complications, in order to be able to predict neurological involvement and quality of life [8].

Another interesting point is that evaluated by Lozada-Martínez et al [9] investigated the prevalence of neuropsychiatric manifestations in health care workers facing the COVID-19 pandemic, finding that post-traumatic stress syndrome (73.4%) and depression (50.7%) were the most prevalent manifestations (vs. anxiety; 29% and insomnia 37.9%) [9]. However, these authors also described the relationship between the activation of proinflammatory immune pathways and mental disorders; therefore, it can be deduced that those health care workers who have suffered COVID-19 and have had neurological or psychiatric manifestations during the acute phase cannot be exposed to mental distress events, since the neuroinflammatory process may worsen the severity of the post-COVID-19 neurological syndrome presentation and the long-term neurological prognosis [5,9]. However, better quality evidence is needed to be able to state with certainty this type of relationship.

Although neurovascular disorders [6] and headache are the most frequently observed conditions during the course of post-COVID 19 neurological syndrome, it cannot be ruled out that neuropsychiatric manifestations such as anxiety, depression, insomnia, post-traumatic stress syndrome, among others [1,5,6], also derive from neurological injury during the acute phase of the disease, rather than being associated with external factors. Therefore, post-COVID 19 neurological syndrome cases should be investigated strictly, and those with neuropsychiatric manifestations and neurological involvement demonstrated by neuroimaging or neurofunctional studies should be prospectively characterized in detail [10]. This is an exciting line of research that needs the highest quality evidence, with the potential to prevent neurological involvement and improve the prognosis of those who present with this syndrome.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] DE Lorenzo R, Cinel E, Cilla M, Compagnone N, Ferrante M, Falbo E, et al. Physical and psychological sequelae at three months after acute illness in COVID-19 survivors. Panminerva Med. 2021. Online ahead of print. doi: 10.23736/S0031-0808.21.04399-8

[2] Perrin R, Riste L, Hann M, Walther A, Mukherjee A, Heald A. Into the looking glass: Post-viral syndrome post COVID-19. Med Hypotheses. 2020;144:110055. https://doi.org/10.1016/j.mehy.2020.110055.

[3] Camargo-Martínez W, Lozada-Martínez I, Escobar-Collazos A, Navarro-Coronado A, Moscote-Salazar L, Pacheco-Hernández A, et al. Post-COVID 19 neurological syndrome: Implications for sequelae's treatment. J Clin Neurosci. 2021;88:219–25. https://doi.org/10.1016/j.jocn.2021.04.001.

[4] Kempuraj D, Selvakumar GP, Ahmed ME, Raikwar SP, Thangavel R, Khan A, et al. COVID-19, Mast Cells, Cytokine Storm, Psychological Stress, and Neuroinflammation. Neuroscientist. 2020;26(5-6):402–14. https://doi.org/10.1177/1073858420941476.

[5] Heneka MT, Golenbock D, Latz E, Morgan D, Brown R. Immediate and long-term consequences of COVID-19 infections for the development of neurological disease. Alzheimers Res Ther. 2020;12(1):69. https://doi.org/10.1186/s13195-020-00640-3.

[6] Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. The Lancet Psychiatry. 2021;8(5):416–27. https://doi.org/10.1016/S2215-0366(21)00084-5.

[7] Bruce SS, Kahan J, Huq T, Santillan A, Navi BB, Merkler AE, et al. Missed cerebrovascular events during prolonged sedation for COVID-19 pneumonia. J Clin Neurosci. 2021;86:180–3. https://doi.org/10.1016/j.jocn.2021.01.008.

[8] Ortega-Sierra MG, Martinez-Imbett R, Del Pilar Zambrano-Arenas MD, Paéz-Escallón N, Lozada-Martínez ID. Letter to the Editor regarding ‘‘Missed cerebrovascular events during prolonged sedation for COVID-19 pneumonia”. J Clin Neurosci. 2021: S0967-5868(21)00241-1. doi: 10.1016/j.jocn.2021.05.023

[9] Lozada-Martínez I, Bolaño-Romero M, Moscote-Salazar L, Torres-Llinas D, Agrawal A. Letter to the editor. Healthcare workers on the edge of sanity due to COVID-19: Rapid review of the results of systematic reviews and meta-analyzes. J Clin Neurosci 2021;83:21–4. https://doi.org/10.1016/j.jocn.2020.11.041.

[10] González-Herazo MA, Silva-Muñoz DC, Guevara-Martínez PA, Lozada-Martinez ID. Post-COVID 19 Neurological Syndrome: a fresh challenge in neurological management. Neurol Neurochir Pol. 2021. Online ahead of print. doi: 10.5603/PJNNS.a2021.0052