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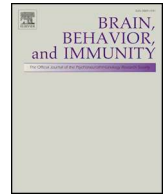
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Letter to the Editor

A brewing storm: The neuropsychological sequelae of hyperinflammation due to COVID-19



To the Editor,

There has been significant focus on understanding COVID-19 symptoms and identifying possible treatments during the current pandemic. The goal of this letter is to highlight the importance of understanding and assessing potential COVID-19 neuropsychological sequelae that may result from the effects of hyperinflammation.

Accumulating evidence suggests that COVID-19 can cause an inflammatory response in multiple organ systems, including the central nervous system (CNS). CNS viral infiltration is suspected to cause neuroinflammation, neurodegeneration, and delirium in some patients (Kotfis et al., 2020). Additionally, a continuous systemic hyperinflammatory response, also known as cytokine storm syndrome (Ye et al., 2020), may result in hypercoagulation and acute respiratory distress syndrome (ARDS; Terpos et al., 2020; Goh, et al., 2020). Patients with severe infection may develop disseminating intravascular coagulation, resulting in both increased blood clots and bleeding, potentially causing ischemic (Lodigiani et al., 2020) and hemorrhagic (Wang et al., 2020) strokes. Further elevating the risk for CNS insult are reports of reduced pulmonary reserve, leading to significant desaturation during intubation followed by prolonged hypoxia (Meng et al., 2020; Yao et al., 2020). For severe cases of COVID-19, the effects of cytokine storm syndrome, coagulation disorders, and hypoxia warrant special attention as potential direct and indirect causes of long-term cognitive impairment.

Existing research reported the cognitive effects of inflammation, stroke, and ARDS. For example, findings showed impairments in memory, attention, processing speed, and executive functioning among patients with ARDS, along with diffuse neuronal loss (Hopkins et al., 2006). Moreover, patients with midlife systemic inflammation have been found to have accelerated cognitive decline decades later (Walker et al., 2019). Future research is needed to evaluate the independent and synergistic effects of the systemic consequences of COVID-19 on cognition in the short- and long-term. Research efforts will need to consider possible iatrogenic complications, as treatments for COVID-19 symptoms, including medications, mechanical ventilation, and prolonged hospitalization, may have unanticipated, adverse effects on cognition. Another complicating factor is the emerging evidence that COVID-19 increases risk for psychiatric and neurological concerns (e.g., mood, anxiety, and trauma or stress-related disorders; Troyer et al., 2020). Psychiatric distress and acquired cognitive deficits following COVID-19 will likely have complex, bidirectional relationships. Impaired cognitive abilities may cause poor occupational and functional outcomes that precipitate or exacerbate mental health concerns, and poor mental health may likewise contribute to cognitive dysfunction. Additionally, future research to investigate possible cognitive problems that may arise from less severe or even subclinical effects of hyperinflammation is needed.

Severe COVID-19 infection triggers a complex inflammatory

response that may result in cytokine storm syndrome, stroke, hypoxia, and/or delirium – each a threat to cognitive health. Research is needed to further clarify the relationships between these medical complications and their neuropsychological sequelae. Better understanding these risk factors may improve both clinical management of patients and long-term neuropsychological outcomes. Meanwhile, screening for cognitive changes with possible referral to neuropsychology, monitoring of potential psychiatric symptoms, and recommending rehabilitation services as needed will likely be beneficial as patients continue to recover from COVID-19.

Conflict of interest

We have no known conflict of interest to disclose.

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