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NEUROLOGICAL IMPLICATIONS OF LONG-COVID-19 — CURRENT KNOWLEDGE AND THE NEED FOR IMPLEMENTING REMEDIES

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According to the Household Pulse Survey conducted by the Census Bureau, over 16.3 million individuals, which accounts for roughly 8% of working-age Americans, are now experiencing LONG-COVID-19. Out of the total number, around 2 to 4 million individuals are unemployed as a direct result of the long-term effects of COVID-19 [1]. Research conducted by Davis et al. [2] using data from 56 countries revealed that 22% of individuals suffering from LONG-COVID-19 had work incapacity as a result of their deteriorating health, while an additional 45% had to decrease their working hours. The prevalence of long-term and chronic neurological symptoms caused by COVID-19, often referred to as LONG-COVID-19, is attracting growing attention. These symptoms may last for many months or even years, impacting a significant number of individuals globally. LONG-COVID-19 often presents in previously asymptomatic persons, especially young adults, and may arise after a mild infection [3]. The most common, long-lasting, and debilitating symptoms of LONG-COVID-19 are related to the nervous system. A significant number of individuals experience fatigue and cognitive dysfunction, including decreased attention span, short-term memory loss, overall memory decline, language and motor skills impairment, decreased encoding and verbal fluency, and executive dysfunction [4]. Several symptoms that may be present include dysautonomia and post-exertional malaise. Post-exertional malaise is a condition characterized by severe tiredness and depletion of energy that people experience even after little physical exertion. Dysautonomia, a disorder marked by impaired functioning of the autonomic nervous system, may present with symptoms such as dizziness, rapid heart rate, high or low blood pressure, and gastrointestinal irregularities [5]. The physiological processes underlying neurological symptoms caused by COVID-19 infection are currently being elucidated. In addition to previously believed long-lasting inflammatory mechanisms, immune dysregulation, microbiota disruption, autoimmunity, clotting and endothelial abnormality, and dysfunctional neurological signalling — neuronal fusion is now considered a potential mechanism for the transmission and spread of the virus [6]. Preserving the distinctiveness of neurons is essential for the optimal operation of the nervous system. Studies suggest that COVID-19 might trigger the activation of viral fusogens, leading to the merging of brain cells in a way that cannot be reversed. This fusing of cells can disrupt the regular connection between neu-

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rons, thereby explaining how the infection can lead to neurological problems. The impact on neuronal fusion will be contingent upon the viral load in the brain and the particular regions infected. For SARS-CoV-2, the fusing of neurons that occurs when they are infected relies on the presence of ACE2, the virus's cellular receptor, as well as other possible entry factors including TMPRSS2 and NRP1 in nearby neurons. Viruses like SARS-CoV-2 can induce the fusion of brain cells, which triggers aberrant behaviour and ultimately results in persistent neurological problems [7]. The administration of COVID-19 vaccines consistently decreased the likelihood of experiencing long-lasting symptoms of COVID-19, underscoring the significance of immunization in preventing persistent symptoms of the disease [8, 9]. The current Moderna and Pfizer-BioNTech vaccines include the whole S protein with two specific mutations — spike S-2P. These mutations involve the insertion of two prolines at locations 986 and 987. The presence of prolines in the protein enhances its structural stability and prevents it from merging with other cells. The spike protein S-2P of the vaccine has been shown to completely lack the ability to fuse with neurons. This unequivocally showcases the efficacy and reliability of mRNA vaccines concerning their safety [10]. Furthermore, it is imperative to establish explicit protocols for the care and handling of individuals experiencing LONG-COVID-19, and to establish specialized institutions specifically designed for the treatment of this particular ailment.

Information and declarations

Author contributions

All authors contributed equally to the manuscript.

Conflict of interest

None.

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