Medical Xpress

COVID-19 infection in crucial brain regions may lead to accelerated brain aging

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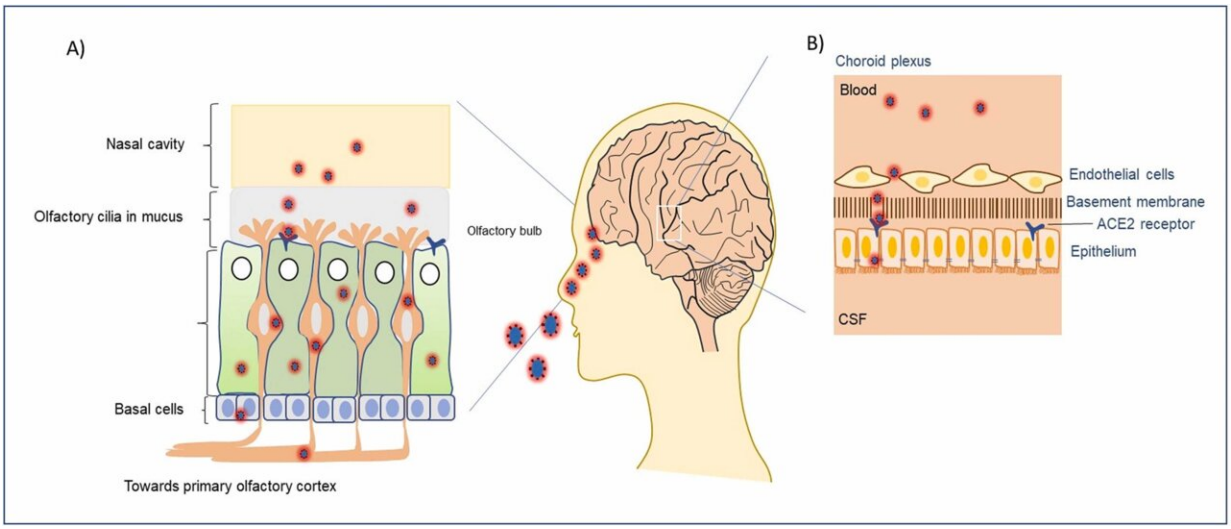

The interaction of SARS-CoV-2 with olfactory cilia for entering the central nervous system (CNS). A) Different layers of cells in the nasal cavity that contain receptors for the very first viral entry into the human host. Some of the olfactory cells express ACE2 receptors that endocytose bound viral particles, before their way to the olfactory bulb in the brain. B) Schematic of the cellular barrier between cerebrospinal fluid and circulating blood in the choroid plexus region. Both endothelial and basement epithelial cells express the ACE2 receptors facilitating the internalization of virions in the brain fluid system. Credit: *Ageing Research Reviews* (2022). DOI: 10.1016/j.arr.2022.101687

A new study by Houston Methodist researchers reviews the emerging insights and evidence that suggest COVID-19 infections may have both

short- and long-term neurological effects. Major findings include that COVID-19 infections may predispose individuals to developing irreversible neurological conditions, may increase the likelihood of strokes and may increase the chance of developing persistent brain lesions that can lead to brain bleeding.

Led by corresponding authors Joy Mitra, Ph.D., Instructor, and Muralidhar L. Hegde, Ph.D., Professor of Neurosurgery, with the Division of DNA Repair within the Center for Neuroregeneration at the Houston Methodist Research Institute, the research team described their findings in an article titled "SARS-CoV-2 and the Central Nervous System: Emerging Insights into Hemorrhage-Associated Neurological Consequences and Therapeutic Considerations" in the journal *Ageing Research Reviews*.

Still a major burden on our daily lives, a great deal of research has shown that the impacts of the disease go far beyond the actual time of infection. Since the onset of the pandemic, COVID-19 has surpassed a death toll of more than 5.49 million worldwide and more than 307 million confirmed positive cases, with the U.S. accounting for almost 90 million of those cases, according to the Our World in Data website.

COVID-19 is known to invade and infect the brain, among other major organs. While a lot of research has been done to help us understand the evolution, infection and pathology of the disease, there is still a great deal that remains unclear about the long-term effects, especially on the brain.

The coronavirus infection can cause long-term and irreversible neurodegenerative diseases, particularly in the elderly and other vulnerable populations. Several brain imaging studies on COVID-19 victims and survivors have confirmed the formation of microbleed lesions in deeper brain regions related to our cognitive and memory

functions. In this review study, researchers have critically evaluated the possible chronic neuropathological outcomes in aging and comorbid populations if timely therapeutic intervention is not implemented.

Microbleeds are emerging neuropathological signatures frequently identified in people suffering from chronic stress, depressive disorders, diabetes and age-associated comorbidities. Based on their earlier findings, the investigators discuss how COVID-19-induced microhemorrhagic lesions may exacerbate DNA damage in affected brain cells, resulting in neuronal senescence and activation of cell death mechanisms, which ultimately impact brain microstructure-vasculature. These pathological phenomena resemble hallmarks of neurodegenerative conditions like Alzheimer's and Parkinson's diseases and are likely to aggravate advanced-stage dementia, as well as cognitive and motor deficits.

The effects of COVID-19 infection on various aspects of the central nervous system are currently being studied. For instance, 20-30% of COVID-19 patients report a lingering psychological condition known as "brain fog" where individuals suffer from symptoms such as memory loss, difficulty in concentrating, forgetting daily activities, difficulty in selecting the right words, taking longer than usual time to complete a regular task, disoriented thought processes and emotional numbness.

More severe long-term effects analyzed in the Houston Methodist review article include predispositions for Alzheimer's, Parkinson's and related neurodegenerative diseases, as well as cardiovascular disorders due to internal bleeding and blood clotting-induced lesions in the part of the brain that regulates our respiratory system, following the COVID-19 symptoms. Additionally, cellular aging is thought to be accelerated in COVID-19 patients. A plethora of cellular stresses inhibit the virus-infected cells from undergoing their normal biological functions and let them enter into "hibernation mode" or even die completely.

The study also suggests various strategies to improve some of these long-term neuropsychiatric and neurodegenerative outcomes, as well as outlines the importance of the therapeutic regimen of the "nanozyme" in combination with various FDA-approved drugs that may prove successful to fight against this catastrophic disease.

However, given the ever-evolving nature of this field, associations like the ones described in this review show the fight against COVID-19 is far from over, say the investigators, and reinforce the message that getting vaccinated and maintaining proper hygiene are key in trying to prevent such long-term and detrimental consequences.

More information: Joy Mitra et al, SARS-CoV-2 and the central nervous system: Emerging insights into hemorrhage-associated neurological consequences and therapeutic considerations, *Ageing Research Reviews* (2022). DOI: 10.1016/j.arr.2022.101687

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