## Even mild COVID-19 may have long-term brain impacts

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esearch presented at the Alzheimer's Association International Conference suggests even mild cases of COVID-19 may be associated with cognitive deficits months after recovery.

One Argentinian study of 234 seniors who previously had COVID-19 found that more than half showed some degree of cognitive impairment months later. One in three had severe "dementia-like" impairments in memory, attention and executive function — a much higher proportion than the 5%–8% of seniors in the general population who have dementia at a given time.

"This could be the start of a dementiarelated epidemic fueled by this latest coronavirus," stated presenting author Dr. Gabriel de Erausquin of the Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases at UT Health San Antonio. Researchers will follow the study participants over the next three to five years to see if these problems resolve or worsen.

The study didn't look at participants' cognitive performance prior to infection. However, those who lost their sense of smell while sick with COVID-19 tended to have more severe cognitive impairments months later, even if their other symptoms had been mild. According to de Erausquin, "once the virus has affected the olfactory bulb and caused effects there — changes that we can see with imaging — then other places in the brain that are connected to it also become abnormal, either in function or structure or both."

Other research presented linked SARS-CoV-2 infection with an uptick in

biomarkers of brain injury, neuroinflammation and Alzheimer disease. One American study of 310 patients with COVID-19 found that those with new neurological symptoms had higher levels of t-tau, NfL, GFAP, pTau-181, and UCH-L1 in their blood, as well as indicators of inflammation such as C-reactive protein, compared to patients without neurological symptoms. "These findings suggest patients who had COVID-19 may have an acceleration of Alzheimer-related symptoms and pathology," according to presenting author Dr. Thomas Wisniewski of the New York University Grossman School of Medicine.

Earlier this year, de Erausquin and others reported that brain inflammation, stroke and other common complications of viral infections have long-standing links with neurodegenerative disorders. "Therefore, it seems likely to expect that COVID-19-related cardio-vascular and cerebrovascular disease will also contribute to a higher long-term risk of cognitive decline and dementia in recovered individuals."

Several recent studies have documented cognitive deficits post-COVID but like the research presented at the Alzheimer's Association conference, data on patients' performance before infection are lacking.

One British study of 81 337 people in *EClinicalMedicine* found that those who previously had COVID-19 tended to score lower on measures of intelligence, reasoning, problem-solving and planning than people who were never infected.

"These results accord with reports of long-COVID, where 'brain fog,' trouble concentrating and difficulty finding the correct words are common," according to the authors. People who had been hospitalized and put on ventilators had the greatest impairments, but even those who had relatively mild symptoms showed some deficit.

In another study of 57 Americans receiving inpatient rehabilitation after hospitalization for COVID-19, four in five had mild to severe cognitive impairments. More than half had deficits in working memory, while two in five had impaired processing speed, divided attention, and trouble switching between mental tasks.

Similar deficits have also been noted in patients after recovery from other coronaviruses. A 2020 systematic review and meta-analysis found that delirium was common in the acute stage of severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19. Following up with patients six weeks to 39 months later, more than 15% reported sleep disorders, mood swings, trouble concentrating, impaired memory and other mental challenges.

Based on this growing body of evidence, British researchers warned in March that health systems will likely see an "influx of patients with psychiatric and cognitive problems who were otherwise healthy prior to COVID-19." They urged doctors to consider detailed cognitive evaluations for anyone reporting new neurological symptoms after infection with SARS-CoV-2.

In the meantime, the Alzheimer's Association has formed an international consortium to study the long-term effects of COVID-19 on the brain.

"These new data point to disturbing trends showing COVID-19 infections leading to lasting cognitive impairment and even Alzheimer's symptoms," stated Heather Snyder of the Alzheimer's Association. "It is imperative that we continue to study what this virus is doing to our bodies and brains."

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