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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2021

COVID-19 ASSOCIATED WITH LONG-TERM COGNITIVE DYSFUNCTION, ACCELERATION OF ALZHEIMER'S SYMPTOMS

DENVER, JULY 29, 2021 — Much has been learned about SARS-CoV-2, the virus that causes the novel coronavirus, since the beginning of the COVID-19 pandemic. However, questions remain about the long-term impact of the virus on our bodies and brains. New research reported at the [Alzheimer's Association International Conference® \(AAIC®\) 2021](#), held virtually and in Denver found associations between COVID-19 and persistent cognitive deficits, including the acceleration of Alzheimer's disease pathology and symptoms.

In addition to the respiratory and gastrointestinal symptoms that accompany COVID-19, many people with the virus experience short- and/or long-term neuropsychiatric symptoms, including loss of smell and taste, and cognitive and attention deficits, known as "brain fog." For some, these neurological symptoms persist, and researchers are working to understand the mechanisms by which this brain dysfunction occurs, and what that means for cognitive health long term.

Scientific leaders, including the Alzheimer's Association and representatives from nearly 40 countries — with technical guidance from the World Health Organization (WHO) — are part of an international, multidisciplinary [consortium](#) to collect and evaluate the long-term consequences of COVID-19 on the central nervous system, as well as the differences across countries. Initial findings from this consortium presented at AAIC 2021 from Greece and Argentina suggest older adults frequently suffer persistent cognitive impairment, including persistent lack of smell, after recovery from SARS-CoV-2 infection.

Other key results reported at AAIC 2021 include:

- Biological markers of brain injury, neuroinflammation and Alzheimer's correlate strongly with the presence of neurological symptoms in COVID-19 patients.
- Individuals experiencing cognitive decline post-COVID-19 infection were more likely to have low blood oxygen following brief physical exertion as well as poor overall physical condition.

"These new data point to disturbing trends showing COVID-19 infections leading to lasting cognitive impairment and even Alzheimer's symptoms," said Heather M. Snyder, Ph.D., Alzheimer's Association vice president of medical and scientific relations. "With more than 190 million cases and nearly 4 million deaths worldwide, COVID-19 has devastated the entire world. It is imperative that we continue to study what this virus is doing to our bodies and brains. The Alzheimer's Association and its partners are leading, but more research is needed."

Cognitive Impairment Correlates with Persistent Loss of Smell in Recovered COVID-19 Patients

Gabriel de Erausquin, M.D., Ph.D., M.Sc., of the University of Texas Health Science Center at San Antonio Long School of Medicine, along with colleagues from the Alzheimer's Association-led global SARS-CoV-2 [consortium](#), studied cognition and olfactory senses in a cohort of nearly 300 older adult Amerindians from Argentina who had COVID-19.

Participants were studied between three and six months after COVID-19 infection. More than half showed persistent problems with forgetfulness, and roughly one in four had additional problems with cognition including language and executive dysfunction. These difficulties were associated with persistent problems in smell function, but not with the severity of the original COVID-19 disease.

“We’re starting to see clear connections between COVID-19 and problems with cognition months after infection,” Erausquin said. “It’s imperative we continue to study this population, and others around the world, for a longer period of time to further understand the long-term neurological impacts of COVID-19.”

COVID-19 Infection Associated with Uptick in Alzheimer’s Biomarkers in the Blood

Certain biological markers in blood — including total tau (t-tau), neurofilament light (NfL), glial fibrillary acid protein (GFAP), ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), and species of amyloid beta (A β 40, A β 42) and phosphorylated tau (pTau-181) — are indicators of injury in the brain, neuroinflammation and Alzheimer’s disease.

To study the presence of these blood biomarkers, neurodegeneration and neuroinflammation in older patients who were hospitalized with COVID-19, Thomas Wisniewski, M.D., a professor of neurology, pathology and psychiatry at New York University Grossman School of Medicine, and colleagues took plasma samples from 310 patients who were admitted to New York University Langone Health with COVID-19. Of the patients, 158 were positive for SARS-CoV-2 with neurological symptoms and 152 were positive for SARS-CoV-2 without neurologic symptoms. The most common neurological symptom was confusion due to toxic-metabolic encephalopathy (TME).

In patients who were initially cognitively normal with and without TME related to COVID-19 infection, the researchers found higher levels of t-tau, NfL, GFAP, pTau-181, and UCH-L1 in COVID-19 patients with TME compared to COVID-19 patients without TME. There were no significant differences with A β 1-40, but the pTau/A β 42 ratio showed significant differences in patients with TME. Additionally, t-tau, NfL, UCH-L1 and GFAP significantly correlated with markers of inflammation such as C-reactive peptide, which may suggest inflammation-related blood-brain barrier disruption accompanying neuronal/glial injury.

“These findings suggest that patients who had COVID-19 may have an acceleration of Alzheimer’s-related symptoms and pathology,” Wisniewski said. “However, more longitudinal research is needed to study how these biomarkers impact cognition in individuals who had COVID-19 in the long term.”

Individuals Recovered from COVID-19 Who Experience Cognitive Decline More Likely to Have Poor Physical Condition, Low Oxygen Saturation

George Vavougiou, M.D., Ph.D., postdoctoral researcher for the University of Thessaly (UTH), and colleagues studied cognitive impairment and related health measures in 32 previously hospitalized mild to moderate COVID-19 patients two months after discharge from the hospital. Among them, 56.2% presented with cognitive decline. Short-term memory impairments and multidomain impairment without short-term memory deficits were the predominant patterns of cognitive impairment.

Worse cognitive test scores correlated with higher age, waist circumference and waist-to-hip ratio. After adjusting for age and sex, worse memory and thinking scores were independently associated with lower levels of oxygen saturation during the 6-minute walk test, which is commonly used to assess the functional capacity of people with cardiopulmonary disease.

“A brain deprived of oxygen is not healthy, and persistent deprivation may very well contribute to cognitive difficulties,” Vavougiou said. “These data suggest some common biological mechanisms between COVID-19’s dyscognitive spectrum and post-COVID-19 fatigue that have been anecdotally reported over the last several months.”

This cohort is also part of the global SARS-CoV-2 consortium.

About the Alzheimer's Association International Conference (AAIC)

The Alzheimer’s Association International Conference (AAIC) is the world’s largest gathering of researchers from around the world focused on Alzheimer’s and other dementias. As a part of the Alzheimer’s Association’s research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

AAIC 2021 home page: www.alz.org/aaic/

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About the Alzheimer’s Association

The Alzheimer’s Association is a worldwide voluntary health organization dedicated to Alzheimer’s care, support and research. Our mission is to lead the way to end Alzheimer’s and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support. Our vision is a world without Alzheimer’s and all other dementia®. Visit alz.org or call 800.272.3900.

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- Gabriel de Erausquin, M.D., Ph.D., M.Sc., et al. Olfactory dysfunction and chronic cognitive impairment following SARS-CoV-2 infection in a sample of older adults from the Andes mountains of Argentina. (Funder(s): Alzheimer’s Association; Fundación de Lucha contra los Trastornos Neurológicos y Psiquiátricos en Minorías (FULTRA); Zachry Foundation Distinguished Chair of Alzheimer’s Clinical Care and Research; Greehey Family Foundation Distinguished University Chair of Alzheimer’s Research)
- Thomas Wisniewski, Ph.D., et al. Plasma Biomarkers of Neurodegeneration and Neuroinflammation in Hospitalized COVID-19 Patients with and without New Neurological Symptoms (Funder(s): National Institutes of Health/National Institute on Aging)
- George Vavougiou, M.D., Ph.D., et al. Investigating the prevalence of cognitive impairment in mild and moderate COVID-19 patients two months post-discharge: associations with physical fitness and respiratory function. (Funder(s): 2020 National Strategic Reference Framework (NSRF) Scholarship)