Study shows COVID-19 infection alters gene transcription of olfactory mucosal cells in Alzheimer's disease

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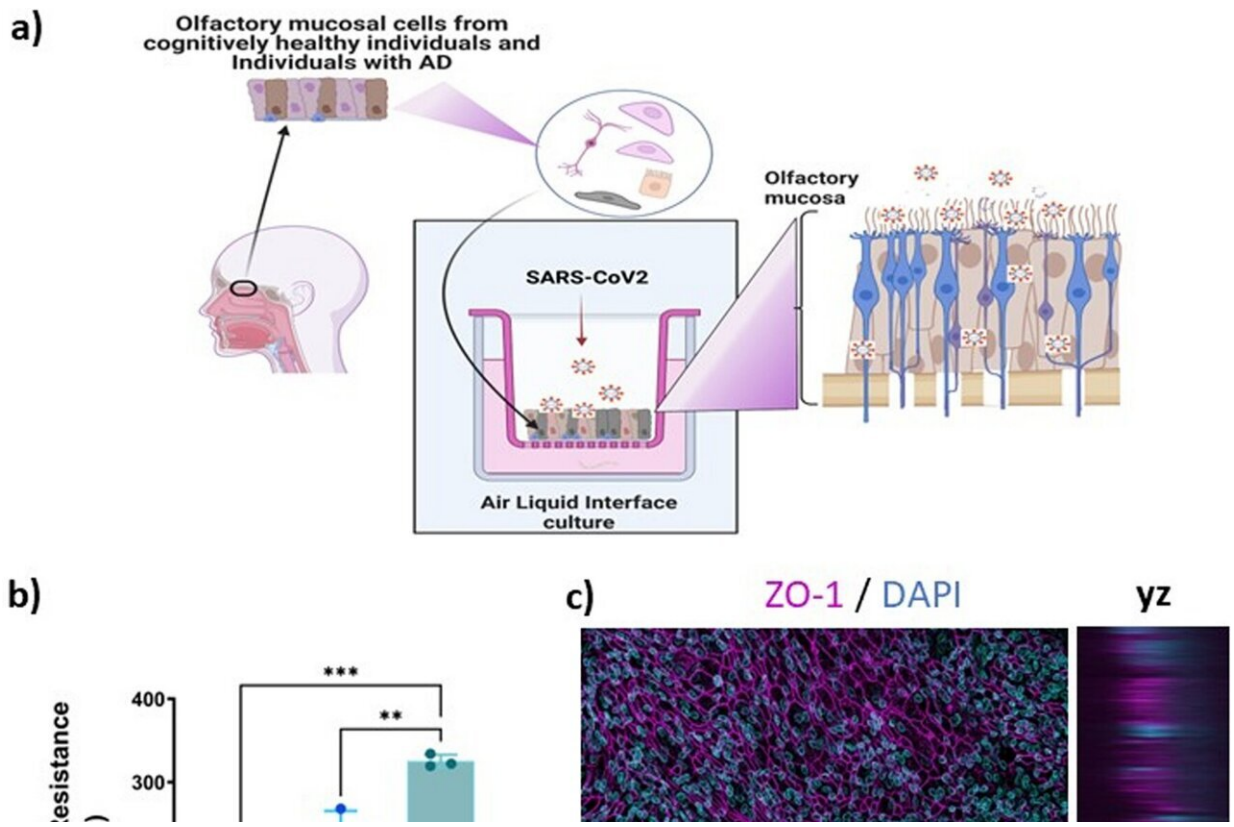

Characterization of the human primary olfactory mucosal cells at air–liquid interface. Credit: *Journal of Neuroinflammation* (2023). DOI: 10.1186/s12974-023-02979-4

A new study identifies alterations in the transcriptomic signatures in human olfactory mucosal cells of individuals with Alzheimer's disease following SARS-CoV-2 infection, potentially contributing to exacerbated COVID-19 outcomes. The study was conducted at the University of Eastern Finland in collaboration with the University of Helsinki and published in *Journal of Neuroinflammation*.

The study was prompted by concerns about the impact of COVID-19 on individuals with pre-existing conditions such as Alzheimer's disease (AD). Olfactory dysfunction, characterized by an impaired sense of smell, is commonly associated with COVID-19 and is also observed in persons with AD.

Exploring the olfactory mucosa as a direct interface between the external environment and the brain, the research aimed to investigate the interaction between SARS-CoV-2 infection and AD within the olfactory mucosa , assessing the potential for this tissue to serve as a plausible entry route for the virus into the brain.

Employing an innovative 3D in vitro model of the olfactory mucosa, the study utilized primary cells obtained from voluntary donors, including both cognitively healthy individuals and those diagnosed with AD. These cells were cultivated at the air-liquid interface (ALI), a technique providing a controlled environment that closely mimics physiological conditions.

The collection of olfactory mucosal biopsies was conducted collaboratively with Kuopio University Hospital. This multidisciplinary research integrated expertise from molecular and cellular biology, neurology, and virology to investigate the effects of various SARS-CoV-2 variants on the olfactory mucosa.

Distinct immune responses after infection between

AD patients and healthy individuals

Contrary to expectations, cells derived from healthy individuals and those with AD exhibited comparable susceptibility to infection by SARS-CoV-2 virus, indicating no significant difference in initial infection rates between the two groups.

However, a significant contrast emerged in the gene activity of infected cells from individuals with AD. Their cells displayed heightened oxidative stress, altered immune responses, and substantial changes in genes related to olfaction when compared to olfactory mucosal cells from cognitively healthy individuals.

"The results suggest a plausible scenario where individuals affected by AD might face potentially more severe COVID-19 outcomes due to pre-existing inflammation in the olfactory mucosa," says Ali Shahbaz, a doctoral researcher in Professor Katja Kanninen's research group at the University of Eastern Finland and the first author of the study.

The present study represents a pivotal advancement in understanding the intricate interplay between COVID-19 and AD.

More information: Muhammad Ali Shahbaz et al, Human-derived air–liquid interface cultures decipher Alzheimer's disease–SARS-CoV-2 crosstalk in the olfactory mucosa, *Journal of Neuroinflammation* (2023). DOI: 10.1186/s12974-023-02979-4

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