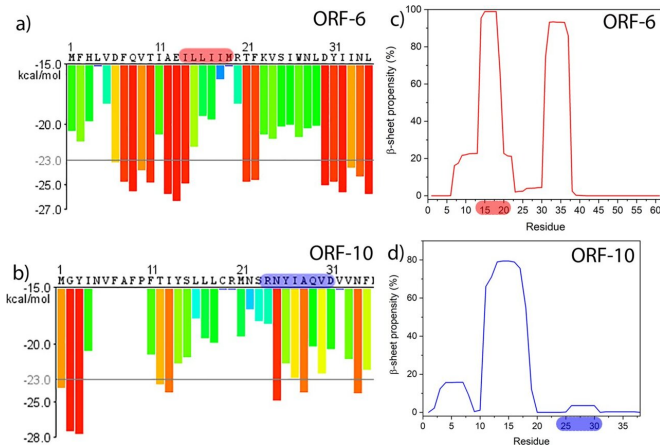


Exploring the cause of long COVID 'brain fog'

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Output from amyloid assembly prediction software for SARS-CoV-2 ORF6 and ORF10 sequences. a, b Outputs from amyloid predicting algorithm ZIPPER identifying hexapeptide fragments predicted to form steric zippers nucleating the assembly of amyloid fibrils. Hexapeptides with Rosetta energies below -23 kcal mol⁻¹ are predicted to be highly amyloidogenic and are shown with red bars. c, d Outputs from amyloid predicting algorithm TANGO indicating sequence regions of high propensity to form β -sheets. Credit: *Nature Communications* (2022). DOI: 10.1038/s41467-022-30932-1

La Trobe University-led research may have uncovered the cause of the neurological conditions seen in patients with long COVID, such as brain fog.

The study, published in *Nature Communications*, provides the first indications that some of the neurological symptoms in long-COVID are being caused by amyloid clumps appearing in the brain that are similar to those that cause Alzheimer's Disease and dementia.

Dr. Nick Reynolds from La Trobe University's Institute for Molecular Science said the research reveals similarities between the effects of

COVID-19 and the early stages of neurodegenerative disease such as Alzheimer's and Parkinson's.

The authors cautioned that the implications of the changes were unclear and did not necessarily suggest people might have lasting damage or that the changes might profoundly affect thinking, memory or other functions.

According to Dr. Reynolds, if further studies confirm that amyloid clumps are contributing towards long-COVID, then drugs which have been developed to combat Alzheimer's and Parkinson's may be repurposed to treat these debilitating neurological symptoms.

"It may be possible that existing drugs may be used to treat the brain fog that affects a significant portion of people who go on to experience long-COVID having been infected with SARS-CoV-2," Dr. Reynolds said.

Long COVID is marked by neurological symptoms such as memory loss, sensory confusion, severe headaches, and even stroke in up to 30 percent of cases, which can persist for months after the infection is over. While there is evidence that the virus can enter the brain of infected people, the precise mechanisms causing these neurological symptoms are unknown.

The researchers investigated if similar amyloid clumps could be formed from fragments of protein from SARS-CoV-2. Finding two such protein fragments that readily form amyloids, called ORF6 and ORF10, and that these are highly toxic to brain cells grown in a lab.

Dr. Reynolds said the findings of aggregates of SARS-Cov-2 proteins in people with long COVID may explain the condition known as "brain fog."

"These toxic clumps of protein, or amyloid

assemblies, appear to be similar to those found in Alzheimer's disease and may be responsible for some of the neurological symptoms of long-COVID," he said. "We suggest that aggregates of SARS-CoV-2 proteins may trigger [neurological symptoms](#) in COVID-19 that many call brain fog," he said.

More information: Mirren Charnley et al, Neurotoxic amyloidogenic peptides in the proteome of SARS-COV2: potential implications for neurological symptoms in COVID-19, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-30932-1](#)

Provided by La Trobe University

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