Long COVID Symptoms Linked to Inflammation

Prolonged inflammation after SARS-CoV-2 infection caused permanent organ damage, affected the brain and correlated with behavioral changes in hamsters.

June 29, 2022 By Larisa Gearhart-Serna, PhD and National Institutes of Health

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The effects of COVID-19 can persist long after the initial symptoms of the illness are gone. These effects, called post-acute sequelae of COVID-19 (or PASC), can include brain fog, fatigue, headaches, dizziness, and shortness of breath. Long COVID—when symptoms last weeks or months after the acute infection has passed—affects about 2.5% of COVID patients. While patients who were hospitalized are more susceptible, even those with mild cases can experience Long COVID.

A research team led by Drs. Benjamin tenOever at the NYU Grossman School of Medicine and Venetia Zachariou at the Icahn School of Medicine at Mount Sinai set out to understand the underlying biology of long COVID. The researchers, who were supported in part by NIH, studied the golden hamster, a widely used small animal model for respiratory infections. The hamsters were exposed to SARS-CoV-2 via their nostrils. For comparison, another group was exposed to a flu virus, influenza A. Various samples were taken for analysis after 3, 14, and 31 days of infection.

Tissues from human donors who had COVID-19 at the time of death or had recovered from COVID-19 but died from other causes were also sampled and analyzed. Results appeared on June 7, 2022, in Science Translational Medicine.

Both SARS-CoV-2 and influenza A infections were largely cleared within two weeks, similar to the course of recovery in humans. Following SARS-CoV-2 infection, however, animals showed much more extensive lung damage and slower recovery than those exposed to influenza A. Those exposed to SARS-CoV-2 also had more kidney damage.

When the scientists sampled different parts of hamster brains to analyze gene activity, they found that SARS-CoV-2 had unique effects on the hamster olfactory system—the parts of the nose and brain responsible for smell. The olfactory epithelium, the lining inside the nose, showed signs of extensive inflammation long after the virus could be detected. SARS-CoV-2 also caused high levels of inflammation in the olfactory bulb, a part of the brain involved in processing smell as well as in emotion and learning. Inflammation in these areas persisted long after the infection was cleared.

Interestingly, chronic inflammation in the olfactory system correlated with behavioral changes in the hamsters thought to reflect mood disorders like depression and anxiety. Although olfactory bulb tissue from people who recovered from COVID-19 and died of other causes is difficult to obtain, the few samples studied were comparable to that of the hamsters. This suggests that the inflammation seen in the hamsters may explain the mechanism responsible for symptoms of long COVID in people. Further research is needed to fully understand the link between brain inflammation, brain activity, and behavioral changes.

“[T]his study suggests that the molecular mechanism behind many long COVID-19 symptoms stems from this persistent inflammation while describing an animal model close enough to human biology to be useful in the design of future treatments,” tenOever says.

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