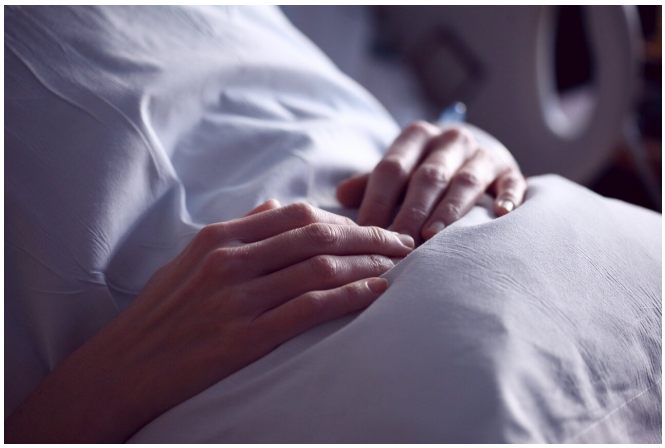
Study finds link between spinal antibodies and neurological COVID symptoms

19 February 2021, by Julie Parry



Credit: CC0 Public Domain

In March of 2020, Shelli Farhadian, MD, Ph.D., assistant professor of medicine (infectious diseases) and neurology, began to see parallels in her pre-pandemic research on neurologic effects in patients with HIV infection and the possibility of neurologic effects on patients with SARS-CoV-2, or COVID-19.

"There was some literature out there that suggested that coronaviruses could have an effect on the brain. So, knowing that that was a potential possibility, even before we had our first case at Yale New Haven Hospital, I worked with other people to set up a protocol where we could consent patients to collect tissue specimens and information to try to see if this was also going happen with SARS-CoV-2," explained Farhadian.

The first COVID-19 positive patient was admitted to Yale New Haven Hospital (YNHH) on March 14, 2020. Farhadian and her infectious diseases colleagues encountered patients with neurological complaints with the absence of other traditional COVID-19 symptoms, who then later tested positive for the disease.

"Large cohort studies in China, France, and New York City, estimated that somewhere around 30% of hospitalized patients with COVID-19 have some sort of neurological component to their illness. So in that context and with our background in studying the neurological effects of systemic infections, we started to ask whether there was inflammation or some other consequence of this infection affecting the brain," said Farhadian.

Patients enrolled in the study underwent a lumbar puncture to drain cerebral spinal fluid from their back, the same fluid that surrounds the brain. Farhadian and her collaborators across Yale School of Medicine and the University of California, San Francisco (UCSF), knew that by looking at the spinal fluid, they would learn what is going on within the brain.

"We took the spinal fluid to try to see if we can get a window into what was going on in the brain.," said Farhadian.

The study, "Exploratory neuroimmune profiling identifies CNS-specific alterations in COVID-19 patients with neurological involvement," currently in preprint on bioRxiv found that unique immune responses were seen in the spinal fluid compared to what was going on in the rest of the body, including increased levels of antibody producing cells than would typically be expected in the spinal fluid. They also found a high level of autoantibodies in the spinal fluid, which suggests that these brain-targeting antibodies are a potential contributor for the neurological complications.

"We found that most of the patients we studied had autoantibodies, or antibodies that target brain tissue, circulating in the spinal fluid. In one case, we found that antibodies that are directed against the virus were also cross-reacting against the brain. We think this might prove to be a link between the virus and the high rates of neurological symptoms that people show during and after COVID-19." Now,

Farhadian and Yale neurologists Dr. Serena Spudich and Dr. Lindsay McAlpine are seeing patients in the Yale Post-COVID neurology clinic who are two to six months out from their COVID diagnosis, and are still having neurological problems. "For example, I saw one a patient last week who is normally a vivacious and active woman, but after her COVID illness, is unable to work. She says she cannot think straight, gets lost easily, and can't do simple tasks like grocery shopping. Are those auto-antibodies contributing to that? That's something that we need to get to the bottom of," said Farhadian.

The researchers are actively enrolling patients with post-COVID neurological problems in their study. For more information on the COVID Mind Study at Yale, visit their website.

Farhadian commended the collaboration in this work, like UCSF neurologists Michael Wilson, MD, Samuel Pleasure, MD, Ph.D., and Christopher Bartley, MD, Ph.D., along with many colleagues at YSM, such as Eric Song, an MD/Ph.D. student in the Iwasaki Lab.

"My UCSF partners, Michael Wilson and Sam Pleasure, are leaders in their field. I knew of them, but hadn't worked with them before. We connected early on in the pandemic and were able to combine my background and interest in neuro-infectious disease with their expertise in auto-immunity, to bring this project together. Here at Yale, I was delighted to collaborate with Eric Song and Akiko Iwasaki in Immunobiology. Eric had been working to develop mouse models of SARS-CoV-2 infection, including mice that specifically had brain infection. It was good opportunity to study the similar phenomenon that we were seeing in our patients in that animal model."

More information: Eric Song et al. Exploratory neuroimmune profiling identifies CNS-specific alterations in COVID-19 patients with neurological involvement, *biorxiv* (2020). DOI: 10.1101/2020.09.11.293464

Provided by Yale University