# Covid-19 virus does not infect human brain cells, study suggests

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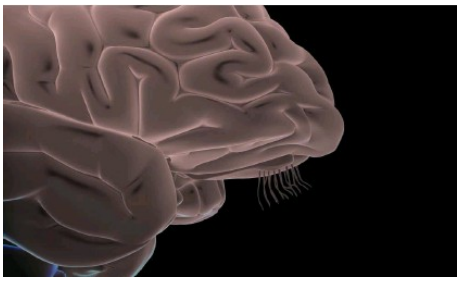
The virus that causes Covid-19 does not infect human brain cells, according to a study published in the journal Cell. The findings will raise hopes that the damage caused by Sars-CoV-2 might be more superficial and reversible than previously feared.



The study contradicts earlier research that suggested the virus infects neurons in the membrane that lines the upper recesses of the nose.

This membrane, called the olfactory mucosa, is where the virus first lands when it is inhaled. Within it are olfactory sensory neurons (OSNs), which are responsible for initiating smell sensations. They are tightly entwined with a kind of support cell called sustentacular cells.

In the new study, Belgian and German researchers claim that the virus infects sustentacular cells but not OSNs. "That is just a critical distinction," said the senior author Peter Mombaerts, who directs the Max Planck Research Unit for Neurogenetics in Frankfurt, Germany. "Once you believe that olfactory neurons can be infected, there is a quick route into the olfactory bulb and then you're in the brain already."

The olfactory bulb, at the front of the brain, is where neural input about odours is first processed. If the virus penetrated this structure it could theoretically spread to deeper brain regions where it could do lasting damage – especially since, unlike OSNs, most neurons are not regenerated once lost.

But if the virus only infects the sustentacular cells, then the damage could be less long-lasting.

Both pathways could explain the olfactory dysfunction that afflicts an estimated half of all Covid-19 patients. In one in 10 of those, the loss or change of smell is long-term, perhaps permanent.

Mombaerts says this could be the result of support for the OSNs breaking down, even if they themselves are not infected. They may function below par, or stop functioning altogether, until the sustentacular cells regenerate.

The group has not looked at other neurological symptoms of Covid-19, such as the fatigue and "brain fog" that accompany long Covid. Nobody doubts that the central nervous system is affected by the disease; the debate concerns whether these effects are due to the virus infecting neurons or some more indirect mechanism, such as an inflammatory response in the blood irrigating the brain – with different implications for prognosis and treatment.

The findings are likely to prove controversial because of the difficulty of studying molecular events unfolding in the moments after infection. Earlier studies made use of animal models, clusters of neural stem cells grown in a dish, and postmortem tissue taken from small numbers of Covid-19 patients. The present study is the largest in Covid-19 patients to date, and it deployed a novel technique for capturing those early events.

Laura Van Gerven, a neurosurgeon at the Catholic University of Leuven in Belgium and another of the paper's senior authors, adapted a form of skull base surgery to remove tissue from the olfactory mucosa and bulb of Covid-19 patients within about an hour of their death. In 30 of the patients, the researchers were able to detect that the virus was still replicating – meaning the patients had died in the acute, contagious phase of the disease.

"It is unquestionably the most thoroughly done bit of work on human postmortem olfactory Covid tissue," said Stuart Firestein, a neurobiologist at Columbia University in New York City.

But Firestein said the results did not shed much new light on how Covid-19 causes olfactory dysfunction. "They do not show any OSNs as being damaged or there being fewer of them, or the OSNs near infected sustentacular cells as being different in any way from those not near infected cells," he said.

Debby Van Riel, a virologist at Erasmus University in Rotterdam, the Netherlands, also praised the study's rigour, but said the authors' claim that SarsCoV-2 does not infect neurons was "pretty bold".

In only six of the 30 patients was the virus detectable in the olfactory mucosa itself. "Overall the numbers are thus really low to make any strong conclusions," she said.

But even if the study isn't the last word on Covid's brain effects, it does indicate that those dire early reports weren't either. If its conclusions are borne out, those experiencing Covidrelated anosmia or parosmia can be reassured that the virus has not infected their brains, and that future therapies targeting the understudied sustentacular cells could alleviate or cure their condition.