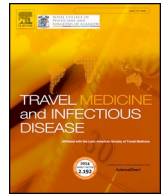




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Sars-Cov-2: Underestimated damage to nervous system

Dear Editor,

Coronaviruses (CoVs) are large enveloped positive-stranded RNA viruses, which generally induce enteric and respiratory diseases in animals and humans [1]. Novel coronavirus pneumonia (NCP, also called COVID-19) emerged in December 2019 in Wuhan, China [1]. This novel CoV(SARS-CoV-2) has caused a national outbreak of severe pneumonia in China, and rapidly spreads around the world.

On March 4, gene sequencing confirmed the presence of SARS-CoV-2 in the cerebrospinal fluid of a 56-year-old patient with NCP in Beijing Ditan Hospital. The patient was diagnosed with viral encephalitis, and the patient's central nervous system was attacked by SARS-CoV-2. This indicates that SARS-CoV-2 can directly invade the nervous system of patients, instead of injuring the nervous system through the immune response to SARS-CoV-2. This is the first evidence that SARS-CoV-2 has directly invaded the nervous system.

Genomic analysis shows that SARS-CoV-2 is in the same Betacoronavirus clade as MERS-CoV and SARS-CoV, and shares highly homological sequence with SARS-CoV [1]. The public evidence shows that COVID-19 shares similar pathogenesis with the pneumonia induced by SARS-CoV or MERS-CoV [2]. Moreover, the entry of SARS-CoV-2 into human host cells has been identified to use the same receptor as SARS-CoV [1]. Previous studies have shown that SARS-CoV and MERS-CoV possess neuroinvasive properties, which can be detected in human brains. CoVs may enter the CNS through two distinct routes: hematogenous dissemination or neuronal retrograde dissemination. I think that the way of neuronal retrograde dissemination is more worrying.

HCoV-OC43 RNA, a kind of human coronaviruses, could be detected for at least a year in the CNS of infected mice that survived the virus-induced acute encephalitis [3]. Therefore, an apparently innocuous human respiratory pathogen may persist in the human CNS as a component of the brain, like herpes simplex virus (HSV) in a large proportion of the population. If SARS-CoV-2 exists for a long time, like HSV, and it will recur again in predisposed individuals.

In addition, the presence of HCoV-229E and HCoV-OC43 was detected in various neurological diseases in humans, including multiple sclerosis (MS) [4]. Multiple sclerosis truly represents a human neurological disease where an infectious agent or agents may play a triggering role, with viruses the most likely culprit in genetically predisposed individuals [5]. If the SARS-CoV-2 is latent in CNS for a long time,

will the cured patients reappear with neurological diseases because of the latentness of the SARS-CoV-2, which is a doubt for the late neurological complications of the cured patients. If the SARS-CoV-2 is latent in the nervous system for a long period of time, will the cured patients reappear with neurological diseases? This is a question for the cured patients. It is worthy of our further discovery and exploration. In addition, we should also be aware of this problem in further clinical work, strengthen the alertness of clinicians, and jointly solve this problem.

### Declaration of competing interest

The authors declare that they have no conflicts of interest.

### References

- [1] Huang Y, Tu M, Wang S, et al. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: a retrospective single center analysis. *Trav Med Infect Dis* 2020:101606.
- [2] Song Z, Xu Y, Bao L, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses* 2019;11(1).
- [3] Jacomy H, Fragoso G, Almazan G, et al. Human coronavirus OC43 infection induces chronic encephalitis leading to disabilities in BALB/C mice. *Virology* 2006;349(2):335–46.
- [4] Arbour N, Day R, Newcombe J, et al. Neuroinvasion by human respiratory coronaviruses. *J Virol* 2000;74(19):8913–21.
- [5] Kurtzke JF. Epidemiologic evidence for multiple sclerosis as an infection. *Clin Microbiol Rev* 1993;6(4):382–427.

Lingyan Zhou<sup>1</sup>

Department of Neurology, The Affiliated Hospital of Qingdao University, Qingdao, 266000, China

Meng Zhang<sup>1</sup>

Department of Neurology, The Affiliated Hospital of Qingdao University, Qingdao, 266000, China

Jing Wang

Department of Rheumatology, The Affiliated Hospital of Qingdao University, Qingdao, 266000, China

Jing Gao\*

Department of Neurology, The Affiliated Hospital of Qingdao University, Qingdao, 266000, China

E-mail address: [sunshinezlyjg@163.com](mailto:sunshinezlyjg@163.com).

\* Corresponding author.

<sup>1</sup> These authors contributed to this work equally and should be regarded as co-first authors.