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.

Although the global COVID-19 pandemic is a public health emergency and presents us with the need to find out as much as we can about the disease as rapidly as possible, we believe that hastily publishing such findings without adequate peer review should be challenged. Especially in times of description of a new disease, much care should be taken to obtain expert review of the findings and any conclusions need to be substantiated by appropriate evaluations and inclusion of controls. Although this literature draw attention to the important question of CNS involvement of COVID-19, the data presented by von Weyhern and colleagues are likely to cause confusion and possibly misdirect future clinical efforts.

We declare no competing interests.

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1 von Weyhern CH, Kaufmann I, Neff F, Kremer M. Early evidence of pronounced brain involvement in fatal COVID-19 outcomes. *Lancet* 2020; **395:** e109.
2 Jortner BS. The return of the dark neuron. A histological artifact complicating contemporary neurotoxicologic evaluation. *Neurotoxicology* 2006; **27:** 628–34.
3 Solomon IH, Normandin E, Bhattacharyya S, et al. Neuropathological features of Covid-19. *N Eng J Med* 2020; **383:** 989–92.

Claus Hann von Weyhern and colleagues[1] describe autopsy findings of six patients who died of COVID-19. Better understanding of the central effects of COVID-19 is crucial, and we read with great interest their findings that included pan-encephalitis and meningitis in all six patients, regardless of whether cause of death was due to cardiorespiratory failure, pulmonary embolism, or intracranial haemorrhage. However, the images provided in the appendix of the Correspondence[1] do not clearly show meningitis or encephalitis. Shrunken neurons are a common histological finding in autopsy brains and are often observed in neurologically normal cases without any specific pathological change, and the small cells indicated as infiltrating lymphocytes are difficult to distinguish from glial cells in the absence of an immunostain showing interstitial lymphocytes. For example, we show similar findings in a section of a normal neocortex (appendix). Although neuron loss was observed by von Weyhern and colleagues, neuronophagia and microglial nodules were not described. Additionally, perivascular lymphocytes are not diagnostic of viral meningitis or encephalitis but perhaps suggest that COVID-19 is associated with vascular alterations.

The findings of published cases and our own limited experience with COVID-19 disease pathology support that when brain pathology is present, it is apparently often associated with vascular changes, such as thrombi or thromboemboli, rather than primary involvement of the CNS. Although instances with neuropathology consistent with severe acute respiratory syndrome coronavirus 2 encephalitis have been reported, these changes are generally mild and variable.[2–4]

We declare no competing interests.

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Authors' reply

We welcome the opportunity to respond to the comments about our Correspondence.[1] To increase the availability of data, we reported our findings, which were produced by a team that included an experienced neuropathologist and was subjected to the *The Lancet*'s peer-review process. The three responses are similar as they all challenge our interpretation of the findings presented. Striking is the fact that the three responses disagree among themselves, with each offering yet another interpretation.

To analyse our findings, we consulted a standard neuropathology textbook, coauthored by one of our critics.[2] In the textbook, one reads that glial cells indeed can be differentiated from non-glial cells, and that hypoxic neurons can be distinguished from dark neurons based on classical haematoxylin and eosin staining.

In the absence of specific morphological alterations, shrinking is often the only indication of necrosis or apoptosis. Aware of the hypoxic origin of similar morphological alterations, we used the general level of hypoxic injury to vulnerable CA1 areas of the hippocampus and Purkinje cells in the cerebellum as a baseline. Because we did not observe hypoxic injury in these areas, we do not attribute the observed morphological alterations to hypoxia.

We concede that the term pan-encephalitis was poorly chosen. In the neuropathological literature, pan-encephalitis refers to a fulminant


Sean Gallup/Staff/Getty Images

See **Online** for appendix