



COVID-19 and neurological disease: implications for neuropathologists

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Introduction

This resource points to a selection of publications (including opinion pieces) related to the role of the central nervous system (CNS) in coronavirus infections. It is meant to provide a starting point for publications on this topic. A number of the hyperlinks refer to non-peer-reviewed articles, for example on *medRxiv*.

It is not intended to be comprehensive or to give an opinion on the levels of evidence presented in the articles, but to serve as an 'entry point' to the topic of neuropathology in relation to COVID-19 and to stimulate discussion. It will be added to as new publications become available.

Starting points

A good starting point into this topic – COVID-19 and its implications for neuropathologists – is a one-page opinion piece in the recently established e-journal freeneuropathology.org.¹ It highlights the role of angiotensin-converting enzyme 2 (ACE2) receptors used by SARS-CoV2 as an entry route^{2,3} and it is suggested that these receptors are expressed in endothelial cells and the brain.⁴

However, it is acknowledged that ACE2 expression levels in the CNS are low⁵ and there are still many uncertainties, and evidence how the CNS is entered remains vague.³

Experimental studies on transgenic mice suggest that SARS-CoV infection is neuro-invasive⁶ and more details on the neuro invasiveness of SARS-Cov and SARS-Cov2 are given in a recent review.⁵

Extensive neuronal pathology of SARS-CoV has been described in autopsy studies.⁷ Undoubtedly, however, one-third of patients with COVID-19 infection had neurological manifestations which have been documented in a retrospective study.⁸

A case report describes a neuroimaging study of COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy.⁹ Despite, but also because of the uncertainties and varied levels of evidence, neuropathology can help understanding CNS complications of SARS-CoV infections.

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