

to make the raw consolidated data from this web-based case report form open access.

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For EAN survey on neurological symptoms in patients with COVID-19 see [https://www.surveymonkey.com/r/eansurvey\\_lancet](https://www.surveymonkey.com/r/eansurvey_lancet)

For more information on how to express interest in the registry see <https://forms.gle/xBbrwjcRTxvQnuzj7>

For the EANcore COVID-19 website see <https://www.ean.org/ean/eancore-covid-19>

## A call from the European Academy of Neurology on COVID-19

The frequency, determinants, and evolution of neurological manifestations associated with coronavirus disease 2019 (COVID-19) remain unknown, because of few available data and the retrospective nature of most reports.<sup>1–4</sup> Furthermore, the possible neurotropic nature of the virus (leading to dyspnoea and respiratory failure) is yet to be confirmed.<sup>5</sup>

Neurologists are facing many other challenges in the current pandemic, including the management of older patients and those with pre-existing neurological disorders for whom ethical decisions about escalation of care (eg,

admission to an intensive-care unit or intubation) might be difficult.

The European Academy of Neurology (EAN) aims to gather evidence about the neurological impact of COVID-19. Encompassing 45 000 European neurologists, 47 European National Neurological Societies, and ten associate National Societies from Africa and Asia, the EAN has created a multidisciplinary task force, the EANcore COVID-19, to develop: diagnostic and treatment recommendations for patients with COVID-19 with all subgroups of neurological condition; an online Neuro COVID-19 survey on neurological complications of COVID-19 (for which more than 4200 responses have been already received as of April 30, 2020); and the EAN Neuro COVID-19 registry, which arises from a collaboration with the Italian, Spanish, and Portuguese neurological societies and aims to collect standardised information about demographics, comorbidities, general and neurological manifestations, and course and outcome of COVID-19. This registry, launched on April 29, 2020, will be offered by the EAN to all interested neurologists, neurology departments, and National Societies, together with the necessary ethical, methodological, and technical support. EAN will also provide a platform for rapid COVID-19-related literature alerts and information.

Difficult times ask for innovative and courageous solutions. Neurologists are called on to play their part. The EAN is ready to support and join international efforts to alleviate the medical consequences and also the burden associated with the COVID-19 pandemic.

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## A call for a global COVID-19 Neuro Research Coalition

Reports are emerging at a rapid pace that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects the nervous system in various ways. Preliminary data from Wuhan, China, suggest that neurological manifestations are present in more than 30% of patients presenting with coronavirus disease 2019 (COVID-19).<sup>1</sup> Neurological features range from quite diffuse neurological signs and symptoms like headache, dizziness, reduced level of consciousness, confusion, diffuse corticospinal tract signs, and paraesthesia, to more specific manifestations, such as seizures, stroke, encephalitis, or meningoencephalitis, and myopathy.<sup>1,2</sup> To date, SARS-CoV-2 has not been detected in the neural

tissue directly, although it has been isolated from the CSF of some patients.<sup>3</sup> The hypothesis of neurotropism with subsequent neuronal injury, either directly or indirectly (through immune mechanisms), is supported by previous findings from other infections with severe acute respiratory syndrome CoV and Middle East respiratory syndrome CoV.<sup>3</sup>

Pre-existing cardiovascular or pulmonary disease and old age increase the chances of contracting SARS-CoV-2 infection and those risk factors are often present in patients with neurological disorders. Individuals with autoimmune diseases, such as multiple sclerosis, who require immunotherapy, might be at increased risk of SARS-CoV-2 infection and neurologists are in need of tailored recommendations for immunotherapy, relapse management, and delivery of care. Patients with Parkinson's disease have an increased risk for cardiovascular complications and can have multiple comorbidities, including cognitive impairment, depression, and psychosis, which can deteriorate during isolation.<sup>4</sup> Also, many patients with cognitive impairment might not be able to follow infection prevention and control recommendations, thereby putting themselves and their caregivers at risk of contracting SARS-CoV-2. Additionally, very little is known about potential interaction between various medications for chronic neurological diseases and drug treatment for COVID-19.

Because the effects of SARS-CoV-2 on the nervous system are largely unknown, estimating the neurological morbidity that might occur from the acute phase of the pandemic is difficult. Also, whether patients might have long-term neurological or cognitive sequelae, or whether pre-existing neurological disease might deteriorate (eg, patients with mild cognitive impairment might have little cognitive reserve and develop dementia early) is unknown. Effects of coronavirus in children seem less severe and often the virus is present but children are

#### Panel: Potential aims for a global COVID-19 Neuro Research Coalition

- To create a platform for global scientific exchange and networking
- To collaborate and partner with our colleagues in low-income and middle-income countries
- To harmonise methods and research tools
- To design joint studies, mobilise research funds, and publish together
- To establish, if appropriate, and to collaborate with existing registries
- To pursue new research translation into policies
- To join forces with national neurological research societies, the European, African, and American Academies of Neurology, the International Child Neurology Association, and the World Federation of Neurology
- To collaborate in a multidisciplinary way with other medical and allied disciplines and their respective societies and networks
- To team up with the brain health unit and COVID-19-related activities of the WHO
- To pursue in all activities a One Health, gender-based and equity-based approach, promoting the vision of Universal Health Coverage and the aims of the Sustainable Development Goals

COVID-19=coronavirus disease 2019.

asymptomatic. Asymptomatic children might still harbour the virus, with so far unknown effects on their health status later in life, including brain development. Additionally, once a vaccine becomes available, careful monitoring across age groups and disease spectra will be required to identify adverse effects and any deterioration of signs and symptoms in patients with neurological diseases. Overall, understanding is needed of whether susceptible groups exist who are at increased risk of deterioration after SARS-CoV-2 infection, how to detect them by use of biomarkers, and whether treatment needs to be specifically targeted in case of neurological signs and symptoms. Systems for clinical surveillance, epidemiological and clinical research, and post-mortem studies will be needed to achieve this aim.

The COVID-19 pandemic necessitates close collaboration on a global scale, with a special emphasis on inclusion of colleagues and partner institutions from low-income and middle-income countries. Inspired by the COVID-19 Clinical Research Coalition described recently in *The Lancet*,<sup>5</sup> our proposal is to build on and link existing international neurology partnerships, such as the Brain Infections Global COVID-Neuro

Network, that provides a network for interested clinicians, a daily update of all publications relating to neurological COVID-19 disease, and freely accessible downloads of case-record forms; the European Academy of Neurology COVID-19 registry; the Lean European Open Survey on SARS-CoV-2 Infected Patients endorsed by the German Neurological Society; and the activities of the World Federation of Neurology around COVID-19. Additionally, WHO can play an important part in building this coalition through identifying priorities and developing harmonised systems for neurological research. We are therefore launching a call for an inclusive and collaborative global COVID-19 Neuro Research Coalition co-created by the research communities around the world (panel). In a first step, we will create a platform of exchange and communication. If you are interested in becoming part of this community, please register at the Center for Global Health, Department of Neurology, Technical University of Munich, Germany, by sending an email to covid19.neuro@med.tum.de.

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For the COVID-19-related resource base of the European Academy of Neurology see [www.ean.org/ean/eancore-covid-19](http://www.ean.org/ean/eancore-covid-19)

For more on the Lean European Open Survey on SARS-CoV-2 Infected Patients see <https://leoss.net>

For more on the COVID-19 related resource base of the World Federation of Neurology see <https://wfneurology.org/covid-19-and-world-neurology>

For the Brain Infections Global COVID-Neuro Network see [www.braininfectionsglobal.tghn.org/covid-neurology-resource/](http://www.braininfectionsglobal.tghn.org/covid-neurology-resource/)

Vaccine programme, Siemens Diagnostics Clinical Advisory Board, Siemens Healthineers Clinical Advisory Board, Data Safety Monitoring Committee of the GlaxoSmithKline Study to Evaluate the Safety and Immunogenicity of a Candidate Ebola Vaccine in Children GSK3390107A (ChAd3 EBO-Z) vaccine, during the conduct of the study. TS has a patent test for bacterial meningitis based on a blood test, filed for patent pending (GB 1606537.7). All other authors declare no competing interests. ASW and SK contributed equally.

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## COVID-19 international neurological registries

The pandemic of coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has already affected more than 2.7 million people and caused more than 192 000 deaths worldwide. Respiratory symptoms are the most common, and neurogenic breathing failure is suspected to be involved.<sup>1</sup> Symptoms such as anosmia, dysgeusia, headache, and muscle pain have been noted, along with reports of central and peripheral nervous system involvement. Mao and colleagues<sup>2</sup>

reported on 214 patients who were admitted to hospital in Wuhan, China, with acute COVID-19. Symptoms were severe in 59% (mean age 58.7 years) of these patients, and non-severe in 41% (mean age 49.9 years). In total, 78 (36%) of 214 patients had neurological compromise, which was more common in severe (46%) than in non-severe (30%) cases and included stroke, impaired consciousness, myopathy, and neuralgic pain. Viral meningoencephalitis with presence of SARS-CoV-2 in CSF by viral genome sequencing has been reported in patients in China<sup>3</sup> and Japan.<sup>4</sup> In the USA, a woman aged between 50 and 60 years developed COVID-19 and altered mental status. Brain MRI on this patient showed bilateral haemorrhagic rim-enhancing lesions within thalami, medial temporal lobes, and subinsular regions characteristic of acute haemorrhagic necrotising encephalopathy.<sup>5</sup> This condition also, but rarely, occurs in influenza and other encephalitides in association with cytokine storm syndrome.

Amid confronting a severe outbreak of COVID-19, the Spanish Neurological Society (Sociedad Española de Neurología) implemented a registry of neurological manifestations in patients with confirmed COVID-19. We applaud this initiative and propose to expand these efforts globally to define the nervous system involvement in COVID-19. The Environmental Neurology Specialty Group of the World Federation of Neurology (ENSG-WFN) is encouraging neurological societies around the world to develop national or regional neuroepidemiological databanks to report all cases of new-onset, acute, delayed, and any long-latency neurological disorders associated with SARS-CoV-2 infection during the COVID-19 pandemic. Late parkinsonism occurred among survivors of the 1918–20 influenza pandemic. Therefore, neurologists must be prepared for the occurrence of delayed neurological manifestations of COVID-19.

For the Spanish Neurological Society registry see <http://www.sen.es/covid-19>

