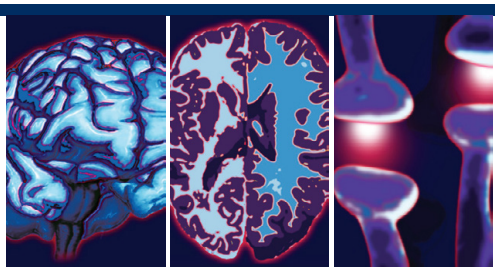
Commentary



Neurological and Neuropsychiatric Complications of Covid-19 Patients

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Introduction

This is the first systematic, nationwide UK surveillance study of the breadth of acute COVID-19 complications in the nervous system that we are aware of, and it was carried out through rapid mobilisation of UK professional bodies representing neurology, stroke or acute medicine, psychiatry, and intensive care. Cases reported by these groups' professional membership came from all throughout the UK, and an exponential rise in cases of COVID-19 neurological and psychiatric squeal coincided with an exponential rise in overall COVID-19 cases recorded by UK government public health bodies.

Future studies on COVID-19 neurological complications, particularly those examining genetic and associated risk factors, would benefit from obtaining notification of all cases of infection admitted to every hospital as a denominator, or a control group of COVID-19 patients without neurological or psychiatric complications. Due to the time constraints faced by busy clinical teams during the pandemic, we concentrated our notification strategy on individuals with neurological or psychiatric problems. Physicians from a variety of disciplines reported instances, and almost all of them fit the case definition of proven SARS-CoV-2 infection.

Cerebrovascular events in COVID-19 patients, which have been well documented elsewhere, were also detected as a significant subgroup within our sample. However, we found a significant number of cases of acute mental status change, including neurological syndrome diagnoses like encephalopathy and encephalitis, as well as main psychiatric syndrome diagnoses like psychosis. Although cerebrovascular events and altered mental status were found in patients of all ages, our cohort confirms that cerebrovascular events are more common in older patients; however, these preliminary findings show that acute alterations in mental status are disproportionately overrepresented in our cohort's younger patients.

Our rates of COVID-19 neurological and psychiatric consequences cannot be generalised to mildly affected patients or patients with asymptomatic infection, particularly those in the community, but they do provide a national perspective on issues severe enough to necessitate hospitalisation.

Our case-finding method has the potential for reporting bias, thus it has to be validated with extensive prospective clinic epidemiological data collecting. Such research should be planned ahead of time in the event of future pandemics, so that they can be mobilised early in the disease's transmission. Our findings may be skewed by a more involved professional membership or individuals who are more accustomed to reporting data to surveillance studies using this method. However, this was the first big national study to adopt a data surveillance technique for clinicians, with a considerable part of our population being notified. The current study also incorporated a priori considerations to establish the strength of the evidence for SARS-CoV-2 infection, and data collection was guided by unambiguous clinical case definitions. Furthermore, we conclude that systematic over ascertainment bias for psychi-

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atric or neuropsychiatric symptoms were unlikely in this sample.

Despite the fact that the RCPsych online portal was introduced 18 days later than the other neurological, stroke, and intensive care unit or more general portals, a substantial number of psychiatric or neuropsychiatric alerts were noted. Indeed, because many COVID-19 patients are treated in intensive care units with sedatives and paralytics, which might conceal and contribute to iatrogenic consequences, our sample may underrepresent the rate of neurological or psychiatric symptoms.
Our sample may underrepresent individuals with milder outpatient symptoms, such as impaired taste or smell, because we deliberately recognised moderate to severe COVID-19 problems as they were reported for inpatient cases by neurologists and psychiatrists. Future hypothesis testing studies based on our findings to infer causative linkages between infection and neurological or neuropsychiatric manifestations should follow basic concepts, such as Bradford Hill's causation criteria for pandemic respiratory illness and brain impacts.

In our analysis, many cerebrovascular events were found, as reported in earlier cohorts and case reports of acute COVID-19 problems. The pathophysiological mechanisms underlying COVID-19 cerebrovascular events need to be investigated further, but there is a biological rationale for a vasculopathy, with a report of SARS-CoV-2 endothelitis in organs outside the cerebral vasculature and cerebrovascular events, in addition to coagulopathy and the traditional risk of stroke during sepsis.

To address this issue, large studies with clearly defined control groups are needed, including patients hospitalised with COVID-19 but without cerebrovascular events and patients hospitalised with cerebrovascular events but not with COVID-19. Detailed prospective longitudinal studies will be required to confirm the relationship between COVID-19 and new acute mental or neuropsychiatric problems in younger patients. Systematic participant evaluation, description of immune host responses, research of genetic correlations, and comparison with adequate controls will be required to understand this association (including patients hospitalised with COVID-19 who do not have acute neuropsychiatric features). Patients brought to the hospital with a serious infection are more likely to have altered mental status, especially those who require intensive care. This symptom, on the other hand, is more common in older people and could indicate the unmasking of latent neurocognitive degenerative illness or much medical comorbidity, which are frequently associated with sepsis, hypoxia, and the need for polypharmacy and sedative drugs. We found a disproportionate number of neuropsychiatric presentations in younger patients and a predominance of cerebrovascular complications in older patients in this study, which could reflect the state of the cerebral vasculature and associated risk factors in older patients, exacerbated by critical illness.

Higher access to neuropsychiatry or psychiatry review for younger patients, as well as increased attribution of altered mental status to delirium in older patients, could explain the high number of patients with altered mental status. Nonetheless, the higher detection of acute changed mental status in COVID-19 patients merits further investigation. Future modelling studies should quantify the exclusion of iatrogenic components such sedatives and antipsychotics. Although the notifying psychiatrist or neuropsychiatric assessed that most mental diagnoses were new in our study, we cannot rule out the potential that they were undiagnosed before the patient developed COVID-19. Our study cohort is a snapshot of hospitalised individuals with COVID-19-related acute neurological or mental problems. Larger, ideally prospective studies should be conducted to identify a larger cohort of COVID-19 patients in and out of hospitals, using capture–recapture analysis and health record linkage to provide more precise estimates of the prevalence of these problems and those at risk. Community studies are also needed to identify persons who are at risk of both COVID-19 and neurological or mental problems, albeit this technique will necessitate widespread serological testing.

Data sharing is being more recognised as critical for facilitating rapid, responsive clinical research, and is especially important during an international emergency like the SARS-CoV-2 epidemic. The Coro Nerve Study Group was made possible by open collaboration between a numbers of universities in the United Kingdom. We believe that sharing data more extensively, across European and worldwide partners, will be beneficial, particularly in low- and middle-income nations. The Brain Infections Global COVID-Neuro Network is assisting data collecting in these countries by making case record forms freely available.