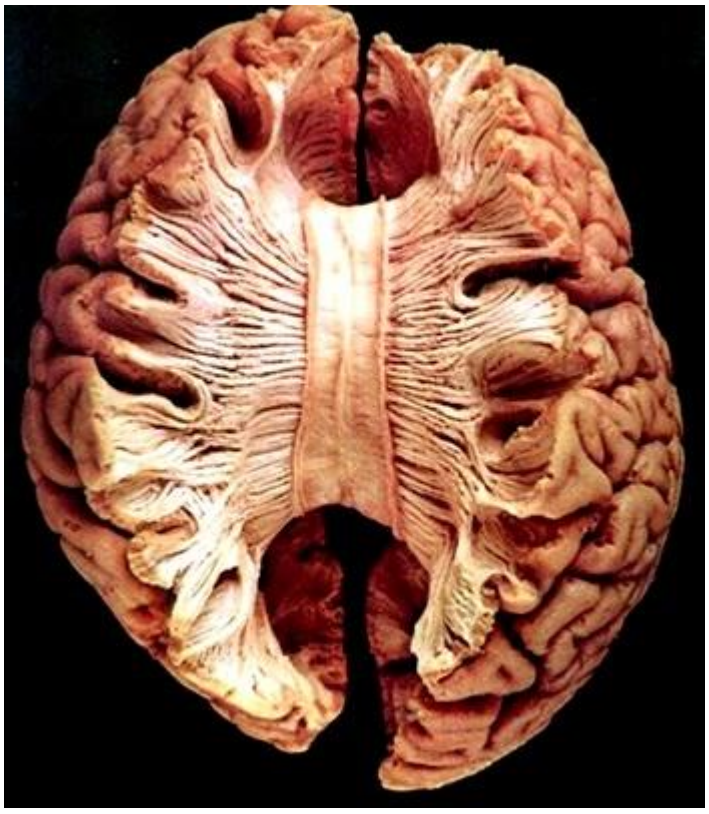
The *corpus callosum (CC)*, as the largest interhemispheric commissure, connects the cortical zones of the left and right hemispheres. The anterior regions of the *CC* contain axons from the frontal premotor and motor cortices, while the posterior regions contain fibers from the somesthetic, parietal, occipital, and temporal lobes. Cytotoxic lesions of the *corpus callosum* (CLOCCs) are a rare clinicoradiologic syndrome characterized by transient and reversible lesions of the *CC* and possibly of the adjacent white matter. CLOCCs have been observed in the context of various diseases, including viral infections. Since CLOCCs were identified as a distinct radiological finding in patients with neuroCOVID, the Chinese researchers in this retrospective study presented the neurological, radiological, and laboratory features of cytotoxic lesions of the *corpus callosum* observed in eight COVID-19 patients.

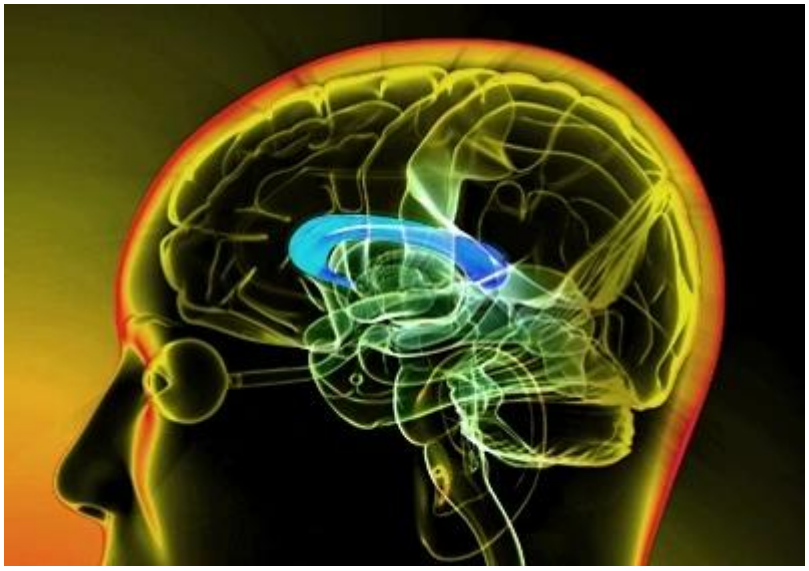


Cytotoxic lesions of the corpus callosum, characterized by transient and reversible lesions of the corpus callosum and possibly of the adjacent white matter, were found in COVID-19 patients (MRI study)

The role of the *CC* has two main aspects. The first aspect suggests that the *CC* is associated

with functional cortical lateralization at the level of interhemispheric inhibition. The second implies that the *CC* contributes to brain symmetry, as impairment of the *CC* leads to intrahemispheric isolation. According to the authors, structural features and characteristics of the blood supply make the *CC* susceptible to damage, including a lack of adrenergic receptors, impaired regulation of water and electrolyte homeostasis, excitatory amino acid toxicity, oxidative stress damage, or inflammatory infiltration mediated by immune dysregulation. However, neurological symptoms, which rapidly emerge after infection and then subside, suggest that disruption of the blood-brain barrier (BBB), leading to direct invasion of the SARS-CoV-2, is unlikely to be the direct cause of CLOCCs. A previous functional brain magnetic resonance imaging (MRI) study investigating brain activation during working memory tasks in patients with neuro-post-COVID revealed differences in brain lateralization. Lower activation was observed in two large clusters localized in the left hemisphere, and higher activation was noted in the right hemisphere, during more challenging tasks in post-COVID patients compared to healthy controls. They also showed poorer performance in the domains of endurance, locomotion, and manual dexterity of the dominant hand, which is controlled by the motor area of the dominant, mostly left hemisphere.
https://discovermednews.com/post-covid-syndrome-and-brain-activation-during-the-working-memory-tasks/

Importantly, COVID-19-related CLOCCs are more common in adolescents and young adults. They also have more severe neurological symptoms, such as impaired consciousness, ataxia, hallucinations, dysarthria, and psychotic disorders, as observed in pediatric cases linked to multisystemic inflammatory syndromes. However, it is important to note that all reported cases had complete remission of neurological symptoms.



About the study and Results

254 COVID-19 patients with an average age of 64.4 years (range: 15-96 years) underwent brain MRI scans. The inclusion criteria were SARS-CoV-2 infection confirmed with positive PCR or antigen testing, as well as CLOCC findings on brain MRI. The exclusion criteria included pre-existing lesions or other causes of the *CC* abnormalities, such as non-COVID-19 infections, acute trauma, pregnancy, epilepsy or antiepileptic medications, chemotherapy, and alcohol intoxication. All patients tested positive for the SARS-CoV-2 virus *via* RT-PCR.

CLOCCs were found in eight COVID-19 patients (four males and four females) with an average age of 31.1 years (range: 15-82 years). More than half of these patients were younger than 20 years. All patients were evaluated by at least two neurologists. Neurological symptoms in all COVID-19 patients diagnosed with CLOCCs developed within three days of COVID-19 onset and included impaired consciousness (5/8), headache (4/8), psychiatric abnormalities (4/8), ataxia (2/8), dysarthria (2/8), pyramidal tract signs (2/8), and visual disturbances (2/8). Two cases had severe COVID-19-related rhabdomyolysis. None of the patients had pre-existing neurological disorders, neurological symptoms, or signs.

MRI Findings

All patients underwent a 3-T brain MRI scan. All MRI images were interpreted by at least one radiologist and one neurologist. Based on the extent of the *CC* lesions on MRI, patients were categorized into three different types of CLOCCs. Type I lesions, which were localized in the splenium of the *CC*, were associated with faster recovery. Type II (cases 6 and 7) and III (case 8), involving the peripheral white matter or anterior *CC*, were associated with more

severe neurological symptoms. These results suggest that the location of the *CC* lesion may influence the clinical presentation and recovery from CLOCCs. Follow-up MRI scans of the brain showed that the *CC* lesions had resolved within 2 to 3 weeks.

Electroencephalography was also performed in cases 2 and 7, which showed epileptic discharges in case 2 and diffuse slow-wave spikes throughout the brain in case 7.

Laboratory Findings

Laboratory testing included a peripheral blood cell count, inflammatory cytokines, markers of cellular lysis (such as lactate dehydrogenase), coagulation parameters, thyroid hormones, creatine kinase, and electrolytes. Peripheral blood samples were taken within six hours after admission.

At the onset of the disease, the CRP-lymphocyte ratio was elevated in all 8 cases, the neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, systemic immune-inflammatory index, and C-reactive protein in 7/8 cases, and IL-6 in 2/4 cases. Importantly, in patients with MRI type II and III of CLOCCs, serum levels of platelet-lymphocyte ratio, systemic immune-inflammation index, CRP, CRP-lymphocyte ratio, and IL-6 were higher than in type I patients. When the *CC* lesions resolved in all patients, the levels of CRP-lymphocyte ratio subsequently declined, suggesting that this marker may serve as a useful indicator of disease activity.

In addition, hyponatremia was found in type II and III patients, particularly those with adjacent white matter lesions, supporting the hypothesis that electrolyte imbalance may contribute to the pathogenesis of CLOCCs.

The cerebrospinal fluid (CSF) samples collected from five patients showed normal cell count, glucose, and chloride concentrations, and elevated levels of total proteins in one patient.

Conclusion

In this study, clinical and radiological findings of eight patients with COVID-19-associated CLOCCs are presented, highlighting the favorable prognosis and the importance of considering CLOCCs in the differential diagnosis of neurological symptoms in neuroCOVID-19 patients. However, the retrospective nature of the study and the small number of patients limit the generalizability of these findings. Given the ongoing threat of SARS-CoV-2 variants, further research is necessary to understand the full range of

neurological effects of COVID-19 and to define future treatment strategies.

This article was published in Brain and Behavior.

Journal Reference

Wan C, Li M, Yu Y et al. COVID-19-Associated Cytotoxic Lesions of the Corpus Callosum in Chinese Patients: A Retrospective Study. Brain and Behavior, 2025; 15: e70547. (Open Access) https://doi.org/10.1002/brb3.70547