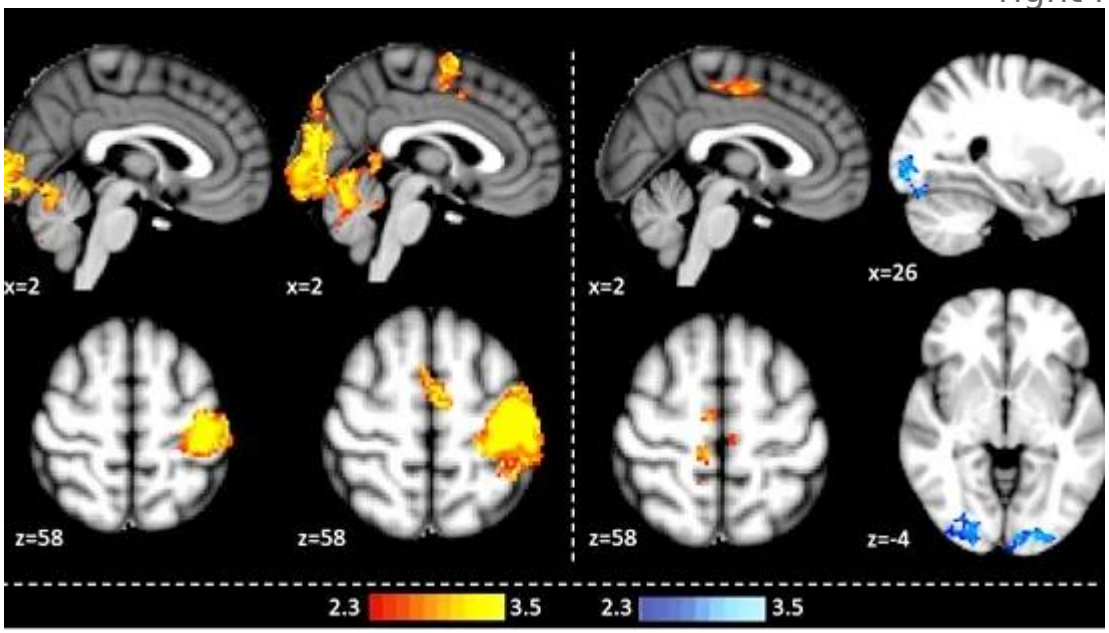
In the post-acute phase of COVID-19, there is an increased risk of neurologic sequelae, affecting the central nervous system (CNS) or the peripheral nervous system (PNS). In this study, researchers from the United States used blood-oxygenation-dependent functional MRI (BOLD-fMRI) to investigate whether patients with post-COVID syndrome and neuropsychiatric symptoms have abnormal brain activation during working memory tasks. They also investigated a possible relationship between abnormal brain activation and performance on three NIH-Toolbox (NIHTB) batteries for cognitive, emotional, and motor functions.

Prior studies have comprehensively mapped the spectrum of neurologic sequelae in post-COVID patients, but there has been no significant progress in understanding the underlying mechanisms. It seems that SARS-CoV-2 uses various neuroinvasive strategies and pathways to invade the CNS, such as infection of the nasal olfactory epithelium and axonal transport along the olfactory nerve, retrograde axonal transport, invasion by compromising the blood-brain barrier (BBB), and the use of infected hematopoietic cells as “Trojan horses” (hematogenous route). It is assumed that the olfactory bulb serves as the main gateway for viruses to enter the brain.

A brain lesion (stroke, for example) induces changes in unaffected brain regions due to deafferentation, removal of inhibition, activity-dependent synaptic changes, changes in membrane excitability, growth of new connections, and unmasking of preexisting connections. After the injury to the primary motor cortex, the recovery process involves functional changes characterized by increased activity in the motor cortex of the unaffected contralateral hemisphere. It is assumed that persistent activation of the contralesional hemisphere correlates with poor recovery and represents maladaptive plasticity, but also that increased activity in the contralesional hemisphere contributes to functional improvement, particularly in less-well-recovered patients. This process represents a kind of adaptation using available resources.



About the study

The authors used BOLD-fMRI to investigate brain activation during a working memory task in participants diagnosed with post-COVID neuropsychiatric symptoms and healthy controls who tested negative for SARS-CoV-2. Patients who developed post-COVID had documented COVID-19 at least six weeks before enrollment. Healthy controls had no history of COVID-19 and tested negative for SARS-CoV-2.

Of the 50 usable fMRI datasets, nine participants (six post-COVID, three controls) had minor abnormalities on their structural MRIs that were not exclusionary. Five individuals (three post-COVID participants, two controls) had slightly more than age-related white matter lesions, two (one in each group) had lacunar infarcts, one control person had microhemorrhages, and one control person had small old infarcts and a microhemorrhage.

Participants were assessed with three NIHTB batteries for cognition (NIHTB-CB), emotion (NIHTB-EB), and motor functions (NIHTB-MB), and selected Patient-Reported Outcomes Measurement Information System (PROMIS) tests.

Results

The study included 50 participants, 29 post-COVID convalescents who developed neuropsychiatric symptoms after the acute COVID-19, and 21 healthy controls who tested

negative for SARS-CoV-2.

Individuals with post-COVID syndrome reported a high prevalence of cognitive disorders, such as concentration problems (93%), memory problems (79%), and confusion (64%). They also had a higher prevalence of neurological symptoms, such as headaches (57%), visual disturbances (50%), gait disturbances (50%), paresthesias (43%), and coordination problems (39%), as well as of other symptoms, such as fatigue (86%), depression/anxiety (68%), sleep disturbances (64%), myalgia (61%), light-headedness (46%), and urinary problems (28%). The NIHTB-EB scores showed significantly worse psychological well-being in post-COVID participants than healthy controls.

BOLD-fMRI findings

BOLD-fMRI findings revealed that brain activation during the 0-back and 1-back tasks did not differ between participants with post-COVID neuropsychiatric symptoms and healthy controls. However, during a more difficult 2-back task, the post-COVID participants had lower activation in several brain regions compared to healthy controls.

Importantly, the two large clusters with lower activation were localized in the left hemisphere, in the postcentral gyrus, insula, precentral gyrus, and inferior parietal lobule. However, all brain regions with higher activation in the 2-back task were localized in the right hemisphere. Interestingly, the long-COVID group had lesser deactivation in the right posterior cingulate cortex and greater activation in the right superior frontal gyrus.

These findings are consistent with the results of a recent resting-state fMRI study on characteristics and changes of the complex network known as brain functional connectome in patients with primarily neurological symptoms of post-COVID syndrome. This study discovered a decreased connectivity of the anterior cingulate cortex and increased connectivity of the posterior cingulate gyrus, a central node in the default mode network, in patients with post-COVID syndrome. According to the authors, a strong correlation between attention test and the hyperconnectivity of the posterior cingulate gyrus could contribute to the deficit of executive cognitive functions in patients with post-COVID syndrome. https://discovermednews.com/changes-in-brain-functional-connectome-in-post-covid-syndrome/

Importantly, the participants with post-COVID neuropsychiatric symptoms performed worse than healthy controls on the NIHTB battery for motor functions in the domains of

endurance, locomotion, and the manual dexterity of the dominant hand (controlled by the motor area of the dominant, mostly the left hemisphere).

According to the authors, these findings indicate suboptimal functioning in the normal network and increased brain activation in the contralateral hemisphere during working memory tasks in individuals who developed post-COVID neuropsychiatric symptoms.

Conclusion

This is the first task-activated BOLD-fMRI study conducted in individuals diagnosed with post-COVID neuropsychiatric symptoms. The results discovered a different brain activity and reorganized working memory networks in post-COVID participants compared to healthy controls who tested negative for SARS-CoV-2. In addition, the participants with post-COVID performed worse than the control group in endurance, locomotion, and dexterity of the dominant hand.

Several brain regions that showed lower activation are located in the left hemisphere. At the same time, the brain regions in the right hemisphere were more used to maintain normal performance.

The authors concluded that BOLD-fMRI was sensitive enough to detect a process of brain reorganization in individuals diagnosed with post-COVID neuropsychiatric symptoms.

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