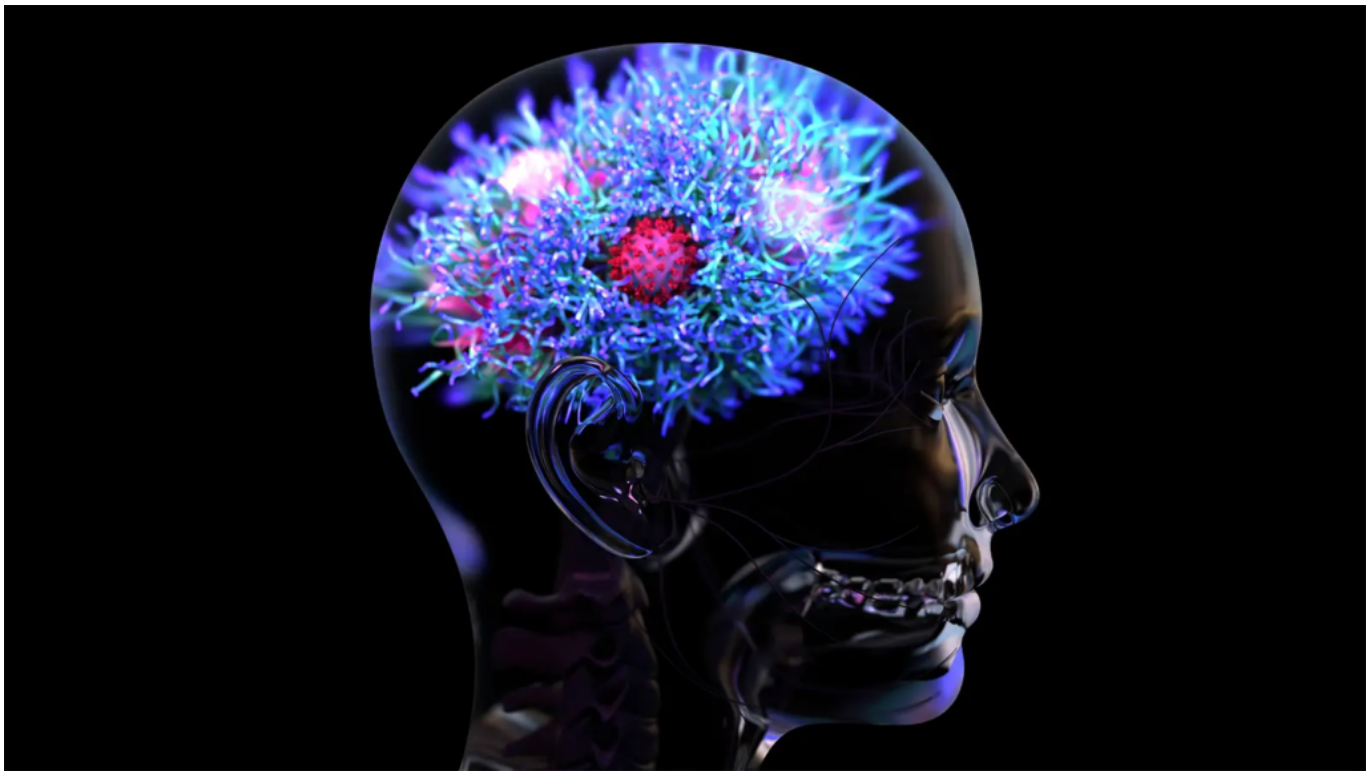
https://www.medpagetoday.com/neurology/longcovid/103108



The hypothesis that long COVID might be related to a functional neurological disorder (FND) remains untested, a systematic review showed.

Across 102 long COVID studies, neurologic symptoms were insufficiently characterized to support or refute a diagnosis of FND, reported Tiago Teodoro, MD, PhD, of St. George's Hospital in London, and colleagues.

Given the characteristics of the disorder, some people with FND might be inappropriately considered to be long COVID patients, which could delay diagnosis and treatment and affect prognosis, the researchers wrote in the *European Journal of Neurology*opens in a new tab or window.

"We remain struck by the similarities between some manifestations of long COVID and functional disorders triggered by acute illnesses," Teodoro told *MedPage Today*.

“Our systematic review shows that the possibility that some people labeled as having long COVID might in fact be experiencing a form of functional neurological disorder has, so far, been largely overlooked in the medical literature,” he said.

“This is a major problem for understanding long COVID but primarily for patient management, as this is a condition with specific diagnostic criteria and for which effective treatments are available,” he added.

FND refers to disorders caused by an abnormality in brain signalingopens in a new tab or window with no significant structural damage in the brain. It occurs in an estimated four to 12 people per 100,000opens in a new tab or window per year.

“These are common neurological conditions caused by malfunctioning of the brain but not directly related with structural damage,” Teodoro noted.

“We have previously seen many patients developing functional neurological symptoms following an acute event such as an injury, an invasive medical procedure, or an infection, among many others,” he said.

“These factors do not directly cause the functional neurological symptoms, but are best understood as triggers, which precipitate this condition in people with a pre-existing predisposition,” Teodoro continued. “In some cases, these functional neurological symptoms might become persistent.”

The analysis by Teodoro and co-authors “seems to be well done, which is not surprising given that the authors are well-known, respected academics,” observed Mark Hallett, MD, emeritus investigator and former chief of medical neurology at the National Institute of Neurological Disorders and Stroke (NINDS), who wasn’t involved with the study.

“Their major conclusion is that it is not known how frequently functional neurological

disorder plays a role in long COVID, if at all, largely because data have not been collected in sufficient detail and the diagnosis has not generally even been considered," Hallett told *MedPage Today*.

"However, it is likely that some long COVID patients do have FND, or FND together with some other pathology," he noted.

"The most important issue is that FND requires its own treatment and that such treatment can be successful," Hallett said. "Physicians should know that FND is a possibility, that it can be diagnosed based on positive features, and that appropriate therapy, as always, depends on making the right diagnosis."

A diagnosis of functional neurologic symptoms is positive and not just based on ruling out other conditions, Teodoro and co-authors emphasized. "A key feature is inconsistency over time, which means that symptoms often occur intermittently and/or with fluctuating severity," they wrote.

Teodoro and colleagues reviewed 102 studies spanning 412,726 who had COVID-19. Of these, 31 studies recruited participants who had long COVID (11,860 patients). The remaining studies looked at people with acute COVID screened for ongoing long COVID symptoms.

Overall, 51 studies were prospective, 33 were cross-sectional, and 12 were retrospective; 18 included a control group. Most (89 studies) defined long COVID as symptoms persisting for 4 weeks or more.

Mean or median age in most studies was between 40 and 59, and the proportions of male and female participants were similar.

Neurologic symptoms reported most consistently were cognitive difficulties, headaches,

pain, dizziness, fatigue, sleep-related symptoms, and ageusia or anosmia.

“Overall, we found no evidence that any authors had systematically looked for positive features of FND,” Teodoro and colleagues wrote. “An exception were three studies describing temporal inconsistency.”

“Moreover, only 13 studies specifically focused on long COVID after mild infection, where the impact of confounders from the general effects of severe illness would be mitigated,” they added.

“There are a growing number of case reports of FNDopens in a new tab or window triggered by COVID-19 infection (and vaccination),” Teodoro and co-authors pointed out. “This is in line with our expectations and makes the absence of patients with FND in the long COVID cohorts we reviewed or that FND was not generally considered by authors as a differential diagnosis even more surprising.”

Researchers and clinicians need to appreciate the likely complexity and heterogeneity of the mechanisms for long COVID symptoms, the researchers noted.

“This includes ensuring that neuropsychiatric and functional explanations for symptoms are considered alongside other explanations without the prejudice that such explanations make symptoms less genuine or disabling, or are less ‘real’ than more traditional biological explanations for symptoms,” Teodoro and co-authors wrote.

“It is also likely that patients may have more than one diagnosis accounting for their multiple symptoms — something which runs the risk of being hidden through the use of a syndromic label such as long COVID,” they added. “Without understanding these issues, it is likely that patients will not be able to access suitable treatment, and development of novel treatments and services will be delayed.”

Disclosures

There was no specific funding involved in this review.

The authors reported no conflicts of interest.

Primary Source

European Journal of Neurology

Source Reference: opens in a new tab or windowTeodoro T, et al "Functional neurological disorder in people with long COVID: a systematic review" Eur J Neurol 2023; DOI: 10.1111/ene.15721.