

A study links long COVID-related fatigue to anxiety and depression for the first time

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Credit: Vera Kratochvil/public domain

The most common symptoms of the post-COVID-19 condition known as long COVID include fatigue, shortness of breath and cognitive dysfunction, according to the World Health Organization (WHO). To be considered symptoms of long COVID, they must be present for at least two months during the three months after the onset of the disease.

A recent study in *Brain and Behavior* showed that the disease had a generalized impact on attention skills, [executive functions](#), learning and long-term memory. Furthermore, the scientific literature estimates that between 9% and 49% of patients present [fatigue](#) four weeks after the onset of symptoms, and it may even persist for a year in at least a third of patients.

Nevertheless, a possible link between fatigue and anxiety or depression in patients with long COVID had not been studied in laboratories. Now, a study by the Universitat Oberta de Catalunya (UOC), which has been published in open access format in the *Journal of Neurology*, has now shown that fatigue in long COVID patients is related to anxiety, depression and apathy.

"Persistent fatigue is very disabling and greatly limits people's quality of life. If someone suffers from fatigue as a result of COVID-19, it's important to study this situation in further depth, and to determine what other symptoms or disorders are associated with this condition," said Marco Calabria, lead researcher of the article, a member of the Cognitive NeuroLab group at the UOC and a member of the Faculty of Health Sciences.

According to the author, now that we know the link between fatigue and depression, "clinicians should explore these aspects to provide a focus for therapeutic guidelines." However, something that this research has not clarified is the direction of the effect: "it's unclear whether fatigue leads to depression, or vice versa," he explained.

Scientists studied a sample of 136 patients with COVID-19 who were suffering from cognitive deficits eight months after contracting the virus. "We found that fatigue is linked to sustained attention, which we use to perform a task for a long period of time and which keeps us focused, and to executive functions, which enable us to temporarily store

information in order to perform tasks such as calculating, or reproducing a phrase that we've heard," said Calabria.

Studying fatigue: a clinical challenge

Fatigue is characterized by excessive tiredness and physical and/or cognitive and muscular weakness. It has been associated with [medical conditions](#) such as post-viral infection and neurological diseases.

Nevertheless, although it could be broadly outlined in these terms, there is no universally accepted definition of this clinical condition, and knowledge of its underlying pathogenic mechanism is limited, which is why it represents a clinical challenge for experts.

Another challenge for the scientists was to separate post-COVID-19 fatigue from the consequences of the specific situation experienced during the pandemic. "Fatigue is a symptom related to viral infections, and this suggested that it'd be one of the possible symptoms of SARS-CoV-2 infection," said Calabria, who believes that it is possible that, in the first waves of the pandemic, isolation may have contributed to the increase in some symptoms. "But some observations tell us that this isn't always the case: fatigue prevents many people from going back to their previous lifestyle, while others continue to suffer from fatigue despite being able to return to pre-pandemic conditions and we found that the prevalence of apathy associated with COVID-19 increased from 17% before infection to 62% after infection."

According to its authors, the results of the study highlight the importance of a holistic approach when evaluating and considering a potential treatment for COVID-19 patients experiencing fatigue. However, there are still many unanswered questions: "how these changes are reflected at the brain level, how long they last, who's more likely to suffer from these symptoms for a long time, and what the individual characteristics that predict recovery are. We'll answer all these questions in the long term,

because this area's something new and unknown," concluded the researcher.

More information: Marco Calabria et al, Post-COVID-19 fatigue: the contribution of cognitive and neuropsychiatric symptoms, *Journal of Neurology* (2022). [DOI: 10.1007/s00415-022-11141-8](https://doi.org/10.1007/s00415-022-11141-8)

Carmen García-Sánchez et al, Neuropsychological deficits in patients with cognitive complaints after COVID-19, *Brain and Behavior* (2022). [DOI: 10.1002/brb3.2508](https://doi.org/10.1002/brb3.2508)

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