



## Long-COVID Headache

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### Abstract

The so-called long COVID-19 is a set of symptoms that accompanies the patient even for months after discharge from the hospital. These symptoms include easy muscle fatigue, moderate breathlessness, persistent headache, the feeling of a foggy head, and the development of psychiatric disorders. In general, the quality of life of at least half of the patients who come out of the COVID-19 syndrome, both mild and severe, shows a markedly worsening despite having passed a difficult physical and psychological test. Among all the neurological disorders that can most frequently be found in the long COVID-19, it is important to consider the persistent headache symptomatology as a possible chronic sequela of the infection. Since there is not a definition in the International Headache Society classification of this type of headache, we must focus our attention on this long-COVID-19 headache especially because clinical studies are being planned to collect big data for the International Headache Society Classification Committee.

**Keywords** Long-Covid-19 · Persistent headache · Neurological sequelae · Pain · Classification

Headache occurs as one of the initial symptoms of infection in COVID-19. It can be spread throughout the skull, giving a feeling of constriction and weight at the top of the head. All this occurs in a large part of subjects who present the first symptoms of COVID-19 in a percentage that varies from 14 to 60% [1–3]. If the infection affects a subject already suffering from migraine, it multiplies the crises and makes recognition not immediate, together with the fever, fatigue, muscle weakness, and respiratory difficulty of the infection [1].

The symptomatology of COVID-19 infection is multifaceted and depends on the involvement of multiple systems and

apparatuses, not just the pulmonary one [4]. In non-severe forms of COVID-19, that can and must be managed and treated by avoiding the hospitalization of the patient, early recognition of symptoms is a fundamental prerequisite for immediate therapeutic management [5].

The so-called long COVID is the set of symptoms that accompanies the patient even for months after discharge from the hospital. These symptoms include easy muscle fatigue, moderate breathlessness, persistent headache, the feeling of a foggy head, and the development of psychiatric disorders [6]. In general, the quality of life of at least half of the patients who come out of the COVID-19 syndrome, both mild and severe, shows a markedly worsening despite having passed a difficult physical and psychological test [7].

The neurological impairment of post-COVID-19 can have different pathophysiological bases: direct neuro-invasion with a damage on the neuronal pathway, indirect effects mediated by hypoxia, hypertension, coagulopathy and cytokine storm on the CNS, up to the worsening of pre-existing brain diseases or new ones (cerebrovascular events, infectious and toxic encephalopathy, meningoencephalitis, Guillain Barré syndrome) [8]. Long-term complications arise from this multifaceted picture.

Among all the neurological disorders that can most frequently be found in the “long COVID-19,” it is not necessary to underestimate the persistent headache for at least 6 months, both as a clinical expression of new onset concomitant with

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cognitive blunting, such as “brain fog,” and as worsening/chronicization of a pre-existing migraine [9]. Although headache does not represent a prognostic picture for the evolution of COVID-19, it must always be taken into consideration as a possible chronic sequela of the infection.

A quite similar clinical picture of sub-continuous headache was already described, as a consequence of other viral infections, as the New Daily Persistent Headache (NDPH), and had been described by Diaz-Mitoma and Walter Vanast of McGill University in Montreal, as headache resulting from Epstein-Barr Virus infection and published in 1987 in *Lancet* [10], headache syndrome lasting >3 months. However, this putative similarity between NDPH and long-COVID headache needs further discussion and data.

In this scientific moment of a not yet incomplete consensus not only on the nosography classification of the sequelae of COVID-19, namely long-COVID, post-acute sequelae of SARS-CoV-2 (PASC, COVID long haulers, etc.), the presence of this multifaceted neurological symptomatology, headache and foggy feeling, even after negativization by COVID-19 infection, must be taken into serious consideration in order to avoid a chronicization of the headache and a further worsening of the patient’s quality of life [11–17]. Furthermore, deranged innate immune signaling and activation of inflammasomes implicated in both COVID-19 headache and migraine [18] could also play a role in long-COVID headache, as well as sleep difficulties associated with long-COVID symptoms also be a significant element determining cognitive problems, poor memory, and chronicity of headaches [19].

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