Movement Disorders Induced by SARS-CoV-2 Infection

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Infections are a significant cause of movement disorders. The clinical manifestations of SARS-CoV-2 infection are variable, with up to one-third of patients developing neurologic complications, including movement disorders.

movement disorders SARS-CoV-2 COVID-19

1. Introduction

Movement disorders are neurologic syndromes with either an excess or a paucity of movement, unrelated to weakness or spasticity. Among the hyperkinetic movement disorders, the most frequent are tremor, dystonia, myoclonus, chorea and athetosis, ballism, tics, and sleep-related movement disorders. Hypokinetic movement disorders include parkinsonism and rigidity.

Infections are a significant cause of movement disorders, as up to 20% of movement disorders are due to an infectious cause [1]. The most frequent agents are beta-hemolytic group A streptococcus, the flavivirus causing Japanese encephalitis, HIV, West Nile virus, and Creutzfeldt–Jakob disease [2].

Two mechanisms were postulated to underly the development of infection-related movement disorders. First, they can be a direct consequence of an active infection in relevant cerebral structures; second, they can be a manifestation of a delayed immune-mediated process secondary to previous infection [3]. In addition, the role of neuroinflammation in neurodegeneration has started to attract interest in recent years. A possible link between neuroinflammation and parkinsonian syndromes such as encephalitis lethargica and postencephalitic parkinsonism [4] was investigated in the context of Spanish flu. Nonetheless, the subject is still under debate, as there is no proven correlation yet. The role of the viral stimulation of microglial activation in neurodegeneration has regained attention in the context of the SARS-CoV-2 infection. Nonetheless, there is a lack of long-term observations, and the question of whether there is any correlation between SARS-CoV-2 and morbidity in parkinsonian syndromes remains open. Meanwhile, recent studies highlighted the impact of the virus on the central nervous system, demonstrating a fast viral spread in the regions connected with the olfactory bulb, including the basal ganglia, with increased neuronal death. These findings indicate the potential for long-term consequences of coronavirus disease 2019 (COVID-19) [5].

Therefore, infection-related movement disorders may have an acute or subacute onset or can be delayed months to years after the infection. However, most movement disorders present about six weeks from the onset of infection

(but depends on the cause) [6][7].

Regarding the treatment, a multifaceted approach is frequently used to control the patient's symptoms. The majority of infection-related movement disorders are a direct consequence of an active infectious process that affects the brain structures implied in the motor network [8]. Therefore, the main treatment consists of disease-specific, infection-targeted medication. In other cases, the movement disorders are caused by a delayed immune-mediated process triggered by a previous infection and may respond to immunomodulatory treatments [7][8][9]. In addition, symptomatic treatment may be used [7][8][9].

The SARS-CoV-2 virus is a novel agent spreading rapidly. The clinical manifestations of COVID-19 are diverse, from asymptomatic to severe disease. Furthermore, up to one-third of the patients with SARS-CoV-2 infection develop neurologic complications, including movement disorders [3]. The most frequent movement disorders were reported to be myoclonus and ataxia [10][11], but patients may also present with chorea, tremor, or dystonia [11]. Interestingly, previous studies reported a predominance of hyperkinetic movement disorders, while hypokinetic disorders were rare [12]. However, due to the novelty of SARS-CoV-2 infection, the management of patients is based mainly on other respiratory infections, principally influenza and other coronaviruses.

2. Movement Disorders Induced by SARS-CoV-2 Infection

The main characteristics on myoclonus in the context of SARS-CoV-2 infection are presented in **Table 1**.

Table 1. Characteristics of myoclonus in the context of SARS-CoV-2 infection.

Article	Databases	Date of Search	Findings	Notes
Brandao 2021 [11]	PubMed	Up to 25 January 2021	59/93 cases presented myoclonus	Investigated movement disorders among patients with SARS-CoV-2 infection.
Chan 2021 [13]	PubMed and Medline	Up to 6 December 2020	51 cases of myoclonus or ataxia	Investigated myoclonus and cerebellar ataxia associated with SARS-CoV-2 infection.
Giannantoni 2021 [14]	PubMed and Cochrane Library	The date is not specified	6 cases	Investigated myoclonus and ataxia in COVID-19 patients.
Hirschfeld 2021 [15]	PubMed	Up to 31 July 2021	33 cases of myoclonus	Among the autoimmune-mediated hyperkinetic movement disorders, the most common was ataxia (83.67%), followed by myoclonus (67.35%).
Roy 2021 [16]	PubMed and Google Scholar	Up to 30 May 2020	4 cases with myoclonus	The main focus of the paper was on the neurological and neuropsychiatric impacts of the COVID-19 pandemic.

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Alcalay, R.N.; Trenkwalder, C. Impact of the COVID-19 Pandemic on Parkinson's Disease and Movement

Article	Databases	Date of Search	Findings	Notes
Salari 2021 [17]	PubMed and Scopus	The date of the search is not specified	64 patients with movement disorders	Limited data on myoclonus.
Schneider 2021 [10]	PubMed and MedRxiv	Up to August 2021	More than 50 cases	The exact number of myoclonus cases is not specified. Narrative review.

Findings may be limited by the quality and breadth of the data in the case reports, which may not be uniform or consistent in all papers. However, case reports represent a relevant, appropriate, and essential study design in promoting scientific knowledge, especially in the case of rare disorders. Although the methodological limitations of case studies in the analysis of treatments and the development of new tests are well known, observing single patients can provide useful insights on the etiology, pathogenesis, natural history, and treatment, especially in rare disorders [18].

Furthermore, case reports and case series have significantly influenced medical knowledge and continue to promoter scientific research and understanding [19]. Although several concerns were raised about the high likelihood of bias associated with single case reports or case series and the weak inferences they may provide, such observations are an important basis for learning by pattern recognition and further progress of medical knowledge [19]. For example, a systematic review of the cases with lipodystrophy enabled authors to propose the core and important clinical features of the disease and to narratively present the data on available treatment options [20].

The key findings will be detailed, allowing their use to inform clinical practice. However, implications for practice may be hampered because of the lack of methodological quality assessment of included studies [21].

To date, several studies on different movement disorders in COVID-19 patients have been performed. However, most studies are up to December 2020, and the studies report only disparate aspects of movement disorders in SARS-CoV-2 infections. Consequently, the outcomes of the evidence-based approach will provide significant information to clinicians and other healthcare professionals, policymakers, and public health scientists.

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