COVID-19 and neurodegeneration: what can we learn from the past?

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Coronaviridae (CoVs) are single stranded RNA viruses. β-CoVs encompass bat coronavirus (BCoV), the human severe acute respiratory syndrome (SARS) virus and the Middle Eastern respiratory syndrome (MERS) virus [1].

In December 2019, a new β-CoV was identified in Wuhan, China, SARS-CoV-2. The genome sequencing demonstrated a 79.5% and 96.2% identity to SARS-CoV and a bat CoV genome, respectively, supporting the interspecies transmission and the origin of this new pandemic [1].

Coronavirus disease 2019 (COVID-19) is linked to severe acute respiratory infection with a pathological role of the angiotensin converting enzyme 2 receptors (ACE2r). Beside the lung expression, ACE2r have been detected in glial cells and neurons.

Neurological manifestations appear in 36.4% of patients and are characterized by acute encephalitis, necrotizing encephalopathy, ischaemic or haemorrhagic stroke, cranial neuropathy (anosmia and ageusia), Guillain–Barré-like syndrome, peripheral neuropathy, myopathy or rhabdomyolysis [2]. Furthermore, neurotropic effects have been related to the morbidity and mortality of COVID-19.

Hyposmia, a classical prodromal non-motor feature of Parkinson disease (PD), has been reported as an early clinical manifestation of COVID-19, but its relevance remains under discussion [3]. Interestingly, olfactory dysfunction could link acute viral infection with increased risk of developing neurodegenerative disorders.

Although the aetiology of PD is still unclear, new insights support a key role of neuroinflammation in dopaminergic neuron dysfunction. Viral infections contribute not only to microglia cytokine release but also to proteostasis dysfunction by viral replication into the host cell.

A meta-analysis identified that some viral infections increase the risk of PD by chronic neuroinflammation. Moreover, according to the 'dual-hit theory of PD' SARS-CoV-2 might trigger PD by modifications of the gut microbiome [4].

In this sense, the most provocative early work was published in 1992 by Fazzini *et al*. [5]. The authors identified a high level of β-murine-CoV antibodies in the cerebrospinal fluid of PD patients. Interestingly, they proposed several concepts that could help our best understanding about SARS-CoV-2 and the risk of developing PD.

The authors reported an acute and chronic persistent infection associated with CoVs, highlighting the interspecies transmission and the possibility of oligosymptomatic or atypical infections, with ≥36% of asymptomatic cases and a variable antigen excretion (days to 2 months for respiratory involvement and several months for patients with gastroenteritis). They also mentioned a potential recurrence associated with a non-protective antibody production and speculated about other new CoVs that may induce a chronic damage of the dopaminergic neurons of the substantia nigra.

It would be interesting to explore whether these statements are applicable to SARS-CoV-2 and its potential role in PD. Although the relation between certain viral infections and PD is still ambiguous, history shows an overlap between the 'Spanish flu' (1918–1920) and the lethargic encephalitis epidemic of 1916–1926 [6].

A new pandemic is being faced. Are the affected individuals at a high risk of developing PD? This needs to be watched carefully, keeping in mind the history lessons, and research needs to be done.

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Ethics statements

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