Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 and selective vulnerability to Parkinson's disease

The current COVID-19 pandemic provides a unique opportunity to investigate the hypothesis that viral infections can precipitate neurodegeneration. Severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1), a pathogenic homolog of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), invades the brain through ACE2,[1] and SARS-CoV-2 might be neurotropic too. SARS-CoV-2 also enters cells via the ACE2 receptor,[1] which is widely expressed in the CNS, including in the striatum,[2] where the virus might precipitate or accelerate neurodegeneration.[3,4] SARS-CoV-2 might infiltrate the CNS directly through the olfactory or vagus nerves, or haematogenously. This infection could, in turn, prompt cytotoxic aggregation of proteins, including α-synuclein. This hypothesis is supported by evidence in animal models that viral infections can trigger α-synucleinopathies in the CNS.[5]

We suspect that neuronal populations are not equally susceptible to degeneration, and that dopaminergic neurons are selectively vulnerable because of their intrinsic properties. For instance, high bioenergetic demands from highly arborised axons, and impaired proteostasis resulting from large axon size, can promote α-synuclein aggregation and result in selective vulnerability to non-cell autonomous factors that promote α-synuclein seeding, such as neuroinflammation and environmental neurotoxins.

α-Synuclein could function as a native antiviral factor within neurons, as shown by an increased neuronal expression of α-synuclein following acute West Nile virus infection.[6] West Nile virus and SARS-CoV-1 are both enveloped, single-stranded, positive sense RNA viruses with analogous viral entry and replication mechanisms.[1,6] Therefore, similar α-synuclein upregulation might occur with SARS-CoV-2 infection. The consequences of this pathological process could be further exacerbated by a peripheral inflammatory response, as occurs in COVID-19. A rodent model of peripheral H5N1 influenza infection showed persistent CNS microglial activation and abnormal α-synuclein phosphorylation, associated with a loss of dopaminergic neurons in the substantia nigra pars compacta.[7] We postulate that antiviral α-synuclein accumulation following SARS-CoV-2 infection might compound pre-existing cell-autonomous vulnerability and lead to α-synuclein propagation and widespread neurodegeneration. Prospective longitudinal studies in survivors of COVID-19 can help to support this hypothesis.

SARS-CoV-2 infection might also interfere with α-synuclein clearance. Other neurotropic viruses, such as H1N1 influenza, can obstruct protein clearance to maintain optimal viral protein levels, rendering infected host cells unable to counterbalance α-synuclein accumulation.[8] SARS-CoV-2 proteins are capable of binding human protein trafficking molecules.[9] One such protein in particular, ORF8, is specifically involved in endoplasmic reticulum regulation.[9] If SARS-CoV-2 can impair proteostasis through ORF8 binding and cause dysregulated endoplasmic reticulum protein trafficking, then α-synuclein could aggregate uncontrollably.

Finally, the bioenergetic stress of SARS-CoV-2 neuroinvasion might be insurmountable for certain neuronal populations. Nigrostriatal dopaminergic neurons display high cellular energy requirements to fuel elevated basal oxidative phosphorylation in the mitochondria, high axon terminal density, and extensive axonal arborisation. Considering this large metabolic energy use, if additional cellular energy reserves are unavailable, the cellular stress of COVID-19 infection might drive these vulnerable neurons over the threshold of neurodegeneration.

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COVID-19 in older people with cognitive impairment in Latin America

The COVID-19 pandemic in Latin America and Caribbean countries (LACs) has failed to capture the attention