Implications for Neuromodulation Therapy to Control Inflammation and Related Organ Dysfunction in COVID-19

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Abstract
COVID-19 is a syndrome that includes more than just isolated respiratory disease, as severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) also interacts with the cardiovascular, nervous, renal, and immune system at multiple levels, increasing morbidity in patients with underlying cardiometabolic conditions and inducing myocardial injury or dysfunction. Emerging evidence suggests that patients with the highest rate of morbidity and mortality following SARS-CoV2 infection have also developed a hyperinflammatory syndrome (also termed cytokine release syndrome). We lay out the potential contribution of a dysfunction in autonomic tone to the cytokine release syndrome and related multiorgan damage in COVID-19. We hypothesize that a cholinergic anti-inflammatory pathway could be targeted as a therapeutic avenue.

Keywords COVID-19 • SARS-CoV2 • ACE2 • Vagus • Vagus nerve stimulation

Abbreviations
α7nAChR α7 nicotinic ACh receptors
ACE2 Angiotensin converting enzyme 2
ACH Acetylcholine
ARDS Acute respiratory distress syndrome
CRP C-reactive protein
DAMPs Danger associated molecular patterns
FABP4+ Fatty acid binding protein 4
nAChR Nicotinic acetylcholine receptor
SARS-CoV2 Severe acute respiratory syndrome–coronavirus 2
sHLH Secondary hemophagocytic lymphohistiocytosis
TNFα Tumor necrosis factor α
VNS Vagus nerve stimulation

As the number of confirmed COVID-19 cases surges over 4 million globally and deaths surpass 280,000, the medical community faces a new challenge expanding at an alarming rate of killing nearly 10,000 patients in a single day. COVID-19 is a syndrome that includes more than just isolated respiratory disease, as severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) also interacts with the cardiovascular, nervous, renal, and immune system at multiple levels, increasing morbidity in patients with underlying cardiometabolic conditions and inducing myocardial injury or dysfunction [1]. As we study patients with COVID-19, it has become clear that COVID-19-