Potential role of memantine in the prevention and treatment of COVID-19: its antagonism of nicotinic acetylcholine receptors and beyond

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Memantine, as an antagonist of α7-nAChR and NMDA receptors, may decrease ACE2 receptor expression and reduce oxidative stress and inflammation. Hence, memantine may potentially reduce SARS-CoV-2 virulence. https://bit.ly/2AZHiVg

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To the Editor:

Recently, Leung *et al.* [1] proposed that α7-subtype nicotinic acetylcholine receptor (α7-nAChR) antagonists might decrease angiotensin-converting enzyme (ACE)2 receptor expression in respiratory epithelium and, hence, prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) invasion of pulmonary epithelial cells. Let us further theoretically evaluate this assertion and contribute to the quest for potential medications that might reduce virulence and pathogenicity of coronavirus disease 2019 (COVID-19). Smoking may be associated with progression and negative outcome of COVID-19 [1]. The receptor-binding domain of the S protein (spike) on the surface of SARS-CoV-2 interacts with the ACE2 receptor, which is an entry point of the virus into host respiratory cells [2]. On the respiratory epithelium cells of smokers and patients with COPD there is higher expression of this "viral receptor" (ACE2 receptor) [1]. Nicotine binds and stimulates nAChR, specifically the α7 subtype, which are localised in lungs and various other tissues, especially in the central nervous system. Increased expression of ACE2 receptors is mediated by stimulation of α7-nAChR. Nicotine, by its agonism on α7-nAChR, might promote entry of SARS-CoV-2 into the respiratory epithelium through ACE2 receptors [1]. Additionally, some evidence suggests that SARS-CoV-2, along with other human coronaviruses, is neurotropic and neurovirulent [3]. Altogether, it is of utmost importance to search for medications that might exert protective effects both at the periphery, at the entry point of SARS-CoV-2 infection, but also in the central nervous system where the virus might propagate.