Can Infection of COVID-19 Virus Exacerbate Alzheimer's Symptoms? Hypothetic Possible Role of Angiotensin-Converting Enzyme-2/Mas/ Brain-Derived Neurotrophic Factor Axis and Tau Hyper-phosphorylation

Hypothesis

During the years of the 2019–2020 outbreak of infection, one of the members of coronavirus, coronavirus disease-19 (COVID-19), becomes a global concern and is a public health emergency.[1,2] Infection by coronaviruses causes mild respiratory tract disorder, such as the common cold, but rare forms of infections with this family of viruses such as severe acute respiratory syndrome, Middle East respiratory syndrome coronavirus, and COVID-19 can be lethal and can remain long-term sequels.[2,3] Unfortunately, there is no enough information on long-term sequels of infection by COVID-19 in an infected person.[3,4] However, based on some indirect evidence and documents, it can be hypostatized that infection with coronavirus family, especially COVID-19, can cause neurological disorder or exacerbate existing disease in an infected person, but it is not proven yet.[4,5] According to recent studies, angiotensin-converting enzyme 2 (ACE2) can be acts as functional and host receptor of COVID-19.[6,7] It seems that some parts of the sequels of COVID-19 in the respiratory and cardiovascular system were mediated via the inhibition of ACE-2, but the mechanism of involvement of this ACE-2 was not exactly clarified.[8,9] On the other way, it was suggested that ACE-2 is one of the main enzymes which by the mediation of some important proteins such as Mas protein regulates normal brain functions such as cognitive activity and release of neurotrophic factors such as brain-derived neurotrophic factor (BDNF).[10,11] Furthermore, there are novel studies that indicate that the reduced activity of the ACE-2/Ang (1–7)/Mas axis is strongly linked to Tau hyper-phosphorylation (inactivation) and aggregation of neural internal microtubules and amyloid-β (Aβ) peptides.[12,13] According to these data, it was established that the reduction of ACE-2 activity or expression can disturb normal brain cognition activity or can exacerbate Alzheimer's disease.[13,14] Thus, according to the mentioned studies, it was hypothesized that infection with COVID-19 can target and reduce ACE-2 activity, and/or expression, and probably its downstream Mas/BDNF axis, in the brain cells, and according to these data, it can be expected that infection by COVID-19 may cause disturbances in cognition activity and also exacerbate cognitive impairment in infected person with Alzheimer's disease [Figure 1].

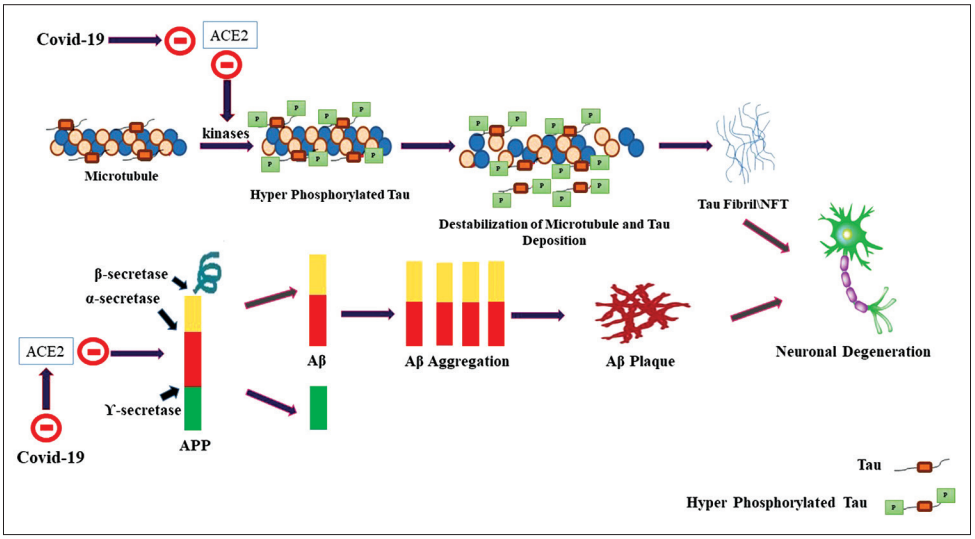

Figure 1: In the pathophysiology of Alzheimer's disease, some intrinsic and extrinsic triggers cause activation of some kinases which led to hyper-phosphorylation of Tau protein. This Tau hyper-phosphorylation causes disability of microtubules, which consequently causes aggregation of tau protein (Tau fibril) and neuro-filaments. On the other way, some intrinsic and extrinsic triggers cause activation of secretase family enzymes which initiate degradation of Amyloid precursor protein and led to production and formation of amyloid-beta. Amyloid-beta, Tau fibril/neuro-filament causes degeneration neural cells which cause Alzheimer's disease or dementia. As mentioned in the text, angiotensin-converting enzyme-2 causes inhibition of secretases family enzymes and kinases enzymes which can inhibit occurrences of Alzheimer's disease, dementia, or cognition impairment. According to some indirect evidence, it seems that infection with the COVID-19 virus can cause inhibition of the angiotensin-converting enzyme-2 signaling pathway, and it might be can have long-term neurological sequels such as activation of Alzheimer's or dementia triggers signaling pathway

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Conflicts of interest

There are no conflicts of interest.

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