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.

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Possible immunity, inflammation, and oxidative stress mechanisms of Alzheimer's disease in COVID-19 patients

Dear Editors,

We have read with great interest the paper from Alomari et al. [1] about the "COVID-19 and the Central Nervous System". With the prevalence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the risks of neurological disease need to be carefully evaluated for neurologists. We found the study very interesting and meaningful, because the authors found affected patients may be at high risk of developing Alzheimer's Disease (AD) after overcoming the COVID-19 infection. The study reported SARS-CoV-2 can disrupt angiotensin-converting enzyme type 2 (ACE2) signaling pathway, with a role of antioxidative stress and anti-neuroinflammation, cause neurodegeneration of dopaminergic neurons or impairment in cholinergic pathways, and may involve in the progression of AD. We highly agree with the authors opinions, are very interested in the AD related to SARS-CoV-2. Here, we want to contribute with some aspects related to AD caused by COVID-19 that may further support the hypothesis of the authors.

First, COVID-19 is associated with a severe innate immune response [2]. As we all known, innate immune activation plays an critical role in AD pathophysiology [3]. Microglia is the brain's major innate immune cells. The SARS-CoV-2 causes the activation of microglia, which produce the Chemokine C-C motif ligand (CCL) 2, and the increase of CCL 2 expression. Overexpression of CCL 2 induces massive increase in interleukin-6 and significant increase of pathogenic tau species, which may contribute to the pathogenesis of AD [3].

Next, SARS-CoV-2 may contribute to blood-brain barrier (BBB)-associated cognitive decline of AD. Endothelial dysfunction at the BBB can be caused by SARS-CoV-2 [4]. It is possible that circulating neurotoxins mediated by inflammatory factors enter the brain through the damaged BBB, which leads to neuronal loss and dysfunction and accelerates the process of developing into AD in the future [5].

Last but not the least, in retort to SARS-CoV-2, reactive oxygen species (ROS), an initiator of toxic innate immune responses, is overproduced. COVID-19 can induce excessive oxidative stress, an imbalance between the ROS and the antioxidant system, and alterations of redox balance in infected cells by altering mitochondrial function [6]. Oxidative stress can induce cell disfunction and cause neuronal death [6], which play an indispensable role in the pathobiology of AD through mitochondrial DNA disturbances including oxidative damage, mutations, and methylation shifts [7]. On the other hand, most people infected with SARS-CoV-2 are elderly, and AD is a age-related neurodegenerative disease. Aging is the most critical risk factor for AD [8]. It is well known that certain cognitive functions decline continuously with age. Continuous accumulation of mediated by ROS-mediated oxidative modifications is one of the potential mechanisms for COVID-19 to induce AD [9].

Consequently, in view of the present situation, the application of antioxidants is particularly necessary to take preventive measures for AD caused by SARS-CoV-2. Some antioxidants such as polyphenols, N-acetylcysteine, and resveratrol may hold a potential role of prevention free from AD caused by SARS-CoV-2 [9]. However, AD is a chronic disease and it takes a long process to develop clinical symptoms and confirm the diagnosis. In spite of this, it remains to be alerted to a possible increase in AD cases in COVID-19 survivors, and it is especially necessary to prevent it in advance.

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We provide consent for publication.

Declaration of Competing Interest

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