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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Correspondence

Reissuing the sigma receptors for SARS-CoV-2

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Dear editor,

Receptor binding is one of the major determinants of tissue tropism for coronaviruses and seems an important mediator of the pathophysiology of COVID-19. With this regard, the emerging review article published in the Journal by Armocida et al. has drawn our special attention to the possible involvement of a broad range of receptors in the neurotropism and neuronal cell entry of SARS-CoV-2 [1]. Despite the effects of SARS-CoV-2 on the central nervous system (CNS) currently remained inconclusive, a foregoing line of evidence supports the hermeneutical notion that the CNS transmission of SARS-CoV-2 might be via either direct viral infiltration or angiotensin-converting enzyme-2 receptors [2,3]. Alternatively and presumably, the recent interactome study by Gordon et al. adumbrated that Sigma1 (σ1) and Sigma2 (σ2) receptors might play a role in the neuronal infectivity of SARS-CoV-2 [4].

Both σ1 and σ2 are widely expressed in the CNS structures including the spinal cord, pons, cerebellum, hippocampus, hypothalamus, midbrain, cerebral cortex and olfactory bulb. Protein architecture of σ1 incorporates cholesterol-binding chaperones that are located in lipid-rich regions of the mitochondria-associated endoplasmic reticulum (ER) membranes (MAMs). These ER-embedded protein microdomains have been attributed to maintaining Ca^{+2} signals and involving in lipid storage and transport in MAMs. These functions of σ1 have also been postulated to take part in the mediation of the early stages of viral RNA replication. Previous research has suggested that pharmacological manipulation of both σ1 and σ2 activity might provide antiviral activity, particularly for RNA viruses including hepatitis C virus (HCV) and human immunodeficiency viruses (HIV). Functional deficiency and reduced expression of σ1 might be associated with decreased intracellular titration of HCV-RNA [5], while a pharmacological selective σ1 antagonist BD1047 has been shown to alter the stimulating effect of cocaine on the intracellular HIV-1 expression in microglia [6]. These findings indicate that σ receptors may also be involved in the neuronal transmission of SARS-CoV-2, which has a genome structure similar to those of HCV and HIV. Clinical observations that many patients with COVID-19 present with anosmia may empirically support our argument as SARS-CoV-2 might have an affinity to olfactor bulb which is enriched in σ receptors. Another important implication of σ receptor involvement in the SARS-CoV-2 infection may lie in the argument that numerous psychotropics likes of haloperidol, fluvoxamine, fluphenazine and chlorpromazine considerably interacts with σ receptors, which may highlight the potential clinical utility of such agents in the management of SARS-CoV-2 infection. Nevertheless, such an argument needs decent support from well-established clinical research. Although abovementioned postulations galvanize our interest in the comprehension of the pathophysiology of CNS involvement of SARS-CoV-2, we disclose that much more work is required to illuminate and guide the specific underpinnings of SARS-CoV-2's brain involvement.

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