



behavior a criminal offense, protecting professionals from similar situations. Brazilian psychiatrists and other health professionals should be vigilant against this emerging and potentially dangerous phenomenon.

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Ayahuasca and its interaction with the sigma-1 receptor: a potential treatment for COVID-19

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SARS-CoV-2 infects alveolar epithelial cells by endocytosis through the angiotensin-converting enzyme II (ACE2) receptor, which initiates virus replication and its effects on the respiratory system.¹ However, ACE2 receptors are also found on glial cells, the olfactory bulb, the hippocampus, the brainstem, and spinal neurons.² Thus, the virus could enter the nervous system through the cribriform plate towards the olfactory bulb, altering the permeability of the blood-brain barrier to easily reach all parts of the nervous system.²

Once the virus enters the interior of the cell through the ACE2 receptors, it interacts with the sigma-1 receptor, which is located in the endoplasmic reticulum, conditioning its structure to create the ideal conditions for replication.³



It is suggested that sigma-1 receptor agonists could serve as a prophylactic treatment, since these drugs, by occupying this receptor, prevent modification of intracellular machinery to the needs of SARS-CoV-2, stopping the inflammatory process induced by the cytokine storm. For this reason, the use of fluvoxamine, donepezil, arketamine, among others, has been proposed.⁴

Preliminary evidence has been found about the effects of antidepressants in relation to severe impairment and death⁵ in Covid-19. Lenze et al.⁶ found that a group treated with fluvoxamine had a lower probability of clinical deterioration. There is a significant association between antidepressant use (whether selective serotonin reuptake inhibitors or not) and a reduced risk of intubation or death.⁷

Ayahuasca, a compound used in South American folk healing rituals, is currently being studied for its therapeutic potential to treat mental illnesses.⁸ It contains β -carbolines (harmine, harmaline and tetrahydroharmine), which are monoamine oxidase inhibitors, and a substance analogous to serotonin called N,N-dimethyltryptamine (DMT), which is responsible for rapid antidepressant and anxiolytic effects.⁹ In relation to Covid-19, preliminary evidence has been published on the use of DMT to treat mental health problems in recovered patients.¹⁰

Various studies have shown that DMT is an agonist of the sigma-1 receptor, which is related to synaptic plasticity in dendritic growth, and that it has anti-inflammatory action, which could attenuate the pathophysiological neuroinflammation mechanism of neuropsychiatric and neurodegenerative diseases.¹¹ Although this evidence supported the therapeutic potential of ayahuasca components for mental illnesses prior to the pandemic, in this new scenario these findings could lead to more effective forms of treatment against SARS-CoV-2 beyond neuropsychiatric diseases.

Finally, by interacting with the sigma-1 receptor, the alkaloids found in ayahuasca might inhibit the replication of SARS-CoV-2 once inside the cell, preventing Covid-19 infection and, ultimately, the development of serious complications. It is an opportune time to develop studies on the evolution of COVID-19 among populations that regularly consume ayahuasca due to its potential preventive effects against SARS-CoV-2 infection.

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