



Psychoactive compounds as multifactorial protection factors against COVID-19

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The SARS-CoV-2 pandemic has raised a number of questions regarding the best treatment options that might be effective in slowing the spread of the illness, specifically in vulnerable patient groups, including patients with psychiatric disorders. Against all odds, in France, units for COVID-19 psychiatric inpatients have remained nearly empty. Moreover, they have been able to effectively manage COVID-19 although patients with psychiatric disorders frequently present with a number of risk factors for a poor COVID-19 prognosis [1]. This, along with the fact that symptomatic COVID-19 cases have been reported far more often in health care workers than in psychiatric inpatients—in France and others European countries—has raised the question whether specific psychoactive drugs might have a protective effect against COVID-19 [2].

Among these drugs, chlorpromazine in particular has been proposed as a potential treatment option against the virus, owing to its anti-MERS-CoV and anti-SARS-CoV-1 properties [2, 3]. However, chlorpromazine is seldom prescribed (2% of prescriptions in France) [4]. Hence, it is unlikely that this antipsychotic drug alone might explain the widespread protective factors found in patients with mental illnesses.

It is important therefore to consider other explanations. Tobacco use for instance could play a role as a protective

factor in patients with psychiatric disorders, whom present with extremely high prevalence rates of tobacco consumption. Indeed, nicotine has been recently put forward as a potential protective factor [5].

Lithium, clomipramine (a tricyclic antidepressant with a pharmacological structure related to that of phenothiazines), and benztropine also seem to have an effect on coronaviruses, whereas haloperidol, paroxetine, and melatonin have been found to have a therapeutic effect on other viruses [6, 7]. Cyamemazine (a phenothiazine, related to chlorpromazine), tropatepine (an anticholinergic drug, structurally and pharmacologically related to benztropine), haloperidol, and alimemazine (a phenothiazine hypnotic drug) are often prescribed in France (20%, 19%, and 14% of prescriptions, respectively) [4].

Given the number of psychoactive compounds found in psychiatric settings more frequently than chlorpromazine [4], we can thus suggest that the potential prophylactic effect of these drugs in patients with psychiatric illnesses is more closely linked to a phenothiazine class effect and to unspecified factors (e.g., related to nicotine and others psychotropics drugs) rather than to chlorpromazine specifically [8, 9].

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All these arguments should lead us to cautiously examine the prophylactic effects of phenothiazines in the treatment of COVID-19. Indeed, the protective factors found in patients with psychiatric disorders are most probably multifactorial and likely due to a number of psychoactive substances found in mental health clinical settings. This is precisely the pharmacological assumption that deserves to be further investigated in future studies in order to gather more understanding regarding the link between exposure to psychoactive substances in psychiatric patients and protection against SARS-CoV2.

Two recent articles mentioned the potentially prophylactic nature of psychotropic drugs by mixing pharmacoepidemiological and pharmacochemical/chemoinformatics data [1, 10].

These studies suggest that some molecules, especially the best-tolerated drugs, could be used as prophylactic agents against SARS-CoV-2 infection (e.g., nicotine or/and antihistamine agents) and could offer new therapeutic perspectives [1].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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