



Authors' Reply to Mazza et al.: "Fluvoxamine for the Early Treatment of SARS-CoV-2 Infection: A Review of Current Evidence"

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Accepted: 1 February 2022 / Published online: 12 February 2022
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Dear Editor,

We appreciated the thoughtful letter by Dr. Mazza positing that the antidepressant effect of fluvoxamine could make it a useful treatment for patients experiencing depression in the wake of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; coronavirus disease 2019 [COVID-19]) infection [1]. This highlights two important points: (1) the critical need to find effective treatments for the neuropsychiatric sequelae of COVID-19 and (2) the potential to repurpose selective serotonin reuptake inhibitors (SSRIs) and other psychotropics towards this goal.

Neuropsychiatric problems are common after COVID-19, including mood and anxiety disorders, cognitive impairment, psychosis, and stroke. A large electronic health record database study found that one in three COVID-19 survivors experienced neuropsychiatric illness after 6 months, including 17% with new-onset anxiety disorder and 14% with new-onset depression [2]. Etiologies include central inflammation, delirium, post-intensive care unit syndrome, cerebrovascular accidents, and psychosocial stress.

Dr. Mazza recently showed that "COVID depression" may be particularly responsive to SSRIs, suggesting that these drugs may have a role in reducing the substantial morbidity of post-COVID neuropsychiatric syndromes [3]. Serotonin reuptake inhibitors (SRIs) have manifold effects

on human physiology, including anti-inflammatory and neurorestorative effects in some studies [4]. Some SRIs have secondary molecular targets, such as the sigma-1 receptor, which motivated our repurposing of fluvoxamine (a strong activator of this receptor) for acute COVID-19.

More studies are needed to confirm and extend the findings of Mazza et al. [1] in COVID-depression and other neuropsychiatric manifestations of this disease.

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Declarations

Conflict of interest Dr. Reiersen and Dr. Lenze are listed on a patent application related to methods of treating COVID-19 that was filed by Washington University in St. Louis. Dr Facente has no conflicts of interest that are directly relevant to the content of this letter.

Funding The original article this letter relates to was supported in part by a gift to the Keck School of Medicine of the University of Southern California by the W.M. Keck Foundation.

Author contributions AMR and EJJ prepared the reply. All authors read and approved the reply.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent to publish Not applicable.

Availability of data and material Not applicable.

Code availability Not applicable.

This comment refers to the article available online at <https://doi.org/10.1007/s40265-021-01636-5>.

This reply refers to the comment available online at <https://doi.org/10.1007/s40265-022-01682-7>.

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