

Letter to the Editor: The Link Between Covid-19-Induced Mental Health Complications And Microbiota Can Exist

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There have been recent reports of mental complications caused by COVID-19. Scientific evidence, on the one hand, tells about the effect that COVID-19 has on mental health directly, as well as the indirect effect that COVID-19 has on people in quarantine, with mental health problems and health care personnel¹.

To the extent that mental health complications are associated with alterations in the synthetic pathways of dopamine and serotonin, it has been hypothesized that this alterations may be related to the pathopsychology of COVID-19². Explaining this influence has been suggested to cause defective expression of the ACE2 gene induced by SARS-CoV2, which may be paralleled by DDC (Dopa Decarboxylase) dysfunction³.

At the same time, research and observation have shown that COVID-19 also causes fatal changes in the intestinal microbiota, especially in elderly patients⁴.

Discussions about the connection between microbiota and mental health complications have been going on for a long time. There is more or less agreement on the existence of gut-brain axis in the scientific community: when a substance produced by bacteria in the gut can cross the blood-brain barrier and induce NMDA-glutamate receptor modulation⁵, which in turn trigger the activation of dopaminergic systems. There are experimental data when application of gut-derived substance produced in animals causes behaviors similar to both epilepsy and autism⁶.

It is known that in human microbiota, due to certain evolutionary conditions, one of the dominant places among bacteria is occupied by Clostridium species. This seems to be related to the change (impoverishment) of the diet of the immediate human ancestor about 7-13 million years ago⁷.

Clostridium produces various neurotoxic substances, among which most interesting is a p-cresol. This toxin, can cross the blood-brain barrier and through inhibition of dopamine beta-hydroxylase affect on dopamine receptors in different areas of the brain⁸.

In addition, there are data on the association of epilepsy, Parkinson's, and intestinal microbiota in the elderly, when a reduction / regulation of intestinal microbiota volume has led to positive shifts in health⁹. There are also frequent reports when dietary changes have a positive effect on weakening epilepsy and autism behaviors in patients.

Consequently, it is quite possible that there is a direct link between the microbiota change induced by Covid-19 and the mental dysfunction induced by COVID-19. This suggestion is additionally supported by the recent findings that *Clostridioides difficile* infection frequently complicates COVID-19¹⁰. Clearly, this requires further experimental/observational research, however, it can be assumed that one of the ways to treat mental dysfunction caused by COVID-19 can occur through microbiota regulation.

References

1. Adhanom Ghebreyesus T. Addressing mental health needs: an integral part of COVID-19 response. *World Psychiatry*. 2020;19(2):129–130.
2. L. Attademo, F. Bernardini. Are dopamine and serotonin involved in COVID-19 pathophysiology? *Eur J Psychiatry*. 2021 January-March; 35(1): 62–63. Published online 2020; Oct 29. doi: 10.1016/j.ejpsy.2020.10.004.
3. Nataf S. An alteration of the dopamine synthetic pathway is possibly involved in the pathophysiology of COVID-19. *J Med Virol*. 2020; doi: 10.1002/jmv.25826.
4. Gu S, Chen Y, Wu Z, et al. Alterations of the Gut Microbiota in Patients With Coronavirus Disease 2019 or H1N1 Influenza. *Clinical Infectious Diseases*. 15 November 2020; 71(10):2669–2678, <https://doi.org/10.1093/cid/ciaa709>.
5. Appleton J. The Gut-Brain Axis: Influence of Microbiota on Mood and Mental Health. *Integr Med (Encinitas)*. 2018;17(4):28-32.
6. Tevezadze G, Nanobashvili Z, Zhuravliova E, et al. Effects of a Gut Microbiome Toxin, p-Cresol, on the Susceptibility to Seizures in Rats. *Neurophysiology*; November 2018: 50(6).
7. Moeller AH, Li Y, Ngole EM, et al. Rapid changes in the gut microbiome during human evolution. *PNAS*. November 18, 2014; 111(46):16431-16435, first published November 3, 2014; <https://doi.org/10.1073/pnas.1419136111>.
8. Tevezadze G, Zhuravliova E, Barbakadze T, et al. Gut neurotoxin p-cresol induces differential expression of GLUN2B and GLUN2A subunits of the NMDA receptor in the hippocampus and nucleus accumbens in healthy and audiogenic seizure-prone rats. *AIMS Neurosci*. 2020; 7(1):30–42.
9. Castillo-Álvarez F, Marzo-Sola ME. Role of the gut microbiota in the development of various neurological diseases. *Neurologia (Barcelona, Spain)*. 2019 Jul. DOI:10.1016/j.nrl.2019.03.017.
10. Granata G, Bartoloni A, Codeluppi M, et al. The Burden of *Clostridioides Difficile* Infection during the COVID-19 Pandemic: A Retrospective Case-Control Study in Italian Hospitals (CloVid). *J Clin Med*. 2020;9(12):3855. doi:10.3390/jcm9123855