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.

Brain, Behavior, and Immunity 87 (2020) 107–108

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Letter to the Editor

Potentially irreversible olfactory and gustatory impairments in COVID-19: Indolent vs. fulminant SARS-CoV-2 neuroinfection

To the Editor:

A recent study by Wu et al. (2020) discussed the neuroinvasive potential of SARS-CoV-2 on the premises of a lack of pathological evidence of definite CNS infiltration, and a predilection for what the authors termed as short-term effects on cerebral functions.

The authors' report is concise, and accurately identifies the scarcity of definitive laboratory evidence for SARS-CoV-2 CNS latency in the literature. There are, however, several aspects of SARS-CoV-2's neurotropism and its significance that are underrepresented in Wu et al' s study. A general outline of these aspects is: (a) consistent SARS-CoV-2 neurotropism, determined by potentially irreversible hypogeusia and reversible hyposmia preceding the onset of respiratory symptoms, (b) the report of at least one case of fulminant CNS disease in the literature, defined by an encephalopathic syndrome associated with the exclusive detection of SARS-CoV-2 RNA in the patient's cerebrospinal fluid (CSF) and (c) selection bias in case definition of SARS-CoV-2 associated CNS manifestations.

Specifically, a recent multicenter study has identified frequent (i.e. more than 80% of the cohort) gustatory and olfactory impairments in included patients. Notably, while olfactory symptoms were mostly self-limiting, gustatory dysfunction persisted after the resolution of the respiratory symptoms in more than 70% of the patients (Lechien et al., 2020). Despite not being a constellation of symptoms exclusive to SARS-CoV-2 infection, hypogeusia and hyposmia are recurrent features of COVID-19 even in retrospective studies, where these symptoms were incidentally rather than systematically documented (Bénézit et al., 2020). These very studies support the concept of indolent SARS-CoV-2 neurotropism as part of COVID-19's natural history, with a nevertheless persistent and significant impairment to neuronal function.

Conversely, the case for fulminant neuroinfection is illustrated in the very first case report of SARS-CoV-2 associated encephalitis by Moriguchi and colleagues, where RT-PCR detected SARS-CoV-2 RNA in the patient's CSF, despite a lack of its detection in the nasopharygeal swab specimen (Moriguchi et al., 2020).

In their study, Wu and colleagues correctly identify a gap of knowledge in our current understanding of SARS-CoV-2's interaction with neurons. The point they raise however also illustrates, by extent, the importance of recognizing mild manifestations of neurotropism in the clinical setting, such as gustatory and olfactory impairment. This point is further exemplified in the studies of Lechien et al. (2020) and Bénézit et al. (2020), where hypogeusia and hyposmia were detected below at 5% retrospectively and more than 80% of the respective cohorts prospectively. In a similar manner, Moriguchi et al.'s (2020) case report indicates that even a fulminant SARS-CoV-2 neuroinfection may escape current case definitions. Taken together, these reports point toward a needed paradigm shift in study design, in order to properly document and phenotype the extent of SARS-CoV-2′s neuroinvasive potential, as well as its possible future consequences.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable/Single Author.

Availability of data and materials

Not applicable.

Funding

No funding source.

Author contributions

Single Author.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

To Dr Maria Chatzi MD, for her steadfast guidance in an ER room.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2020.04.071.

https://doi.org/10.1016/j.bbi.2020.04.071
Received 23 April 2020; Received in revised form 25 April 2020; Accepted 26 April 2020
Available online 27 April 2020

References

Wu, Y., Xu, X., Yang, L., Liu, C., Yang, C., 2020. Nervous system damage after COVID-19 infection: presence or absence? Brain Behav. Immun. https://doi.org/10.1016/j.ijid.2020.03.062.

Lechien, J.R., Chiesa-estomba, C.M., De siati, D.R., et al., 2020. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur. Arch. Otorhinolaryngol. https://doi.org/10.1007/s00405-020-05965-1.

Bénézit, F., Le turnier, P., Declerck, C., et al., 2020. Utility of hyposmia and hypogeusia for the diagnosis of COVID-19. Lancet Infect. Dis. https://doi.org/10.1016/S1473-3099(20)30297-8.

Moriguchi, T., Harii, N., Goto, J., et al., 2020. A first Case of Meningitis/Encephalitis associated with SARS-Coronavirus-2. Int. J. Infect. Dis. https://doi.org/10.1016/j.ijid.2020.03.062.

George D. Vavougios[a,b,c,*]

[a] *Department of Neurology, Athens Naval Hospital, Athens, Greece*

[b] *Scientific Research Associate, Department of Respiratory Medicine, University of Thessaly, Larisa, Greece*

[c] *Postdoctorate Research Fellow, Department of Computer and Electrical Engineering, Volos, Greece*

E-mail address: dantevavougios@hotmail.com.

* Address: 70 Deinokratous Street, Athens 11125, Greece.