Received: 14 July 2021 | Accepted: 3 August 2021

DOI: 10.1002/alz.12460

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

AUTHOR REPLY

Reply to "Post-COVID 19 neurological syndrome: A new risk factor that modifies the prognosis of patients with dementia"

We thank Dr. Lozada et al. for their commentary. We agree that our findings demonstrated clearly the significant increased risk for COVID infection and for poor outcomes for patients diagnosed with dementia compared to those without a diagnosis of dementia, even after controlling for demographics, and demonstrated COVID-19 factors including hypertension, obesity, cardiovascular disease, diabetes, and congregant living, among others.[1] We find the mechanism for this increased risk suggested by Dr. Lozada et al. entirely plausible. However, our study, by itself, identifies associations and cannot be used to infer causation.

We do, however, have evidence that supports the concept that inflammation is important in the pathogenesis of Alzheimer's disease (AD). Tumor necrosis factor (TNF) is a major component of the hyperinflammatory response in COVID-19.[2] Anti-inflammatory therapy with TNF antagonists was shown to delay or prevent AD in populations treated for systemic inflammatory disorders including rheumatoid arthritis.[3] COVID-19-mediated inflammatory responses may contribute to the pathogenesis of AD and dementia, and therefore it is also important to track new diagnoses of dementia including AD among survivors of COVID-19.

We strongly agree that further studies should be undertaken to define the mechanism and progression of neurodegenerative disease promoted by neurotropic viruses such as SARS-CoV2. The concept of an infectious etiology of AD has been postulated for years.[4] The COVID-19 pandemic offers a real opportunity and a large-scale experiment of nature for researchers to investigate whether and how SARS-CoV2 viral infection triggers new onset of AD in COVID-19 survivors. Future studies could include follow-up real-world informatics studies on large populations, prospective cohort studies where it is possible to collect specific information in a more uniform manner longitudinally to test specific hypotheses, and possibly studies of pathology as samples become available. It will be important to identify demographic risk factors as well as biologic risks such as inflammatory diseases, and to develop protective strategies for the most vulnerable populations. We agree that long-term follow-up is essential. Indeed, in our large-scale population study using informatics analytics, we intend to follow up the long-term impact of COVID-19 on populations diagnosed with dementia.

ACKNOWLEDGMENTS

This work was supported by NIH National Institute of Aging (grant numbers AG057557, AG061388, AG062272) and The National Center for Advancing Translational Sciences the Clinical and Translational Science Collaborative (CTSC) of Cleveland (grant number UL1TR002548-01).

CONFLICTS OF INTEREST

Pamela B. Davis has served as a consultant for Trinity College, Dublin, Ireland, participated on the University of Chicago External Advisory Board, served as member of the board of directors of BioEnterprise, Cleveland OH, and member of the board of directors of Judson Foundation, Cleveland OH. QuanQiu Wang and Rong Xu have no outside interests to declare.

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