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Reply to: Neurological, Cognitive and Behavioral Disorders During COVID-19: The Nitric Oxide Track

To the Editor: We read with great interest the letter of Annweiler et al.[1] They propose an intriguing mechanism for cognitive impairment related to coronavirus disease 2019 (COVID-19). We would like to clarify a couple of points related to our case. First, although we wanted to exclude COVID-19 encephalitis as a possibility, this was not possible without cerebrospinal fluid analysis and magnetic resonance imaging, which was refused by our patient. Our patient fulfilled the Confusion Assessment Method criteria for delirium on admission, which was our working diagnosis.[2] In fact, the rapid improvement in his cognitive function might argue against COVID-19 encephalitis. Second, our patient's usual medication included lisinopril, an angiotensin-converting enzyme 2 inhibitor, for treatment of hypertension in the context of diabetes mellitus, type II. Possibly, the mechanism proposed by Annweiler et al[1] pertaining to the nitric oxide track could explain the rapid improvement in our patient's cognition following just a brief period of supportive management.

It is important to emphasize that delirium is a heterogeneous entity caused by multiple causative factors and complex underlying pathogenesis.[3-5] In fact, nitric oxide has long been implicated in the pathogenesis of delirium and cognitive impairment.[6,7] Whether the nitric oxide track will prove to have a central role in the acute manifestations of COVID-19–related cognitive impairment remains to be seen. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection could activate multiple downstream molecular pathways affecting each individual distinctly.[7] We propose that the underlying mechanism of COVID-19 central nervous system manifestation or delirium depends on the interaction between SARS-CoV-2 activated molecular pathways and the individual related factors, including age, COVID-19 severity, individual's underlying genetic susceptibility, vascular risk factors, premorbid cognitive function, use of certain medication, and comorbidities.

Several other mechanisms have been linked to COVID-19 neurological and cognitive manifestations.[8,9] However, the retrospective design of the study by Mao et al limits our ability to infer the causal mechanism of cognitive decline in COVID-19 patients.[8] We propose possible mechanisms of COVID-19–related cognitive dysfunction (Table 1), which could help researchers in studying the specific pathways associated with each possible mechanism. Finally, the core message of our study is for clinicians to proactively screen for delirium in hospitalized older adults.[10] Once delirium is identified, a comprehensive individualized assessment should

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Table 1 Possible mechanisms of COVID-19–related cognitive dysfunction

Indirect CNS involvement through inflammatory or immune response
Viral encephalitis due to direct CNS invasion
COVID-19–related organ failure (lung, heart, kidney, or vasculature) and metabolic dysfunction
COVID-19 ICU-related delirium
Large-vessel stroke or lacunar stroke syndrome
Exacerbation or unmasking of underlying cognitive impairment or neurodegenerative process
Medication-related adverse reaction
Other unknown mechanism

Abbreviations: CNS, central nervous system; COVID-19, coronavirus disease 2019; ICU, intensive care unit.

be pursued, including COVID-19 testing during this pandemic.[10]

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Addressing Hearing Loss to Improve Communication During the COVID-19 Pandemic

To the Editor: Change occurs quickly in emergencies. The coronavirus disease 2019 (COVID-19) response has resulted in rapid modifications in healthcare delivery. Home-based medicine and telemedicine are swiftly evolving and being promptly deployed, as is in-room videoconference technology for inpatients. Necessary precautions, including distancing and personal protective equipment (PPE), have become the norm.[1,2] Importantly, these changes may exacerbate communication barriers faced by persons with hearing loss.

Hearing loss affects half of all adults older than 60 years.[3] However, little consideration is given to addressing hearing loss for effective communication.[4,5] Hearing loss limits communication via poor auditory encoding of speech signals, resulting in reduced clarity of speech. Cognitive processing, especially working memory, may also be impacted as adults with hearing loss attempt to make sense of poor signals. The stressful, busy, and noisy hospital[6] environment exacerbates problems, leading to limited treatment understanding and increased frustration.

Importantly, poor communication may mediate the association between hearing loss and health outcomes. Adults with hearing loss have increased risk of 30-day readmission, experience longer length of stay, and are less satisfied with care.[7,8] Moreover, hearing loss is associated with poor functional recovery following intensive care unit admissions.[9] Sensory deprivation may increase risk to experience delirium as older adults are cut off from communication and their environment.

The current extended use of PPE during the COVID-19 pandemic limits visualization of the mouth, preventing lipreading, and acts as a general sound barrier. Even when using videoconferencing equipment, lag and poor image quality may cause significant visual barriers. Coupled with noisy hospital environment (e.g., alarms and constant communication among staff), these visual barriers render the natural sensory substitution compensation methods used by adults with hearing loss as futile. Additionally, distancing may limit access to caregivers or interpreters (American Sign Language) to facilitate conversations during visits.

Thoughtful consideration of addressing barriers is needed (Figure 1). In the outpatient and telehealth setting,

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