Response to Letter Regarding Article, “Sleep Fragmentation, Cerebral Arteriolosclerosis, and Brain Infarct Pathology in Community-Dwelling Older People”

We thank Dr Kawada for his interest in our study, which showed that sleep fragmentation is associated with postmortem evidence of arteriolosclerosis and subcortical infarcts. We collected objective measures of sleep fragmentation in the community-setting from more than a 1000 older participants in the Rush Memory and Aging Project—a volunteer cohort in which all participants agree to brain donation on death and in which the autopsy rate is $\approx 90\%$. Because this was a selected cohort, we agree that it will be important to replicate these findings in more diverse populations.

Residual confounding and ambiguity on causality are limitations of all observational cohort studies. Nonetheless, our novel brain autopsy results from a large number of well-characterized older adults will allow the field to refine hypotheses for experiments and clinical trials that will provide more unambiguous delineation of causality.

Although, we have previously shown that kRA, a sleep fragmentation metric derived from actigraphy that roughly corresponds to the probability per 15-second epoch of having a movement after a sustained period of rest (ie, sleep), is correlated with standard polysomnographic metrics of sleep fragmentation, we agree that sleep fragmentation whether measured by actigraphy or polysomnography may be because of many causes. Moreover, sleep fragmentation can accompany common causes of sleep and circadian disruption, such as sleep apnea that affect millions of older Americans. Further studies concurrently collecting multiple sleep and circadian metrics from well-characterized older adults and combining this with brain tissue measures are essential to elucidate the mechanisms, which link sleep and circadian disruption to brain health in older adults.

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Disclosures

None.

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