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LETTERS TO THE EDITOR

Time to regroup and redirect? Sleep fragmentation and hypoxia may not be where we should focus our efforts in looking for causal pathways to cognitive deficits in OSA

Response to Lajoie AC, Kaminska M. Cognitive profiles in obstructive sleep apnea and their relationship with intermittent hypoxemia and sleep fragmentation. *J Clin Sleep Med*. 2021;17(2):337. doi:10.5664/jcsm.8910

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The Letter to the Editor by Lajoie and Kaminska[1] in response to our article[2] was thought-provoking. The authors make 2 astute points about our analysis that, if carried out, may have led to a more defined picture of the relationship between nocturnal symptoms of obstructive sleep apnea (OSA) and the cognitive profiles that emerged. They state that (1) assessing hypoxemia with multiple measures may have provided a more precise understanding of how hypoxemia impacts cognition (eg, CT90) and (2) using scoring criteria that exclude hypopneas with an associated oxygen desaturation from the apnea-hypopnea index and retaining hypopneas with an associated arousal may have further elaborated the role of sleep fragmentation in cognitive dysfunction.

Our response to their comments is 2-fold. While, substantively, we agree with the authors and encourage this further analysis, for the paper we wrote we aimed to explore if profiles were present and replicable in disparate samples. To this end, we used measures of hypoxemia and sleep fragmentation available in both the clinic and community samples. As these samples demonstrated the same 3-profile solution in clinic and community samples of individuals with OSA, this indicates strong statistical support for these disparate profiles. With this groundwork, it is now possible to build upon these analyses with further explorations of these relationships using different measures of hypoxemia and sleep fragmentation. Such additional analysis would have required post hoc exploration of secondary hypoxemia parameters in just one of the samples. We would not be comfortable taking such an approach.

Second, although Lajoie and Kaminska make considered recommendations of ways to parse out hypoxemia and sleep fragmentation, we take the view that perhaps it is time for us to redirect our efforts. Hypoxia and sleep fragmentation may not be the best focus for exploring causal pathways to cognitive deficit in OSA. While sleep fragmentation and hypoxemia certainly impact the body and health, other factors may be more directly involved in leading to cognitive change. The field needs to consider a range of OSA factors that have seen little or no consideration, such as the longevity of disease and the downstream effects of long-standing undiagnosed or untreated OSA on, for example, intrathoracic pressure changes exacerbating poor glymphatic clearance and, ultimately, metabolite build-up,[3] increased inflammation,[4] cerebrovascular and cardiovascular damage,[5] and eventually, detrimental brain changes to areas including the raphe nucleus,[6] which lead to the cognitive impairment witnessed. Certainly, after 20 years of research on cognition and OSA, and now 5 years after a defined cognitive profile, we are in a position to now identify causal pathways to cognitive damage. It is time to direct greater precision to capturing these aspects of cognitive harm through transcranial Doppler sonography or functional magnetic resonance imaging of cerebrovascular changes, assessments of amyloid β in cerebrospinal fluid, and the development of ways to measure length of exposure to disease in OSA in order to more directly capture factors that may lead to cognitive impairment in OSA.

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REFERENCES

1. Lajoie AC, Kaminska M. Cognitive profiles in obstructive sleep apnea and their relationship with intermittent hypoxemia and sleep fragmentation. *J Clin Sleep Med*. 2021;17(2):337.
2. Olaithe M, Pushpanathan M, Hillman D, et al. Cognitive profiles in obstructive sleep apnea: a cluster analysis in sleep clinic and community samples. *J Clin Sleep Med*. 2020;16(9):1493–1505.
3. Ju YE, Finn MB, Sutphen CL, et al. Obstructive sleep apnea decreases central nervous system-derived proteins in the cerebrospinal fluid. *Ann Neurol*. 2016;80(1):154–159.
4. Kheirandish-Gozal L, Gozal D. Obstructive sleep apnea and inflammation: proof of concept based on two illustrative cytokines. *Int J Mol Sci*. 2019;20(3):459.

5. Prilipko O, Huynh N, Thomason ME, Kushida CA, Guilleminault C. An fMRI study of cerebrovascular reactivity and perfusion in obstructive sleep apnea patients before and after CPAP treatment. *Sleep Med.* 2014;15(8):892–898.
6. Andrade AG, Bubu OM, Varga AW, Osorio RS. The relationship between obstructive sleep apnea and Alzheimer's disease. *J Alzheimers Dis.* 2018;64(Suppl 1):S255–S270.

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All authors have seen and approved the manuscript. Work for this manuscript was performed at the University of Western Australia. The authors report no conflicts of interest.