



## REPLY

## Reply to Hunasikatti commentary: Reinventing polysomnography in the age of precision medicine-Not at cost of discarding the hard data



We heartily thank Dr. Hunasikatti for his letter [1] that conveys his interest in our technical review [2] and for highlighting several relevant discussion topics.

Obstructive sleep apnea (OSA) is a highly heterogeneous disorder with different subtypes, thus fundamentally, our message is to supplement the apnea hypopnea index (AHI) with the abundance of information that can be obtained from the polysomnogram (PSG) to identify OSA subtypes. Dr. Hunasikatti highlights studies where the AHI can be informative when studying OSA. To better understand the heterogeneity of OSA we need multidimensional data, including data that can be acquired using tools described in our review [2]. Ultimately, the goal is to assist clinicians practice precision sleep medicine for the individual from the assessment to management of OSA.

Current OSA treatment management is largely a “one-size-fits-all” approach with positive airway pressure (PAP) as the primary therapy [3]. We envision that with better characterization of the heterogeneity of OSA, therapies such as mandibular advancement devices, medications and hypoglossal nerve stimulators would become primary therapies in certain individuals, based on their OSA subtype. For example, a patient with low hypoxic burden, very high arousal index and insomnia symptoms may have more fragmented sleep if treated with PAP only, but if arousal threshold reducing medications (with or without PAP) were used we could reduce sleep fragmentation. The benefit of using subjective (e.g., symptoms from questionnaires) and objective (e.g., novel and conventional PSG biomarkers) data to inform OSA management is minimization of trial and error selection of an appropriate therapy and hopefully improve clinical outcomes.

We agree with Dr. Hunasikatti that the role of wearable technology to characterize OSA is an important part of precision sleep medicine [4,5]. Today, many different systems and technologies are available such as apps on smartphones, smartwatches, wearables, and contact-free recording of sleep and sleep disorders. As the signal quality of these systems are improving quickly, we anticipate in the near future they will provide cost-effective and convenient ways to screen for OSA. Another benefit of wearables is providing valuable longitudinal data that dynamically accounts over time for an individual's age, body-mass index, newly diagnosed co-morbidities and medications.

In addition to using more information from the PSG, the sleep field needs to formalize a platform that integrates non-PSG data to better characterize OSA heterogeneity. Additional data to

integrate into this platform include symptoms [6], structural biomarkers (e.g., physical exam [7] and radiological exams [8]), molecular biomarkers (e.g., genomic, transcriptomic, proteomic and metabolomic profiles) and wearable technology. Collectively, this multidimensional data could be used to predict individual future risk of known OSA consequences (e.g., cardiovascular, neurodegenerative, cancer or metabolic diseases).

In conclusion, we agree with Dr. Hunasikatti that the AHI is part of multidimensional data that better characterizes an individual's OSA subtype. As scientists around the world elicit which symptoms, structural, molecular, and physiological biomarkers are significant, we will have more data to understand OSA heterogeneity. Lastly, but most importantly, more trained physician-scientists are needed to determine the clinical relevance of these biomarkers and support their implementation into routine practice.

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