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## In Response

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Response to Letter to the Editor on "Best Practices for Postoperative Brain Health: Recommendations From the Fifth International Perioperative Neurotoxicity Working Group".

Miles Berger, Martin S. Angst, Deborah J. Culley, Catherine E. Price, David A. Scott, Robert A. Whittington, Roderic G. Eckenhoff for the Perioperative Neurotoxicity Working Group

We thank Dr. Sinclair for his comments<sup>1</sup> on our recent article "Best Practices for Postoperative Brain Health: Recommendations From the Fifth International Perioperative Neurotoxicity Working Group".<sup>2</sup> We understand Dr. Sinclair's frustration that we could not make more definitive practice recommendations, as the current state of knowledge does not

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allow making firmer, evidenced-based recommendations. We faced a tension between the limits of our current knowledge, versus the preference of practicing clinicians to have firm guidance on what to do when caring for older adults. Our article represents our best attempt to provide guidance to practicing clinical anesthesiologists, while not going beyond the extent of published evidence and/or advice that makes intuitive sense based on first principles (such as monitoring the brain during anesthesia, since the brain and CNS are the target organ of most if not all sedative/hypnotic anesthetic agents). However, an important contribution of our Best Practices Paper<sup>2</sup> is to document such limitations and provide directions for the research that should be done to produce more specific guidelines.

We also agree with Dr Sinclair's point that there are multiple delirium screening instruments, including the AWOL instrument.<sup>3</sup> Further research should help determine which delirium screening instruments have the highest sensitivity, specificity and take the least time for use in the perioperative environment.

Dr. Sinclair's third point centers on the evidence basis for the age-associated decline in MAC; he correctly notes that published studies (to date) and meta-regression analyses of age dependent changes in MAC have only included 80-some patients over age 65. However, the slope for the age dependent change in MAC are actually based on a much larger sample size of patients both younger and older than age 65, and the slope of this age dependent decline in MAC of ~6–7% does not substantially change when excluding patients over age 65. As discussed in the first paragraph above, our recommendation that clinicians should monitor age-adjusted MAC fraction is based on the best currently available evidence for how inhaled anesthetic dosage requirements change with age. Nonetheless, we agree that it would be helpful for the field to have more data on MAC requirements in older adults, on the underlying mechanistic basis for the age-dependent change in MAC, and on the extent to which MAC changes with age itself versus with disease processes and/or conditions that themselves increase in frequency with age (such as neurodegenerative diseases and/or frailty).

Lastly, while Dr. Sinclair notes that his clinical experience has been that elderly patients often have low BIS values and low MAC fractions, clinicians (at least at one of our institutions) do not fully reduce inhaled anesthetic dosage in older adults in accord with known age-dependent decreases in MAC.<sup>4</sup> Further, BIS values actually increase with age, even in response to increasing age-adjusted end tidal MAC fractions.<sup>4</sup>

## **Acknowledgments**

In closing we thank Dr. Sinclair for his interest in our work, and we hope future research will provide more definitive evidence-based recommendations for promoting postoperative brain health for older adults, an important ASA Brain Health Initiative goal.

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