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Too little or too much anesthesia: Age paradox of electroencephalogram indices

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Editorial

Too little or too much anesthesia: Age paradox of electroencephalogram indices

A patient's age affects all aspects of the perioperative continuum, [1] and excessively deep anesthesia in elderly patients is associated with postoperative cognitive dysfunction and delirium. In the search for the optimal perioperative treatment leading to enhanced recovery after surgery (ERAS) [2–4], emerging data indicate that quantitative indices such as electroencephalogram (EEG)-guided anesthesia may play a potential role in anesthetic depth monitoring [5]. Accumulating evidence suggests, but does not yet conclude that anesthetic delivery titrated with EEG acquisition devices reduces the incidence of postoperative cognitive dysfunction/delirium [6–10].

The ageing human brain changes both structurally and neurophysiologically over the years. The cortex thins, skull conductance decreases, and the cerebrospinal fluid volume increases. These changes presumably attenuate EEG amplitude and coherence [11]. In fact, older age is associated with significant spectral and entropic changes under general anesthesia, with a predominant shift of the EEG activity pattern towards higher frequencies, with more irregular and oscillatory components [12]. Given that EEG signals change with age, it may be conceivable that these changes have critical implications for the utility of EEG-guided indices—especially in the elderly. However, currently available commercial devices/indices are not age-adjusted, and are rather derived heuristically and validated with a database deriving from a young and healthy population [13]. Moreover, the target range thresholds for EEG acquisition devices were constructed under the assumption that a similar index range defines an equivalent anesthetic state—irrespective of the patient's age.

In a recent study published in the *Journal of Clinical Anesthesia*, Obert and colleagues addressed this significant gap using post-hoc observational analysis [14]. The authors evaluated and compared the effect of age on the neuromonitoring indices of commercially available devices—the bispectral index (BIS), the Response Entropy/State Entropy (RE/SE), the qCON/qNOX (Quantium Medical, Barcelona, Spain), the Triton Brain Activity Index (AI; Triton Electronic Systems Ltd. Ekaterinburg, Russia), and the Narcotrend index. In 180 adult patients who received propofol-sevoflurane anesthesia, the dependency of the indices on age was investigated by linear regression analysis and the findings were presented elegantly in a graphical format for each monitor. The authors report an increase of around 0.2 index points per year for the BIS, qCON/qNOX, and SE/RE—implying that the observed effect of age on indices can be associated with varied target ranges for adequate anesthesia. For instance, the BIS device is probably most familiar in intraoperative settings and is normally targeted between 40 and 60 for awareness prevention.

Let us say, for argument's sake, that in a 70-year-old individual, a modest shift to the right with an approximate increase of 10 points or more in both upper and lower limits might be expected. In other words, elderly patients paradoxically display higher EEG thresholds. The authors caution that targeting the familiar operating range of EEG indices in the elderly population would likely result in inappropriately high anesthetic delivery and may lead to harm.

This finding adds an intriguing layer to our understanding of the need to consider age-corrected target ranges for EEG indices in vulnerable patients—or to explore parameters that are independent of age. One difficulty is the need for rapid calculation of 0.2 index points change per year from the reference age. Another caveat is the practicability with concomitant anesthetics—such as ketamine and dexmedetomidine since they trigger varied EEG patterns. As such the current observation is limited to anesthesia with propofol and sevoflurane only. Another conclusion is that the practical application from this observation may be restricted to awareness prevention while other applicability such as prevention of movement or autonomic surgical responses are limited due to the fact that the authors did not evaluate EEG characteristics during surgical stimulation.

These findings provoke a sense of “déjà vu”. Not that long ago, age-adjusted minimum alveolar concentration (MAC) was introduced with an adjustment factor of 6–7% per decade, which nowadays is automatically computed by a gas analyzer. Although the effect of age on MAC is fundamentally different from the effect of age on EEG indices, a recent study found that elderly patients were shown to have higher BIS values, despite increasing anesthetic delivery [15]. Since all patients in the presented cohort were anesthetized at age-adjusted 0.9 MAC, we might assume that the higher observed EEG indices are indicative of age-dependent changes [14]. As one might expect, with rising age-adjusted MAC, the EEG indices would fall. Interestingly, in the present study, the authors did not observe any significant increase or decrease of age-adjusted MAC with age across all indices. It is also possible that a relative overdose of anesthetics occurred, because the clinicians were titrating anesthetics based on relatively higher EEG indices. Obert and colleagues also performed a correlation analysis between the indices and revealed a strong positive correlation between BIS, SEF, qCON, and SE with the patient's age. It is certainly difficult to titrate anesthetics based on just one modality, and no currently available indices reliably detect awareness. However, current research raises concerns over the possibility of anesthetic overdose in the vulnerable elderly population with conventional titration methods. Maybe the complete solution lies in a “context-sensitive” or “individualized indices” approach.

We still do not know to what extent these age-dependent changes in EEG indices affect actual clinical outcomes, and the investigation by Obert reveals that more evidence is required. Two recent investigations—“ENGAGES” and “Balanced Study”—suggest that the clinical

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outcome is not different when elderly patients are exposed to light or deep anesthesia [6,7]. Overall, perioperative clinical outcomes are likely to remain related to baseline risk factors. If age-related indices demonstrate clinical benefits in an elderly population, wide applicability of age-corrected technology in the next generation of depth-of-anesthesia monitors appears plausible. We assume that the age-corrected EEG indices will translate to improved clinical outcomes. New target-processed EEG parameters will be required in the future to provide adequate age-adjusted anesthesia.

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