Does the use of processed EEG monitoring (i.e. depth of anesthesia monitoring) during general anesthesia reduce the risk of post-operative delirium?

Processed EGG may have a role in reducing the risk of delirium and other neuro-cognitive outcomes by allowing anesthesiologists to target specific depths of anesthesia, reducing exposure to anesthetic agents (1). Processed EEG (BIS) has good evidence for the improvement of drug delivery and emergence, as well as the prevention of awareness, but its utility in preventing post-operative delirium is less clear (1).

The most significant review of the subject remains the 2018 Cochrane review, which included six randomized controlled trials and 2929 participants examining processed EEG or evoked-potential indices-guided anesthesia alongside usual-care anesthesia (1). The primary outcomes were the occurrence of postoperative delirium and post-operative cognitive dysfunction. The review concluded there was moderate quality-evidence to suggest that EEG could reduce the risk of delirium in patients over 60 after non-cardiac from 21.3% to 15.2% (NNT 17) and non-neurological procedures, and evidence that post-operative cognitive dysfunction was reduced at three months from 9.1% to 6.4% (NNT 38). Notably, however, the was little to no evidence that processed EEG reduced length of stay or post-operative all-cause mortality, both important sequelae of post-operative delirium. Several important limitations include the exclusion of patients under the age of 60, heterogeneity the lack of blinding of anesthesia providers and incomplete data outcome in three of the included studies.

Since 2018, several further studies have been published exploring this question. ENGAGES, published in 2019, is an RCT of 1232 patients aged 60 or older comparing the use of processed EEG to usual anesthetic care; the study notably stratified on both cardiac surgery and a history of falls as both are known risk factors for post-operative delirium and potential confounders (2). No difference in post-operative delirium was found between study arms. ENGAGES has been criticized for the relatively minimal difference in amount of administered anesthetic between arms and a lack of published BIS values, suggesting a possible bias toward the null hypothesis (3).

A 2021 sub-study within the BALANCED trial, an RCT looking at the effect of processed EEG and anesthetic depth on a wide variety of perioperative outcomes, compared a targeted depth of 35 (deep anesthesia) to 50 (light anesthesia) on the effect of post-operative delirium and longer-term cognitive outcomes in 515 patients (4,5). The BALANCED substudy found a reduction of post-operative delirium from 28% in the deep anesthesia group to 19% in the light anesthesia group (NNT 11) (5).

Some studies have restricted their scope to particular procedures. STRIDE is a 2018 study comparing light to heavy propofol sedation during hip fracture repair (6); although the depth of sedation was primarily observer-assessed, significant separation of the two groups by BIS values was noted (82 vs. 57) (6). While no difference in post-operative delirium was noted at the primary analysis, a secondary analysis suggested that patients with no comorbidities may benefit from the use of light sedation with respect to post-operative delirium. eMODIPOD was a 2021 study that looked at the use of SedLine in laparoscopic surgery in patients over the age of

50 receiving propofol-remifentanil anesthesia; no difference in incidence of post-operative delirium was found between groups(7).

In summary, there is low-to-moderate quality evidence that the use of processed EEG may reduce the risk of post-operative delirium. This is consistent with a mechanistic understanding that excessive doses of anesthesia may damage the brain through either a directly toxic effect (8) or augmenting the neuroinflammatory response to surgery (9). Recommendations for use of processed EEG have appeared in guidelines, however with recognition that there is limited evidence for its use. In studies where processed EEG has been found helpful, the NNT is relatively low, suggesting it may be beneficial in a reasonably large number of patients.

The recommendation of processed EEG use has multiple caveats. Its use in patients under 60 is generally not studied, although these patients are less likely to experience post-operative delirium. It is also not clear which patients may necessarily benefit from this: while many clinicians may select patients whose co-morbidities suggest they are at high risk of post-operative delirium, the STRIDE trial counterintuitively found benefit in patients with no comorbidities instead (6). While processed EEG has low risk of harm, it is a disposable monitor with an implementation cost and environmental impact. It is also unclear if it may allow for cost savings, such as reducing OR time or length of stay. Furthermore, many of these results are at risk of publication bias as there are many studies that have been registered with clinicaltrials.gov but have not completed or published, calling into the question of missing data (10). In addition to other anti-delirium measures, such as avoidance of benzodiazepines, adequate pain control, appropriate fluid administration and maintenance of sleep-wake cycles, processed EEG may provide an additional data point for the prevention of delirium.

Editor's Note: The current highest quality data does not convincingly support the use of pEEG to reduce post operative delirium risk. The fundamental tenants of prevention remain avoiding polypharmacy (including benzodiazepines and meds with central cholinergic activity), hypothermia, anemia, dehydration, sleep disruption, pain, and immobilization. Customized, multidisciplinary care team approaches for high risk individuals (such as the Hospital Elder Life Program) are likely to be of benefit.

References

- 1. Punjasawadwong Y, Chau-in W, Laopaiboon M, Punjasawadwong S, Pin-on P. Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults. Cochrane Database Syst Rev [Internet]. 2018;(5). Available from: https://doi.org//10.1002/14651858.CD011283.pub2
- 2. Wildes TS, Mickle AM, Abdallah A Ben, Maybrier HR, Oberhaus J, Budelier TP, et al. Effect of electroencephalography-guided anesthetic administration on postoperative delirium among older adults undergoing major surgery the engages randomized clinical trial. JAMA J Am Med Assoc. 2019;321(5):473–83.

- 3. Evered L, Atkins K, Silbert B, Scott DA. Acute peri-operative neurocognitive disorders: a narrative review. Anaesthesia. 2022;77(S1):34–42.
- 4. Short TG, Campbell D, Frampton C, Chan MT V, Myles PS, Corcoran TB, et al. Anaesthetic depth and complications after major surgery: an international, randomised controlled trial. Lancet (London, England) [Internet]. 2019;6736(19):1–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31645286
- 5. Evered LA, Chan MTV, Han R, Chu MHM, Cheng BP, Scott DA, et al. Anaesthetic depth and delirium after major surgery: a randomised clinical trial. Br J Anaesth [Internet]. 2021;127(5):704–12. Available from: https://doi.org/10.1016/j.bja.2021.07.021
- 6. Sieber FE, Neufeld KJ, Gottschalk A, Bigelow GE, Oh ES, Rosenberg PB, et al. Effect of Depth of Sedation in Older Patients Undergoing Hip Fracture Repair on Postoperative Delirium: The STRIDE Randomized Clinical Trial. JAMA Surg. 2018;153(11):987–95.
- 7. Wang E, Wang L, Ye C, Luo N, Zhang Y, Zhong Y, et al. Effect of electroencephalography spectral edge frequency (sef) and patient state index (psi)-guided propofol-remifentanil anesthesia on delirium after laparoscopic surgery: The eMODIPOD randomized controlled trial. J Neurosurg Anesthesiol. 2021;00(00):1–10.
- 8. Culley DJ, Xie Z, Crosby G. General anesthetic-induced neurotoxicity: an emerging problem for the young and old? Curr Opin Anaesthesiol. 2007 Oct;20(5):408–13.
- 9. Vacas S, Degos V, Feng X, Maze M. The neuroinflammatory response of postoperative cognitive decline. Br Med Bull. 2013;106(1):161–78.
- 10. Evered LA, Goldstein PA. Reducing perioperative neurocognitive disorders (PND) through depth of anesthesia monitoring: A critical review. Int J Gen Med. 2021;14:153–62.