1 Perioperative Neurocognitive Disorders Defined

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Objective: Cognitive change affecting patients after anesthesia and surgery has been recognised for more than 100 yr. Research into cognitive change after anesthesia and surgery accelerated in the 1980s when multiple studies utilised detailed neuropsychological testing for assessment of cognitive change after cardiac surgery. This body of work consistently documented decline in cognitive function in elderly patients after anaesthesia and surgery, and cognitive changes have been identified up to 7.5 yr afterward. Importantly, other studies have identified that the incidence of cognitive change is similar after non-cardiac surgery. Other than the inclusion of non-surgical control groups to calculate postoperative cognitive dysfunction, research into these cognitive changes in the perioperative period has been undertaken in isolation from cognitive studies in the general population. This study aimed to develop similar terminology to that used in cognitive classifications of the general population for use in investigations of cognitive changes after anesthesia and surgery.
Participants and Methods: A multispecialty working group followed a modified Delphi procedure with no prespecified number of rounds comprised of three face-to-face meetings followed by online editing of draft versions. Two major classification guidelines [Diagnostic and Statistical Manual for Mental Disorders, fifth edition (DSM-5) and National Institute for Aging and the Alzheimer Association (NIA-AA)] are used outside of anesthesia and surgery and may be useful for the inclusion of biomarkers in research. For clinical purposes, it is recommended to use the DSM-5 nomenclature.
Results: The working group recommends that 'perioperative neurocognitive disorders (PND)' be used as an overarching term for cognitive impairment identified in the preoperative or postoperative period. This includes cognitive decline diagnosed before operation (described as neurocognitive disorder); any form of the acute event (postoperative delirium) and cognitive and functional decline diagnosed up to 30 days after the procedure (delayed neurocognitive recovery (dNCR)) and up to 12 months (postoperative neurocognitive disorder (postoperative NCD).1 Further, the working group has undergone a further Delphi process to expand these recommendations for research purposes which will also be covered.
Conclusions: Perioperative neurocognitive disorders are the most common complication for patients aged 65y or more undergoing anesthesia and surgery. Moreover, they are associated with significant morbidity, mortality, loss of functional independence and extreme economic costs. A multi-disciplinary approach to PND, including neuropsychologists, is critical to reducing and preventing these disorders. Evered L, Silbert B, Knopman DS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. Br J Anaesth 2018; 121: 1005-12

Categories: Aging
Keyword 1: delirium
Keyword 2: neurocognition
Keyword 3: memory disorders
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2 From Bench to Bedside: How Tau Protein is Altered by Perioperative Factors

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Objective: Postoperative neurocognitive disorder is common after all forms of surgery in older adults. The mechanisms are multifactorial, and probably require pre-existing neuropathology, whether the patient is symptomatic or not. In Alzheimer's disease (AD) and other tauopathies, the microtubule-associated protein tau can undergo aberrant hyperphosphorylation potentially leading to the development of neurofibrillary pathology, one of the neuropathological hallmarks of the disease. Preclinical and human CSF studies suggest that anesthesia and surgery elicits an increment in CNS tauopathy, which may accelerate any pre-existing neuropathology and produce a risk of delirium and the commonly reported changes in cognition.

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Participants and Methods: In this session, the author will present a bench to beside review of how tau protein is altered by perioperative factors and its potential relationship to the impairment of cognition after surgery and anesthesia. Published and ongoing studies will be reviewed to result in a discussion as to why changes in tau protein are concerning in perioperative disorders of cognition.
Results: The presenter will initially review pre-clinical studies focusing on the impact of anesthetics and surgery-induced inflammation on tau pathology and how the impairment of resolution of surgery-induced inflammation, notably decreased lipoxin A4 signaling, is altered by aging, gender, or an increase in the tau pathology burden. These preclinical studies have partially informed a multi-center federally funded observational clinical study, currently in progress, involving neuroimaging to determine whether pre-operative CNS tauopathy, as reflected by PET imaging, predicts delirium and other cognitive and functional outcomes. This translational study will also examine whether anesthesia and spine surgery produces a longitudinal change in the brain tau burden in older adults, as compared to control, non-operative patients.
Conclusions: Bench to bedside research is needed in order to promote evidence-based care for patients at risk for ADRD.

Categories: Aging
Keyword 1: delirium
Keyword 2: aging disorders
Keyword 3: neurocognition
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3 Anesthesia as a Stress Test for the Aging Brain: Understanding the Implications of Unexpected Anesthetic-Induced Brain Activity Patterns for Delirium and Dementia Risk

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Objective: Recent work has shown that dysfunctional brain EEG responses to anesthetic drugs can be an indicator of both preoperative cognitive impairment and postoperative delirium risk. However, since excessive anesthetic dosage can also cause abnormal EEG brain responses, it is unclear how to tell to what extent such abnormal brain EEG responses reflect latent neurocognitive impairment versus excessive anesthetic dosage. Further, it is unclear what underlying mechanisms might underlie the link between phenotypes (such as delirium and cognitive impairment) and these abnormal neurophysiologic responses to anesthetic drugs.
Participants and Methods: Dual center prospective cohort design. 139 total older surgical patients from two academic centers underwent intraoperative EEG monitoring with the bispectral index (BIS) EEG monitor during anesthesia and surgery, and postoperative delirium screening by geriatrician interview (Duke cohort) or by trained research staff (Mt Sinai cohort). We developed the Duke Anesthesia Resistance Scale (DARS), defined as the average BIS EEG values divided by the quantity 2.5 minus the age adjusted end tidal anesthetic gas concentration). We then examined the relationship between the DARS and postoperative delirium risk using the Youden index to identify an optimal low DARS threshold for delirium risk, and we used multivariable logistic regression to control for potential confounders.
Results: Neither BIS scores nor inhaled anesthetic dosage differed significantly between patients with vs without postoperative delirium. Yet, patients with delirium had lower DARS scores than those who did not develop delirium (27.92 vs 32.88, p=0.015). A DARS threshold of 28.7 maximized the Youden index for the association between the DARS and delirium. In multivariable models adjusting for site (Duke vs Mt Sinai) and individual patient risk factors, DARS values <28.7 were associated with a 3.79 fold increased odds ratio (95% CI 1.63-9.10; p=0.03) for postoperative delirium. These results remained unchanged after adjusting for intraoperative medications including opioids, benzodiazepines, propofol, phenylephrine and ketamine. Patients with structural/functional MRI or CSF biomarker evidence of preclinical/prodromal Alzheimer's disease and/or neurovascular pathology were more likely to show altered anesthetic-induced EEG activity patterns.
Conclusions: Lower scores on a processed EEG-based scale of neurophysiologic resistance to anesthetic induced brain activity changes were independently associated with a nearly 4-

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