

Participants and Methods: In this session, the author will present a bench to bedside 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-

fold increased delirium risk. The altered anesthetic-induced brain EEG patterns in patients who go on to develop postoperative delirium may reflect latent pre-clinical/pro-dromal Alzheimer's disease and/or neurovascular pathology.

Categories: Aging

Keyword 1: electroencephalography

Keyword 2: neurocognition

Keyword 3: neural circuitry

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4 Characterizing Cognitive Profiles and Postoperative Cognitive Risk in Older Adults Presenting for Elective Surgery

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Objective: Older adults represent 50% of surgical patients and are disproportionately at risk of poor cognitive outcomes after surgery including delirium, accelerated cognitive decline, and dementia. Delirium alone is estimated to occur in up to 50% of older adults postoperatively, while research indicates it is preventable in 30-40% of cases. Individuals with pre-existing cognitive impairments or neurodegenerative diseases are at the highest risk of such outcomes, but (1) cognitive diagnoses are grossly underrepresented in patients' medical records, and (2) routine preoperative cognitive clearance remains rare. The purpose of this presentation is to demonstrate the extent and nature of cognitive vulnerability in older adults preparing for elective surgery within a tertiary care hospital. A case series is also reviewed to illustrate varying surgical outcomes with and without consideration of preoperative cognitive risk.

Participants and Methods: This presentation incorporated IRB-approved and data honest broker management to assess diagnoses and cognitive profiles of adults age 65 and older electing surgery with anesthesia between January 2018 and December 2019. Data were assessed across two phases of the Perioperative Cognitive Anesthesia Network (PeCAN) program within the University of Florida and UF Health. First, data from the

preoperative anesthesia clinic were reviewed for the percentage of patients with cognitive difficulties within the patient problem list. Second, based on neuropsychological domains, the cognitive profiles of patients assessed by neuropsychologists within the preoperative anesthesia clinic were divided into primary attention, primary memory, or combined memory attention. From these patients, the presenter highlight cases to demonstrate how individuals with cognitive difficulties can be provided care by a multidisciplinary team to mitigate the presence of postoperative complications.

Results: Of 14,794 older adults entering the tertiary care medical center for surgical procedures, 4% (n=591) of the sample had ICD cognitive or neurodegenerative codes in the record. When a comprehensive neurobehavioral assessments were conducted on 1,363 of these presurgical patients, 70% had confirmed cognitive deficits on neuropsychological testing. These deficits included primary attention and executive deficits (12%), primary memory impairment (27%), or both attention and memory impairment (31%). Cases from these patients are reviewed and highlight how preoperative cognitive risk status can inform conservative perioperative practices including opioid-sparing analgesia, depth of anesthesia monitoring, and postoperative inpatient geriatric medicine consultation.

Conclusions: Medical records listed cognitive diagnoses in 4% of hospital preoperative medical records, yet neuropsychological assessment of a subset of cases revealed a markedly higher rate of impairment. Patients with preoperative cognitive assessment show cognitive symptoms consistent with known neurological disorders of aging including Alzheimer's disease and cerebrovascular disease. Appreciation of pre-existing neurocognitive disorders can alter perioperative practices to prevent or reduce the risk of delirium and other postoperative neurocognitive changes. These data and cases reviewed will highlight how neuropsychology can be involved in perioperative care and champion perioperative interventions for perioperative "rescues".

Categories: Aging

Keyword 1: delirium

Keyword 2: dementia - Alzheimer's disease

Keyword 3: cerebrovascular disease