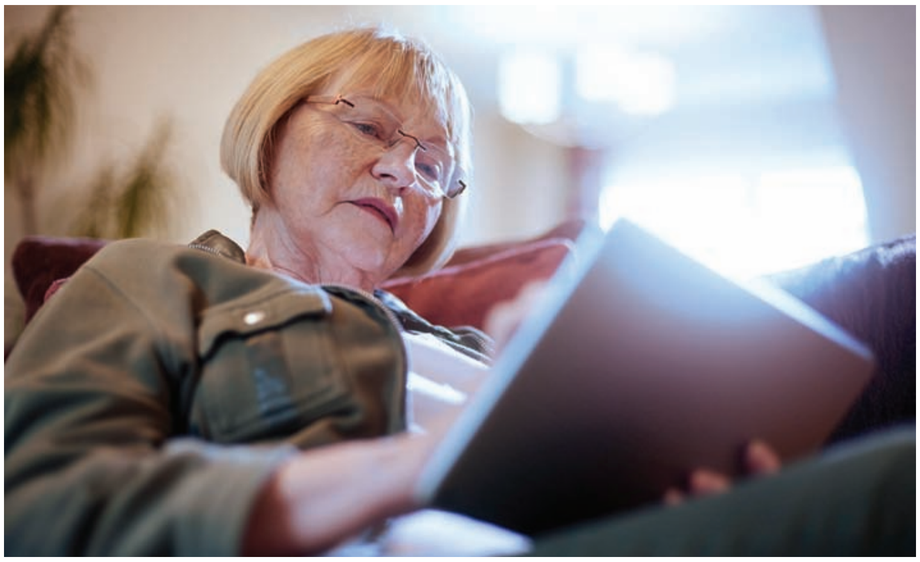
Your Patient's Brain

Cognitive Prehabilitation and Postoperative Brain Health

Michelle L. Humeidan, MD, PhD   Daniel J. Cole, MD, FASA

During my (MH) medical school rotation in anesthesiology, the importance of optimizing specific organ systems prior to surgery was a fundamental aspect of what I was taught. If a patient had congestive heart failure, diuresis would be considered; for reactive airway disease, inhalers would be administered; and appropriately timed dialysis was key for end-stage renal disease patients. *But no one ever talked about optimizing the brain!* I may have been biased as I was fresh off a long stint in graduate school studying neuronal aging in the hippocampus, an important brain structure for learning and memory; but this seemed like an obvious gap. At that time, it was recognized that patients may experience alterations in thinking and behavior after surgery, but this was largely dismissed as an accepted response to anesthesia medications. I was disappointed, but what an opportunity to close this gap with science and improve the health of our patients.

My "scientist" lens would make each anesthetic I witnessed as a medical student seem like an experiment, complete with hypothesis-testing, variables, and data. I became perplexed at the repeated experience of having two "well-controlled" experiments with similar patients, procedures, anesthetics, and operative courses, yet very different outcomes in terms of brain health. Patient A would be normal when I visited them postoperatively, and Patient B would be noticeably different than I remembered from my preoperative evaluation, displaying altered consciousness and cognition. Addressing this phenomenon of postoperative delirium (POD) has become a priority for ASA, demonstrated by inception of the Perioperative Brain Health Initiative. We have learned much about risk factors for POD, both predisposing and precipitating. Some are modifiable, others not. Age is a major risk factor for POD, and the population aged 65 and older in the United States has grown by over a third in the last decade and is expected to double to 95 million by 2060. Today, while this group represents 16% of the American population, it accounts for 40% of the more than 50 million surgical procedures performed each year. With associated increases in morbidity and mortality, POD is becoming a significant concern for older patients undergoing surgery.

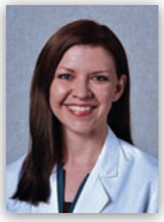


During my PhD work, I was introduced to the concept that an active mind is a protected mind. There were many prominent researchers in my department studying dementia, and smack in the middle of what would be 17 years of post-high school education before accepting my first full-time faculty position, I remember thinking, "if being a lifelong learner is protective against dementia, I am good!" Just prior to starting my postgraduate training in anesthesiology, I got the idea for the Neurobics Trial. It was as simple as connecting my observations that "brain" optimization was not part of standard anesthesiology practice, POD was common, especially in older patients, and an "active" brain had a lower risk of dementia. Could increasing brain "activeness" prior to surgery protect against postoperative cognitive decline?

A few years later, I formalized my hypothesis for the Neurobics Trial (*Clin Ther* 2015;37:2641-50). From the literature at that time, it was known that 1) Preexisting cognitive dysfunction (i.e., low cognitive reserve) increases risk of developing POD; 2) Surrogates for baseline "high cognitive reserve" like regular reading and singing are associated with decreased POD risk; and 3) Cognitive function in older individuals can be improved with a variety of activities ranging from "play-therapy" to computer games. Presumably through increasing cognitive resilience, the Neurobics Trial was designed to investigate if preoperative brain exercise could modify the risk of POD in older patients having major surgery. The intervention, a tablet-based game application targeting the cognitive domains of memory, speed, attention, flexibility, and problem-solving, was chosen to dynamically challenge participants and allow verification of patient participation, as opposed to assigning crossword puzzles or the like to complete at home. To avoid confounding factors, only patients with normal baseline cognition were to be randomized. A rigorous delirium evaluation construct was included, the lack of which had limited interpretation of other studies due to the unpredictable presentation of POD.

From 2015 to 2019, Neurobics Trial researchers randomized 268 patients between control and intervention groups. Final evaluation of the primary outcome, incidence of delirium between postoperative day 0 to 7 or discharge, included 251 patients. Two things struck me immediately about our data. First, almost 97% of patients in the intervention group did participate in the brain exercise, but the majority had difficultly completing the suggested 10 hours of activity (median 4.6 hours). Second, possibly from general improvements in surgical care at our institution, the rate of POD in the control group was lower than expected (29 of 126 patients, 23%). Nonetheless, only 18 of 125 patients (14.4%) in the intervention had POD, and interestingly two of those 18 were from the small cohort of intervention patients who were completely noncompliant with the brain exercise (N=4). Post-hoc analysis of only compliant patients revealed a delirium rate of 13.2% (16 of 121 patients, P=0.04). Despite wide variability in game usage and overall less-than-desired brain exercise time commitment by patients, the intervention still lowered POD risk in patients who were at least minimally compliant. Though the trial was not designed to examine dosage effects, it is interesting that patients who completed more than five hours of cognitive exercise had about half the incidence of delirium of those who completed less than five hours (*JAMA Surg* 2021;156:148-56).

What is next for cognitive exercise and the prevention of POD? More research! The ideal types of brain exercise activities, effective dose, and perioperative timing will require several additional studies. Furthermore, what opportunities exist for using brain exercise in patients who present for surgery with preexisting cognitive dysfunction, which we now know is a significant number (*Anesthesiology* 2017 Nov;127:765-74)? In the meantime, the Perioperative Brain Health Initiative continues to facilitate implementation of strategies to decrease postoperative delirium based upon consensus guidelines and expert opinion and is a great resource for provider and patient educational materials (*J Am Coll Surg* 2016;222:930-47; *Anesth Analg* 2018;127:1406-13). I look forward to the day when optimizing the brain is standard practice, just as we now do for the heart. Brain exercise can be incorporated into other prehabilitation programs that are becoming more widespread for care of older surgical patients. It won't hurt – and it just might help! ■



Michelle L. Humeidan, MD, PhD

Associate Professor, Neuroanesthesiology, Department of Anesthesiology, Medical Director, Enhanced Surgical Recovery, and Associate Faculty, Institute for Behavioral Medicine Research, The Ohio State University Wexner Medical Center, Columbus.

Daniel J. Cole, MD, FASA

Professor of Clinical Anesthesiology, Department of Anesthesiology and Perioperative Medicine, David Geffen School of Medicine, University of California, Los Angeles.