The Devil Is in the Details

Comparison of Postoperative Delirium and Neurocognitive Dysfunction

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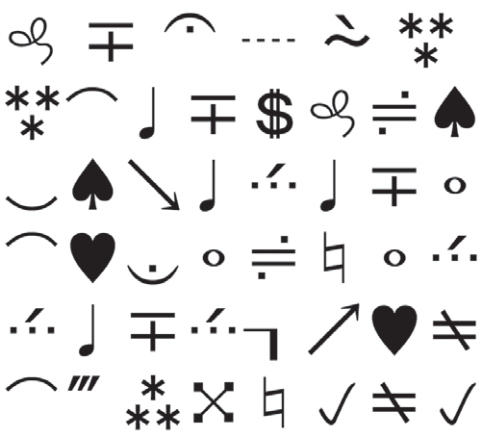
Evaluating cognitive change within individuals (and in groups) has bedeviled neuropsychologists, biostatisticians, and clinicians for ages. In this issue of Anesthesiology, a study by Daiello *et al.*[1] illustrates quite well some of the difficulties inherent in how we define and assess "clinically meaningful" postoperative cognitive outcomes and the practical impact those difficulties can have on determining the association between postoperative delirium and postoperative cognitive dysfunction—two conditions frequently associated with heightened risk for mortality within 1 yr after surgery, longer-term cognitive decline, and dementia.[2–4]



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In their examination of in-hospital postoperative delirium and postoperative cognitive dysfunction at 1, 2, and 6 months after noncardiac surgery in Successful Aging after Elective Surgery study participants,[5] Daiello *et al.*[1] report a weak association between in-hospital postoperative delirium and the risk of lingering postoperative cognitive dysfunction at 2 months of recovery (odds ratio = 1.30, $P = 0.062$) and a lack of association at 6 months of recovery (odds ratio = 1.07, $P = 0.744$). Their results suggest that the risk of significant postoperative cognitive dysfunction is really highest at 1 month in patients with in-hospital delirium (relative risk = 1.34, $P = 0.010$). Even then, only a small proportion of patients with both conditions at 1 month were found in their large surgery sample (75 of 548 patients; 14%) compared to the total patients with postoperative cognitive dysfunction at 1 month (256 of 548 patients; 47%). More patients developed postoperative cognitive dysfunction during the early stages of recovery *without* a history of in-hospital postoperative delirium. Although 12.5% of patients with postoperative cognitive dysfunction at 1 month were still evincing moderate to severe cognitive decline at 6 months of recovery, a history of postoperative delirirum was not predictive of persistent cognitive deficits. These findings demonstrate that postoperative delirium is poorly predictive of postoperative cognitive dysfunction after 1 month of recovery and beyond, suggesting that postoperative delirium and postoperative cognitive dysfunction are separate clinical conditions, rather than shared conditions reflecting two sides of the same coin.[6]

One fundamental conundrum is determining how we define postoperative cognitive dysfunction, as differing definitions can have notable impact on the frequency of postoperative cognitive dysfunction in a given study. For instance, when Daiello *et al.*[1] defined postoperative cognitive dysfunction as a mild rather than moderate change in cognition from presurgical baseline, the incidence of postoperative cognitive dysfunction at 1 month recovery rose from 47% to 60%. These cognitive change considerations, while seemingly arcane, are salient to clinicians' assessment of patient risk and long-term outcomes and patients' understanding of their condition and expectations for recovery. Importantly, a newly proposed perioperative neurocognitive disorders diagnostic nomenclature[7] has started a robust debate about what to call postoperative cognitive dysfunction, yet significant work remains on how to best measure, discriminate, and define the clinically meaningful cognitive change suggested for mild and major perioperative neurocognitive disorder diagnoses.

Image: J. P. Rathmell.

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The lingering uncertainty in how we characterize the cognitive change associated with postoperative cognitive dysfunction is an uncomfortable truth often lost in translation and buried in study methods. Is postoperative cognitive dysfunction reflective of global cognitive impairment or more selective to particular cognitive domains (*e.g.*, memory, attention, and others), or could it be both? It seems sensible to capture both possibilities, but doing so allows for greater heterogeneity in cognitive performance patterns that may, in turn, complicate our efforts to determine if there are critical cognitive deficits that bridge between delirium and postoperative cognitive dysfunction. We know that many of the same presurgical risk factors for delirium are shared with postoperative cognitive dysfunction, particularly those involving frontal/executive functioning,[8] and it has also been observed that functional declines are greatest in patients with postoperative cognitive dysfunction characterized by selective memory and executive dysfunction.[9] Why, then, would we expect to observe a global decline in cognitive performance, which is often derived from averaging or summing individual test variables in a battery? Doing so may only serve to dilute and obscure potentially more sensitive indicators of postoperative cognitive dysfunction, which could include deficits like those observed in delirium (*e.g.*, inattention). Alternatively, maybe we should consider the possibility that postoperative cognitive dysfunction exists on a spectrum and therefore prioritize quantifying cognition change as a continuous variable? Whatever side of the debate on which we land, we should seek to optimize postoperative cognitive dysfunction detection for what is unusual for the patient. Depending upon an individual's age, presurgical cognitive abilities, occupational complexity, and levels of psychosocial support, even a mild cognitive decline from presurgical baseline could have severe functional consequences.

The debate about how to best capture and characterize cognitive change is significant because the clinical impact of postoperative delirium and postoperative cognitive dysfunction can be devastating, with both conditions associated with worse cognitive decline 3 to 5 yr later,[10] decreased quality of life, and increased 1-yr postoperative mortality risk.[2] For any patient, this could range from not being able to complete a work project on time, to loss of independent living, or even death 1 yr after surgery/anesthesia. Although the impact of delirium and postoperative cognitive dysfunction is significant, we still lack a complete understanding of their pathophysiologic underpinnings; thus, it is unclear whether delirium and postoperative cognitive dysfunction truly represent distinct conditions. If delirium and postoperative cognitive dysfunction are two separate conditions (but with similar predisposing factors), as the findings of Daiello *et al.*[1] suggest, one could argue that two clinical strategies should be employed to prevent delirium and postoperative cognitive dysfunction. First, potentially modifiable predisposing factors should be identified and addressed before surgery. Known predictors of delirium and postoperative cognitive dysfunction such as age and years of education are virtually immutable, but other predictors such as frailty, depression, obstructive sleep apnea, and presurgical cognition may be modifiable to a degree through treatment or "prehabilitation." We hope that continued research on these potentially modifiable factors will guide preoperative optimization strategies to prevent postoperative delirium and postoperative cognitive dysfunction. Second, distinct postoperative strategies to reduce delirium and postoperative cognitive dysfunction should be employed. For example, validated strategies to reduce in-hospital delirium, such as medication avoidance (*e.g.*, benzodiazepines, anticholinergics, meperidine), encouraging sleep hygiene, performing early mobilization, preventing sensory deprivation, and encouraging family presence might not be effective in preventing postoperative cognitive dysfunction later in the postoperative period. Instead, perhaps strategies to reduce postoperative cognitive dysfunction severity or duration should focus on cognitive stimulation therapies and aerobic exercise interventions, which have the potential to reduce cognitive decline.

Overall, the study by Daiello *et al.*[1] reveals the difficulties inherent in ascertaining what is "meaningful" postoperative cognitive change and reminds us that often the devil is in the details. The study also suggests that delirium and postoperative cognitive dysfunction are distinct clinical entities, for which differential clinical management will be needed to guide anesthesiologists as we move forward to optimize perioperative brain health.

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Competing Interests

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