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## Neurological complications of surgery and anaesthesia

G. A. Mashour<sup>1\*</sup>, D. T. Woodrum<sup>1</sup> and M. S. Avidan<sup>2</sup>

## **Editor's key points**

- In this narrative review, the authors describe the potentially devastating neurological complications that may arise around the time of anaesthesia.
- They review recent advances in the field, and provide guidance on the prevention of adverse outcomes.

**Summary.** Injury to the central and peripheral nervous systems is often permanent. As such, adverse neurological outcomes of surgery and anaesthesia can be devastating for patients and their families. In this article, we review the incidence, risk factors, outcomes, prevention, and treatment of a number of important neurological complications in the perioperative period.

**Keywords:** anaesthesia; delirium; neurological complications; neurological outcomes; postoperative cognitive dysfunction; postoperative visual loss; spinal cord ischaemia; stroke; surgery

Neurological injury during the course of surgery can be devastating to patients and their families. Importantly, there is neither a temporary nor sustainable alternative to native neurological function as there is with other organs such as the kidney (dialysis machine, transplant), heart (ventricular assist device, transplant), liver (transplant), lungs (extracorporeal membrane oxygenation, transplant), or skeletal system (artificial joints). Despite the importance of the central and peripheral nervous systems, it could be argued that the field of anaesthesiology has systematically ignored neural function in the perioperative period. This provocative assertion is meant to highlight the fact that there is no standard monitor for the brain or other neural structures during surgery and anaesthesia, while standard monitors for the cardiovascular and respiratory systems have been used routinely for decades. This gap in clinical care is even more striking considering the fact that the brain and spinal cord are the primary therapeutic targets for both anaesthetics and analgesics. In other words, we have traditionally focused the least on what is arguably the field's most important physiological system, comprised organs that are the most difficult to heal or replace if injured.

In this article, we provide a concise review of five neurological complications of surgery and anaesthesia. Given the extensive literature and significant number of possible neurological outcomes, we have chosen to focus on adverse events that are common (delirium), controversial [postoperative cognitive decline (POCD)], and potentially catastrophic [stroke, spinal cord ischaemia, and postoperative visual loss (POVL)]. The objective of this review is to familiarize practicing anaesthetists with the incidence, risk factors, outcomes, prevention, and management of important neurological complications in order to heighten attention and improve care in the perioperative period.

#### **Delirium**

Delirium is an acute and fluctuating neurological disorder that reflects a change from baseline cognition and is characterized by the cardinal features of inattention and disorganized thinking (Table 1).<sup>12</sup> Delirium is arguably one of the most important post-operative complications because (i) it is common, affecting up to 70% of patients older than 60 undergoing major inpatient surgeries and (ii) it is associated with adverse outcomes, including mortality, persistent cognitive decline, and prolonged intensive care and hospital length of stay.<sup>3–8</sup> Delirium or agitation upon emergence from general anaesthesia occurs frequently, especially in children,<sup>9</sup> but will not be discussed in this section. Instead, we will focus on postoperative delirium because of its significance as a complication associated with increased morbidity and mortality.

In many patients, postoperative delirium is a marker of brain vulnerability and its occurrence suggests the possibility of underlying neurological disease, such as early or preclinical dementia. <sup>6</sup> <sup>10</sup> <sup>11</sup> Despite its high incidence and serious implications, delirium is frequently undiagnosed because it presents with a hypoactive rather than hyperactive phenotype (Fig. 1). <sup>12</sup> <sup>13</sup> Furthermore, without targeted questioning, patients may appear normal or perhaps slightly lethargic. In order to promote diagnosis of delirium, reliable and user-friendly diagnostic algorithms have been developed. The Confusion Assessment Method and the Confusion Assessment Method for the Intensive Care Unit (for patients unable to speak) are the approaches that have been most widely adopted. <sup>14–17</sup>

Anaesthetists have historically not focused on delirium because it typically manifests when patients are no longer under their direct care. Delirium causes distress to patients and their families, and is a frustrating problem for clinicians as no treatments have been available to decrease its incidence

<sup>&</sup>lt;sup>1</sup> Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, MI, USA

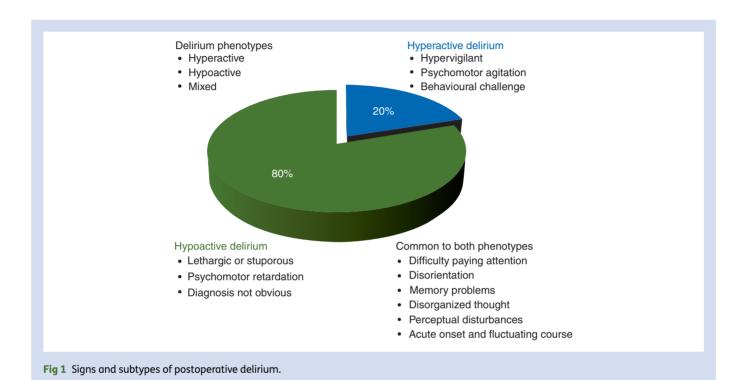
<sup>&</sup>lt;sup>2</sup> Department of Anesthesiology, Washington University School of Medicine, St. Louis, MO, USA

<sup>\*</sup> Corresponding author: Division of Neuroanesthesiology, Department of Anesthesiology, University of Michigan Medical School, 1UH247, University Hospital, SPC-5048, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5048, USA. E-mail: gmashour@umich.edu

Table 1 Diagnostic criteria for delirium (from the Diagnostic and Statistical Manual of Mental Disorders-5, pp. 599-600)

(A) There is a disturbance in attention, manifesting as a decreased ability to focus, shift, direct, and sustain attention. Patients may be either agitated (hyperactive) or letharqic (hypoactive)

- (B) It develops over a short period of time, typically hours to days, and tends to fluctuate in its severity, and is often worse in the evening and night
- (C) There is a cognitive change. This typically manifests as memory problems, disorientation, or hallucinations
- (D) Delirium should not be diagnosed in the context of coma, but acute-onset low arousal states are compatible with delirium with severe inattention
- (E) It is associated with an acute insult, such as a medical illness or a major surgery, which leads to neurophysiological perturbation



or mitigate its duration. One of the reasons that delirium is difficult to prevent or treat is that several pathological pathways have been implicated, including neurotransmitter imbalance, neuroinflammation, endothelial dysfunction, impaired oxidative metabolism, and altered availability of large neutral amino acids. 10 18 19 With such complexity, no single intervention is likely to be a panacea. Nonetheless, there are important risk factors for delirium that should be prevented or alleviated. These include pain, acute medical conditions, sleep disturbance, sensory impairment, social isolation, daylight deprivation, infections, withdrawal syndromes, dehydration, blood loss, blood transfusion, electrolyte abnormalities, acid-base abnormalities, hypoxaemia, temperature derangements, seizures, and endocrine dysfunction. 11 20-22 Certain drugs commonly used in the perioperative period such as atropine, antihistamines, corticosteroids, benzodiazepines, propofol, and opioids—can precipitate delirium and should be minimized in vulnerable patients.<sup>23</sup> <sup>24</sup>

Given that postoperative delirium is so common, any approach that prevented it or lessened its consequences would have major clinical impact. Evidence has recently emerged from randomized controlled trials that guiding both total i.v.

anaesthesia and volatile-based general anaesthetic administration with a processed EEG might decrease incident post-operative delirium.<sup>25–27</sup> A theoretical mechanism by which this could occur is that a processed EEG prevents relatively excessive anaesthetic administration to vulnerable patients. However, if slightly deeper anaesthesia in vulnerable surgical patients were to increase the risk of postoperative delirium, we would expect regional anaesthesia to be associated with a considerably lower incidence of postoperative delirium than general anaesthesia. A meta-analysis of small trials that randomized surgical patients to regional (albeit with light sedation) or general anaesthesia surprisingly found no increased risk for delirium with general anaesthesia (odds ratio, 0.88; 95% confidence interval, 0.51–1.51).<sup>28</sup> This apparent paradox warrants further exploration through a large, pragmatic clinical trial.

Various perioperative pharmacological agents have been investigated for the prevention of delirium and some success has been noted with low-dose haloperidol, subanaesthetic dose ketamine, and perioperative dexmedetomidine.<sup>29–31</sup> Of these interventions, dexmedetomidine for postoperative or intensive care unit sedation has been most rigorously investigated, and might be superior to benzodiazepines and

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