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[Better Patient Care Through Research](#)**Regional Anesthesia and Analgesia and Postoperative Central Nervous System Dysfunction***Christopher J. Jankowski, M.D.*[Calendar for Meetings](#)[Career Center](#)[Clinical Information](#)[Continuing Education Resources](#)[Links of Interest](#)[News Archives](#)[Office of Governmental & Legal Affairs](#)[Patient Education](#)[Patient Safety](#)[Practice Management](#)[Press Room](#)[Providers of Anesthesia](#)[Publications & Services](#)[Related Organizations](#)[Residents & Medical Students](#)

It is well-known that the population is aging and that older patients have a disproportionately high rate of surgery. Those over 85 years old are the fastest-growing segment of the population and will number more than 20 million in the United States by 2050.<sup>1</sup> Postoperative central nervous system (CNS) dysfunction is among the most common complications in elderly surgical patients. For example, up to 60 percent of older surgical patients experience postoperative delirium (POD).<sup>2</sup> Delirium is associated with increased medical morbidity, mortality and costs. More relevantly for older patients and their families, it is associated with a loss of independence.<sup>3</sup> Thus postoperative CNS dysfunction is a significant public health issue, one that is of particular concern to anesthesiologists. What can we do to influence cognitive outcomes in elderly patients? Should we choose general or regional anesthesia? Does postoperative analgesic management matter?

Postoperative CNS dysfunction in the elderly was first reported more than 50 years ago.<sup>4</sup> Unfortunately, despite being common and representing impairment in the target organ system for general anesthetic agents, comparatively little research was done on the subject. In part, this may have been because of a lack of appreciation of the frequency of the problem; signs and symptoms of postoperative CNS dysfunction often present well after anesthesiologists have completed their postoperative rounds. In addition, the study of postoperative CNS dysfunction is difficult. Standardized tools for detecting delirium were not available until decades later,<sup>5</sup> and there still remains no universally accepted definition of postoperative cognitive dysfunction (POCD). However, the aging population and recent laboratory evidence that volatile anesthetics induce changes in neurons consistent with Alzheimer disease<sup>6-7</sup> have renewed interest in postoperative CNS dysfunction both for the lay public<sup>8</sup> and within our specialty.

There are two main forms of postoperative CNS dysfunction: delirium and POCD. In contrast to emergence delirium (which occurs immediately following general anesthesia), the onset of POD occurs between postoperative days one to three. POD is a disturbance of consciousness that develops over hours to days, tends to fluctuate in intensity and cannot be explained by a previously existing dementia. Risk factors for POD include age, type of operation, severe metabolic abnormalities, and poor preoperative medical, physical and cognitive status. Many drugs used in the perioperative period are associated with delirium, including opiates, benzodiazepines, anticholinergics, corticosteroids and some antibiotics. In addition, the incidence of POD is higher when pain is poorly controlled. The mechanism of delirium is not well understood. There are, however, a number of theories involving neurotransmitter imbalances (especially in the cholinergic system), cytokines and hormones.

The definition of POCD is evolving. Generally it consists of deficits in one or more cognitive domains following surgery, and diagnosis requires neurocognitive testing. Unlike delirium, patients with POCD tend to be alert and oriented. Like POD, however, little is known about the etiology of POCD. Age, major surgery and pain are risk factors.

The March 2007 issue of *Anesthesiology* contains selected reports from the Journal Symposium on Postoperative Cognitive Dysfunction, which was held at the 2006 ASA Annual Meeting in Chicago. It also includes two excellent reviews of postoperative CNS dysfunction. The first, by Jeffrey H. Silverstein, M.D., and colleagues examined the general topic of postoperative CNS dysfunction.<sup>9</sup> In the other, Stanton Newman, D. Phil., and colleagues systematically reviewed literature pertaining to POCD.<sup>10</sup> Interested readers should refer to these articles for more information.

Regional anesthetic techniques are intuitively attractive options for patients at risk for postoperative CNS dysfunction. They minimize exposure to drugs associated with CNS dysfunction, blunt the surgical stress response and provide excellent pain control. In theory all of these effects may contribute to a reduction in the incidence and severity of postoperative CNS dysfunction. Unfortunately, in studies to date, regional techniques have not been associated with decreased incidence of either POD or POCD.

For example, in a trial published in 1995, Williams-Russo and colleagues randomized 262 patients undergoing total knee arthroplasty to receive either epidural or general anesthesia. Patients were evaluated with standardized neurocognitive tests on postoperative days one through seven and at

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one and six months. There was no difference in the incidence of POD or early or late POCD between groups. In fact there was a trend toward more delirium in patients who received an epidural anesthetic.<sup>11</sup>

More recently the International Study of Postoperative Cognitive Dysfunction (ISPOCD) investigators examined the effect of regional versus general anesthesia on POCD on patients undergoing a variety of noncardiac surgical procedures. Four hundred twenty-eight patients from 12 institutions were randomized to receive either regional or general anesthesia. The investigators found no difference in the incidence of POCD at three months between groups.<sup>12</sup>

A systematic review of 24 trials examining the effect of regional versus general anesthesia on postoperative CNS dysfunction also concluded that choice of intraoperative anesthetic does not influence the incidence of POCD. The authors noted, though, that methodological and design concerns in the available studies prevented their results from being definitive.<sup>13</sup> For example, in both the Williams-Russo and ISPOCD group studies, postoperative analgesia was not standardized.

There are a number of reasons why the timing of the use of regional techniques may be important. For instance, parenteral postoperative analgesic regimens often include drugs associated with CNS side effects (e.g., opiates) and may not provide optimal pain control. Because of this, they may contribute to postoperative CNS dysfunction. Thus for regional anesthetic techniques to confer a benefit on postoperative cognitive outcomes, it may be necessary to continue them into the postoperative period. The key issue with regard to preventing postoperative CNS dysfunction may be the *analgesic* rather than the *anesthetic* regimen.

Epidural catheter infusions are a mainstay of regional analgesic techniques. When properly managed, their benefits include reductions in opiate requirements and excellent pain control.<sup>14</sup> In addition they modulate the surgical stress response.<sup>15</sup> Unfortunately epidural catheters cannot be used in patients receiving certain forms of thromboprophylaxis because of the risk of spinal hematoma. They also are associated with undesirable side effects, including urinary retention and difficulties with ambulation.

For appropriate procedures, catheter-based continuous peripheral nerve blockade is an attractive alternative to neuraxial analgesia. First described more than 60 years ago,<sup>16</sup> advances in catheters and placement methods have led to increased popularity in recent years. These techniques provide excellent pain control and reduce opiate consumption.<sup>17</sup> In addition they encourage ambulation, can be used with a variety of thromboprophylactic regimens and do not lead to urinary retention. Thus they may be ideal for use in the elderly.

There is a paucity of data on the impact of continuous peripheral nerve catheter analgesia on cognitive outcomes. Preliminary evidence suggests, however, that their use may result in a substantial reduction in the incidence of POD. In an observational study of elderly patients undergoing major lower-extremity joint replacement, the use of continuous postoperative peripheral nerve catheters was associated with a more than 58-percent decline in the incidence of POD.<sup>18</sup>

Will regional techniques play a role in improving neurocognitive outcomes in elderly surgical patients? Possibly.

The issue is far from settled, though, and more study is needed. Rather than focusing solely on whether intraoperative management affects postoperative CNS dysfunction, future trials also should consider the impact of postoperative analgesic care. As the population ages, improving our understanding of the influence of perioperative management on postoperative CNS dysfunction will be increasingly important and may allow us to improve outcomes for older patients.

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