Study shows increased Alzheimer's biomarkers in patients after anesthesia and surgery

October 4 2011

(Medical Xpress) -- The possibility that anesthesia and surgery produces lasting cognitive losses has gained attention over past decades, but direct evidence has remained ambiguous and controversial. Now, researchers at the Perelman School of Medicine at the University of Pennsylvania provide further evidence that Alzheimer's pathology may be increased in patients after surgery. The new research is published in the October 2011 issue of the journal *Anesthesiology*.

"We have long sought a clearer picture of the true impact of anesthesia and surgery on the central nervous system," said lead study author Roderic Eckenhoff, MD, Austin Lamont Professor of Anesthesia at Penn. "Although not definitive, this human biomarker study gives some credibility to the notion that anesthesia and surgery produce an inflammatory insult on the brain and accelerate chronic neurodegenerative diseases like Alzheimer's."

Clinical observation of postoperative cognitive dysfunction in patients and studies in animals have long suggested that anesthetics could interact with Alzheimer neuropathology, but the decades-long refractory period, when Alzheimer pathology is developing in the absence of detectable cognitive symptoms, has made research difficult.

With advances in diagnostic tests led by Penn Medicine's Leslie Shaw, PhD, professor of Pathology and Laboratory Medicine, there is now a

validated biomarker test that is able to detect the presence of Alzheimer's disease (AD) biomarkers found in cerebral spinal fluid (CSF). This 'signature' combination of Alzheimer's disease indicators – amyloid beta and tau protein – can find disease markers before Alzheimer's symptoms appear and reliably predicts which patients will progress from mild cognitive impairment to full blown Alzheimer's disease. Generally speaking, highly increased CSF tau protein and decreased beta-amyloid are indicative of AD pathology.

To further examine the impact of anesthesia and surgery on CSF in real time, Dr. Eckenhoff and colleagues at Penn set out to analyze the 'signature' indicators of Alzheimer's disease by collecting CSF from patients undergoing routine surgical procedures. A total of 11 patients, all undergoing endoscopic nasal surgery, were included in the study.

At the beginning of the study, there was no evidence of cognitive impairment and infection, and no patients were taking central nervous system (CNS)-active medications. The first, or baseline, CSF sample was taken at the beginning of the procedure. Another CSF sample was taken at the end of the procedure, and additional samples were taken at 6, 24, and 48 hours after that.

Mean CSF amyloid beta concentrations fluctuated by less than 10 percent in either direction and were statistically unchanged throughout the 48 hour postoperative period. However, total tau was significantly increased after 6 hours, and was still increasing at 48 hours when most of the spinal catheters were removed. An injury biomarker, S100B, and inflammatory biomarkers Interleukin-10, IL-6, and tumor necrosis factor, were also significantly increased over time after surgery suggesting neuroinflammation as a possible mechanism.

These findings together suggest significant changes in CSF biomarkers in a direction that is consistent with Alzheimer's disease progression and

enhanced neuroinflammation.

The researchers also found that the use of the inhaled volatile anesthetic sevoflurane was associated with significantly higher CSF concentrations of inflammatory biomarkers than was associated with injectable anesthetics such as propofol and remifentanil. Although this suggests anesthetic management might make a difference in post-surgery neuroinflammation, the authors caution the study was too small to make a definitive connection; larger studies are needed to examine this concept.

"The evidence for anesthesia per se being responsible for the changes we saw in this study is not definitive – in fact, our work in animal models of Alzheimer's is beginning to suggest that the surgical procedure itself produces a larger effect than anesthesia," said Dr. Eckenhoff. "The next step in this line of research is to determine whether anesthetic management can modulate the neuroinflammation caused by surgery, whether this brief inflammatory insult can actually change the trajectory of something like AD, and given that surgery is usually not strictly elective, development of a strategy to reduce the inflammatory insult to the brain.

More information:
journals.lww.com/anesthesiology/pages/default.aspx

Provided by University of Pennsylvania School of Medicine