

Maxillofacial and brain surgeries and stress response

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ABSTRACT

Despite significant improvement in diagnostic and therapeutic technology over the past decades, mortality rates after cancer surgery (including brain tumor resection) remains high. Perioperative stress on the nervous system and the resultant central nervous system (CNS) changes are likely to be causative for altered behaviors that are seen postoperatively, including chronic pain, posttraumatic stress disorder, and learning difficulties. Improving the ability of the anesthesiologist to control all four components of acute perioperative stress could potentially reduce the negative impact of surgery on the brain.

Keywords: anesthesia, neurosurgery, spine, stress, drugs.

TEXT

Anesthetics may influence cancer recurrence and metastasis following surgery by modulating the neuroendocrine stress response or by

directly affecting cancer cell biology.¹⁻⁸ Saito et al.¹ summarized the current evidence on whether commonly used anesthetics potentially affect postoperative outcomes following solid organ cancer surgery with particular focus on neurological malignancies. Postoperative delirium (POD) is a common complication following surgery and anesthesia.² Mitochondrial dysfunction, which is demonstrated by energy deficits and excessively activated oxidative stress, has been reported to contribute to POD.^{2,9-15} The dynamic balance between mitochondrial fusion and fission processes is critical in regulating mitochondrial function. However, the impact of Surgery/Anesthesia on mitochondrial fusion/fission dynamics remains unclear.^{2,16-21} The anesthesia/surgery induced greater postoperative delirium-like behavior, increased brain IL-6 levels, decreased PSD-95 and synaptophysin levels, and mitochondrial dysfunction in 18 than 9 months old mice.²² Treatments with Lactobacillus and probiotic mitigated the anesthesia/surgery-induced changes. These data suggest that microbiota dysbiosis may contribute to neuropathogenesis of postoperative delirium and treatment with Lactobacillus or a probiotic could mitigate postoperative delirium.^{3,5,19,22} Despite significant improvement in diagnostic and therapeutic technology over the past decades, mortality rates after cancer surgery (including brain tumor resection) remains high.¹ With regards to brain tumors, interaction between microglia/macrophages and tumor cells by multiple biological factors play an important role in tumor progression and metastasis.^{1,4,22-30} Preclinical studies have demonstrated an association between anesthetics and brain tumor cell biology, and a potential effect on tumor progression and metastasis has been

revealed.^{1,31-35} However, in the clinical setting, the current evidence is inadequate to draw firm conclusions on the optimal anesthetic technique for brain tumor surgery.^{1,36-38} The anesthesia/surgery increased brain IL-6 levels in aged mice. These findings are consistent with the clinical observation that the elevation of plasma IL-6 level is associated with postoperative delirium in patients.³⁹⁻⁴⁵ However, the results from the current studies and our previous studies also showed that the increases in mouse brain and plasma levels of IL-6 were age-dependent.^{45,46-50} These findings would lead to future mechanistic investigation in animals to illustrate the underlying mechanism and clinical studies in patients to reveal the clinical relevance of the age-dependent changes in IL-6 levels.⁴⁵ Given the findings that the anesthesia/surgery was able to increase BBB permeability to small, but not big, molecules, next, we compared the effects of the anesthesia/surgery on the levels of β -catenin, tight junction proteins claudin, occludin, and ZO-1, and adherent junction proteins VE-cadherin, E-cadherin, and p120-catenin in cortex and hippocampus of 18-month-old mice.⁵¹ Anesthesia is a state of drug-induced unconsciousness with suppression of sensory perception, and consists of both hypnotic and analgesic components.⁵²⁻⁶⁰ The anesthesiologist monitors the clinical response to noxious stimuli and adjusts drug dosage to achieve an adequate depth of anesthesia, with the aim of reducing operative stress. Acute stress in the perioperative period has four major contributors: anxiety, pain, the surgical stress response, and the potential neurotoxicity of anesthetic agents. Any or all of these may act deleteriously on multiple systems in the brain and have known significant effects on brain regions such as the hippocampus and the hypothalamic-pituitary-adrenal axis.^{52,61,62} Perioperative stress on the nervous system and the resultant central nervous system (CNS) changes are likely to be causative for altered behaviors that are seen postoperatively, including chronic pain, post-traumatic stress disorder, and learning difficulties. Improving the ability of the anesthesiologist to control all four components of acute perioperative stress could potentially reduce

the negative impact of surgery on the brain. Currently, there is no objective measurement for any of these stressors.^{52,63,64} In conclusion, surgery/anesthesia disturbed mitochondrial fission/fusion dynamics and then impaired mitochondrial function in the brain of aged mice; these effects may be involved in the underlying mechanism of POD. Further studies are needed.

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