LSU HealthNewOrleans School of Medicine

Neuroscience Center of Excellence

Special Seminar

in Neuroscience

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Mechanisms and Resolution of Neuroinflammation in Postoperative Cognitive Dysfunction

Cognitive decline following surgery and acute illness is a common complication without defined etiology. Major surgery exposes patients to extensive trauma, blood loss and tissue injury; all of these factors effectively modulate the immune system to ultimately trigger an inflammatory response. Activation of the innate immunity, cytokines, and neuroinflammation are putative mechanisms to underlie cognitive dysfunction in preclinical models. Using a murine model of orthopedic surgery we earlier demonstrated that systemic release of TNFα is upstream of IL-1 and provokes its subsequent production in the brain. Peripheral blockade of TNFα is able to limit the release of IL-1 and prevent neuroinflammation and cognitive decline. We furthered the role of TNFα and NFκB activation in myeloid cells in mediating neuroinflammation through disruption of the blood-brain barrier (BBB) and infiltration of peripheral macrophages in the hippocampus. Through stimulation of the cholinergic endogenous anti-inflammatory pathway (α7 nACh) we prevented BBB disruption, macrophage infiltration in the CNS, and memory dysfunction after surgical trauma.

Recently, we explored the role of specialized pro-resolving mediators (SPM) and described a novel and unexpected role of in preventing cognitive decline, further illustrating how peripheral surgery interferes with memory processes and neuronal function. Perioperative administration of aspirin-triggered resolvin D1 (AT-RvD1), a SPM biosynthesized from docosahexaenoic acid, effectively prevent surgery-induced cognitive decline by modulating synaptic plasticity and long-term potentiation (LTP) in hippocampal neurons. Treatments with resolvins or maresins also counter regulate the excessive release of pro-inflammatory cytokines in plasma and oxidative stress signaling in monocytes in-vitro. Ongoing studies are looking into anti-inflammatory and pro-resolving pathways with an overarching aim of translating these findings into clinical studies and biomarker discovery for predicting at-risk patients. Overall, administration of SPM in the perioperative period may represent a safe and effective therapeutic option to modulate the inflammatory sequelae and restore neuronal-glial function after trauma.

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