Aspirin-Triggered Resolvin Protects Against Cognitive Decline After Surgery

Resolvins are molecules naturally produced by the body from omega-3 fatty acids – a process that can be jumpstarted by common aspirin. In a new study, published in *The FASEB Journal*, researchers at Karolinska Institutet describe how resolvins could protect against the cognitive impairment that often affects recovery of surgical and critically ill patients. The study adds new knowledge on how peripheral surgery affects the brain and neuronal function contributing to the processes of cognitive decline.

Hospitalization for surgery or critical illness can lead to cognitive dysfunction in some patients, especially the elderly. This is often reported as inattention, disorganized thinking, altered consciousness and prolonged disruptions in learning and memory functions. The mechanisms whereby surgery and/or anesthesia may lead to cognitive impairment remain unclear, but the researchers behind the current study have previously demonstrated that inflammation and release of pro-inflammatory molecules, like cytokines, play an important role in causing brain inflammation and cognitive decline after surgery.

Today there is no effective treatment for postoperative cognitive dysfunctions. However, the results now presented in *The FASEB Journal* suggest that it is possible to prevent and treat this condition by turning off and 'resolving' the inflammation that underlies surgery-induced cognitive decline. In the current preclinical study, treatment with a single dose of aspirin-triggered resolvin D1 (AT-RvD1), a substance from the omega-3 fatty acid docosahexaenoic acid (DHA), protected the brain from memory dysfunction after surgery.

The treatment also had an effect on neuronal function when given 24 hours after surgery. In their study, the researchers also further describe how surgery affects brain function in general, contributing to processes of neuroinflammation and memory impairment.

"We report a novel role for AT-RvD1 in restoring memory dysfunction after surgery", says Dr. Niccolò Terrando, Assistant Professor at the Department of Physiology and Pharmacology, who lead the study. "It was remarkable that AT-RvD1 displayed such unexpected effects on the central nervous system when administered at very low doses in the systemic circulation using this surgical model."

"Aspirin works as an anti-inflammatory by lowering the levels of prostaglandins and thromboxanes but in the presence of essential omega-3 fatty acids can also increases the body's own production of various lipid mediators, including resolvins like AT-RvD1, which promote resolution of inflammatory processes", says Professor Lars I Eriksson, head of the research group behind these findings at the Section of Anesthesiology and Intensive Care Medicine at Karolinska Institutet. "These

molecules, aside from reversing inflammation, also promote healing and tissue regeneration that are of relevance to patient safety and recovery. We hope to apply these therapies to prevent cognitive decline in at-risk surgical patients by translating our findings into patient care."

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