Aspirin-triggered resolvin D1 prevents surgery-induced cognitive decline.

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Abstract
Hospitalization for major surgery or critical illness often associates with cognitive decline. Inflammation and dysregulation of the innate immune system can exert broad effects in the periphery and central nervous system (CNS), yet the mechanisms underlying memory impairment after surgery remain poorly understood and without effective therapy. Endogenous regulation of acute inflammation is providing novel approaches to treat several disease states including sepsis, pain, obesity and diabetes. Resolvins are potent endogenous lipid mediators biosynthesized during the resolution phase of acute inflammation that display immunoresolvent actions. Here, using a mouse model of surgery-induced cognitive decline we report that orthopedic surgery affects hippocampal neuronal-glial function, including synaptic transmission and plasticity. Systemic prophylaxis with aspirin-triggered resolvin D1 (AT-RvD1: 7S,8R,17R-trihydroxy-4Z,9E,11E,13Z,15E,19Z-docosahexaenoic acid, as little as 100 ng dose per mouse) improved memory decline following surgery and abolished signs of synaptic dysfunction. Moreover, delayed administration 24 h after surgery also attenuated signs of neuronal dysfunction postoperatively. AT-RvD1 also limited peripheral damage by modulating the release of systemic interleukin (IL)-6 and improved other clinical markers of tissue injury. Collectively, these results demonstrate a novel role of AT-RvD1 in modulating the proinflammatory milieu after aseptic injury and protecting the brain from neuroinflammation, synaptic dysfunction and cognitive decline. These findings provide novel and safer approaches to treat postoperative cognitive decline and potentially other forms of memory dysfunctions.

KEYWORDS: astrocytes; dementia; inflammation; long-term potentiation; resolution

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