Neuroinflammation in surgery-induced cognitive decline: Can we prevent it?

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Major surgeries expose patients to extensive trauma, blood loss and tissue injury; all of these factors effectively modulate the immune system to ultimately trigger an inflammatory response. Cognitive decline following surgery in older individuals is a major clinical problem of uncertain mechanism; a similar cognitive decline also follows severe infection, chemotherapy, or trauma and is currently without effective therapy. Activation of the innate immunity, cytokines, and neuroinflammation are putative mechanisms to underlie cognitive dysfunction. A variety of mechanisms have been proposed and exploring the role of inflammation we reported on the role of IL-1β after surgery in mice with postoperative cognitive dysfunction. We demonstrated that TNF-α is upstream of the IL-1 response and provokes its production in the brain. Peripheral blockade of TNF-α is able to limit the release of IL-1 and prevent neuroinflammation and cognitive decline in a mouse model of surgery-induced cognitive decline. TNF-α appears to synergize with MyD88, the IL-1/TLR superfamily common signaling pathway, to sustain postoperative cognitive decline. More recently we reported on the role of endogenous anti-inflammatory pathways, via cholinergic regulation, in resolving surgery-induced neuroinflammation and preventing both blood-brain barrier disruption and macrophage infiltration in the CNS after peripheral surgery.

Biography

Dr. Terrando is Assistant Professor at the Karolinska Institutet, Stockholm, Sweden. He received his Ph.D. from Imperial College London in 2009 and did his postdoctoral training at the University of California, San Francisco (UCSF). His research focuses on the identification of the pathogenic mechanisms underlying surgery-induced cognitive decline, with a particular interest between cytokine release at the site of intervention, neuroinflammation and cognitive dysfunction and the identification of putative targets for effective treatment and prevention.

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