Resolvins promote resolution of brain inflammation via microglia polarization

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The brain innate immune system is mainly composed of microglial cells. Microglia are activated in response to an immune or inflammatory stimuli or a trauma, and then produce pro- and anti-inflammatory factors. These factors drive the innate immune response and can modulate neuronal activity and in fine, learning and memory. Although brain innate immune system defends brain tissue from aggression, chronic activation of microglia can also be deleterious. In the adult brain, chronic production of inflammatory cytokines can contribute to the pathogenesis of neurodegenerative diseases. Limiting the production of pro-inflammatory cytokines and enhancing the production of anti-inflammatory cytokines are crucial for neuron survival. New molecules have recently been identified. Lipidic mediators derived from n-3 polyunsaturated fatty acids (PUFAs), and more precisely from docosahexaenoic acid (DHA) which is the main PUFA in the brain include the resolvin D1 (RvD1). Its involvement in the resolution of inflammation in microglial cells and the mechanisms by which it influences are unknown. Herein we studied the effects of RvD1 on the resolution of inflammation in microglial cells stimulated with systemic lipopolysaccharide. Our results indicated that RvD1 inhibited the production of pro-inflammatory cytokines and enhanced the production of anti-inflammatory cytokines. Moreover, the receptor of RvD1 was overexpressed, reinforcing the idea that this molecule is involved in the resolution of inflammation. We also showed that RvD1 promoted a phenotypic switch in microglial polarization toward a M2-like phenotype. These findings illustrate novel mechanisms through which DHA conferred anti-inflammatory and proresolving actions in inflamed brain.

Inflammation is an essential host defence against infection, but can be damaging when excessive. Limiting the production of pro-inflammatory cytokines and enhancing the production of anti-inflammatory cytokines are crucial. New molecules have recently been identified. Lipidic mediators derived from n-3 polyunsaturated fatty acids (PUFAs), and more precisely from docosahexaenoic acid (DHA) which is the main PUFA in the brain include the resolvin D1 (RvD1). RvD1 is an endogenous immunoresolvent that regulates acute inflammation and orchestrates resolution at the periphery. Its involvement in the resolution of inflammation in the brain and the mechanisms by which it influences are unknown.