Role Of Bioactive Lipids In Plasticity Of The Prefrontal Cortex

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Calcium-independent phospholipase A2β (iPLA2β) releases docosahexaenoic acid (DHA) from brain phospholipids which is then metabolized by downstream 15-Lipoxygenase-1 (Alox15) to produce resolvins and protectins. Existing literature led us to hypothesize that DHA and its metabolites may be involved in synaptic plasticity in the prefrontal cortex (PFC) and its modulation of learning and memory and pain. In this study, we investigated the role of PFC iPLA2β in learning and memory, studied the distribution of Alox15 in the CNS, and investigated the role of Alox15 in learning and memory and pain in the PFC. Disruption of this pathway of lipid metabolism leads to disturbances in learning and memory (long-term potentiation) and spatial working memory. Together, results provide evidence for a key role of anti-inflammatory molecules generated by Alox15 and DHA (e.g. resolvin D1) in memory and central antinociceptive pathways and implicate them in neuroinflammatory brain disorders, chronic neurodegeneration and chronic pain/anxiety. In total, results of this study show the involvement of iPLA2 and Alox15 in the effect of DHA and its metabolites on plasticity in the prefrontal cortex and suggest novel pharmaceutical targets for neurodegenerative and pain disorders.

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