The role of eicosanoids in the brain.

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The brain contains two main polyunsaturated fatty acids (PUFA), arachidonic acid (AA) and docosahexaenoic acid (DHA). These PUFA are located almost exclusively in the sn2-position of phosphoglycerides which are found in the neural cell membranes. Liberation of these PUFA from the phosphoglycerides occurs via the action of specific phospholipases (PLA2). Free AA can be metabolised by cyclooxygenases to prostaglandins and thromboxane, while both AA and DHA can be metabolised by lipoxygenases to form hydroxy derivatives and leukotrienes. AA is also metabolised to lipoxins via the 5-lipoxygenase pathway. The eicosanoids formed play important roles in neural function including sleep induction (PGD2), long term potentiation, spatial learning and synaptic plasticity (PGE2), resolution of inflammation (lipoxins) and anti-inflammatory and neuroprotective bioactivity (dihydroxy-docosatriene, neuroprotectin D1, formed from DHA). COX-inhibitors have been shown to reduce oxidative stress and cognitive impairment. Additionally, drugs which are used to treat depression have been shown to reduce the turnover of AA to PGE2 in the brain. Diets deficient in omega 3 PUFA lead to reduced DHA in the brain and increased turnover of AA to eicosanoids, an effect which is overcome by restoring the omega 3 PUFA to the diet. In neural trauma and neurodegenerative diseases, there is a dramatic rise in the levels of AA-derived eicosanoids. In contrast, DHA-derived compounds can prevent neuroinflammation. Clearly, the eicosanoids are very important for the normal functioning of the brain, while the PUFA themselves are important in membrane structure and function.