# Alterations in dietary n-3 and n-6 fatty acids for treating chronic headaches

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Many patients with chronic pain continue to experience substantial pain and impaired quality of life despite taking multiple medications. It is therefore essential to investigate novel mechanisms and complementary approaches to manage pain. As major components of myelin, glial, and neuronal cell membranes, n-3 and n-6 fatty acids can be endogenously converted to several families of bioactive lipid autacoids with pro- or antinociceptive properties (eg, eicosanoids, endocannabinoids, endovanilloids, resolvins). With several notable exceptions, mediators derived from n-6 linoleic (LA) and arachidonic (AA) promote nociception, while mediators derived from n-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) promote anti-nociception. Thus, an imbalance of mediators derived from n-3 and n-6 fatty acids is a plausible mechanism that may contribute to the development and maintenance of chronic pain disorders including headaches. In a small randomized trial in 67 patients with chronic headaches, we found that increasing dietary n-3 with concurrent reduction in n-6 fatty acids (the H3-L6 diet) produced statistically significant improvements in headache frequency and severity, psychological distress and function. These clinical improvements were accompanied by increases in pathway precursors for n-3 derived lipid mediators of anti-nociception, and reductions in n-6 derived mediators of nociception in circulation. Therefore, targeted alterations in dietary n-6 and n-3 fatty acids may be able to modulate nociceptive lipid mediators to reduce physical pain. However, current understanding of the molecular pathways and specific lipid autacoids linking diet to physical pain is limited. In this presentation I will review emerging preclinical and clinical evidence and highlight key gaps along the proposed causal chain linking dietary n-3 and n-6 fatty acids to the etiology of chronic pain.