The effect of eicosapentaenoic acid on brain and platelet produced bioactive lipid mediators. The effect of eicosapentaenoic acid, docosapentaenoic acid and other polyunsaturated fatty acids on the eicosanoids and endocannabinoids produced by rat brain and human platelets using electrospray ionisation tandem mass spectrometry-based analysis.

Thesis title

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Keywords

Eicosapentaenoic acid, docosapentaenoic acid, eicosanoids, endocannabinoids, liquid chromatography tandem mass spectrometry, brain, platelets

Abstract

Eicosapentaenoic acid (EPA) is a polyunsaturated fatty acid (PUFA) with neuroprotective and cardioprotective properties. It is thought that some of the actions of EPA may be attributed to its elongated metabolite, the PUFA docosapentaenoic acid (DPA). Docosahexaenoic acid (DHA) and arachidonic acid (AA) are bioactive PUFA ubiquitously expressed in neural tissues. EPA and AA can be converted by cyclooxygenase (COX) to prostanoids and by lipoxygenase (LOX) to hydroxy fatty acids. PUFA can also be converted to ethanolamides in the brain. These mediators are involved in physiological and pathological processes in many bodily systems.

The purpose of this study was to examine the production of eicosanoids, hydroxy fatty acids and fatty acid ethanolamides in young and aged rat brain following EPA or DPA enriched diets. The effects of specific PUFA on human platelet eicosanoid production were also investigated as these mediators play a role in adhesion and aggregation. Liquid chromatography coupled to tandem mass spectrometry (LC/ESI-MS/MS) assays were developed and used to measure lipid mediators in rat brain and human platelets.

Ageing in rat brain was accompanied with several changes in the prostanoid and hydroxy fatty acid profiles. Supplementing the diet with EPA or DPA at a daily dose of 200 mg/kg for 8 weeks prevented these changes and decreased levels of PGE_2. DPA changed the profile of hydroxy fatty acids synthesised in the brain tissue of young animals. This study has shown that levels of eicosapentaenoylethanolamide (EPA-EA) increase in the brain as a result of ageing and that this is accompanied by an increase in levels of anandamide. Feeding aged animals EPA or DPA further increased the levels of EPA-EA but prevented any change in the level of anandamide.

Niacin is used to treat hypercholesterolaemia although it is associated with an unpleasant PGD_2 mediated skin flush. This exploratory study has shown that human platelets treated with niacin did not show any changes in their prostanoid and hydroxy fatty acid profiles. Platelets treated with EPA showed increased production of TXB_3 and 12-HEPE. Niacin augmented the effects of EPA on human platelet mediator synthesis.

Overall, this study has demonstrated that EPA can change brain and platelet lipid mediator synthesis and has provided evidence that could explain some of the neuroprotective and cardioprotective actions of this PUFA.

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