

Abstract

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Omega-3 fatty acid supplementation and reduction of traumatic axonal injury in a rodent head injury model.

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OBJECTIVE: Traumatic brain injury remains the most common cause of death in persons under 45 years of age in the Western world. Recent evidence from animal studies suggests that supplementation with omega-3 fatty acid (O3FA) (particularly eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) improves functional outcomes following focal neural injury. The purpose of this study is to determine the benefits of O3FA supplementation following diffuse axonal injury in rats.

METHODS: Forty adult male Sprague-Dawley rats were used. Three groups of 10 rats were subjected to an impact acceleration injury and the remaining group underwent a sham-injury procedure (surgery, but no impact injury). Two of the groups subjected to the injury were supplemented with 10 or 40 mg/kg/day of O3FA; the third injured group served as an unsupplemented control group. The sham-injured rats likewise received no O3FA supplementation. Serum fatty acid levels were determined from the isolated plasma phospholipids prior to the injury and at the end of the 30 days of supplementation. After the animals had been killed, immunohistochemical analysis of brainstem white matter tracts was performed to assess the presence of beta-amyloid precursor protein (APP), a marker of axonal injury. Immunohistochemical analyses of axonal injury mechanisms-including analysis for caspase-3, a marker of apoptosis; RMO-14, a marker of neurofilament compaction; and cytochrome c, a marker of mitochondrial injury-were performed.

RESULTS: Dietary supplementation with a fish oil concentrate rich in EPA and DHA for 30 days resulted in significant increases in O3FA serum levels: 11.6% +/- 4.9% over initial levels in the 10 mg/kg/day group and 30.7% +/- 3.6% in the 40 mg/kg/day group. Immunohistochemical analysis revealed significantly ($p < 0.05$) decreased numbers of APP-positive axons in animals receiving O3FA supplementation: 7.7 +/- 14.4 axons per mm² in the 10 mg/kg/day group and 6.2 +/- 11.4 axons per mm² in the 40 mg/kg/day group, versus 182.2 +/- 44.6 axons per mm² in unsupplemented animals. Sham-injured animals had 4.1 +/- 1.3 APP-positive axons per mm². Similarly, immunohistochemical analysis of caspase-3 expression demonstrated significant ($p < 0.05$) reduction in animals receiving O3FA supplementation, 18.5 +/- 28.3 axons per mm² in the 10 mg/kg/day group and 13.8 +/- 18.9 axons per mm² in the 40 mg/kg/day group, versus 129.3 +/- 49.1 axons per mm² in unsupplemented animals.

CONCLUSIONS: Dietary supplementation with a fish oil concentrate rich in the O3FAs EPA and DHA increases serum levels of these same fatty acids in a dose-response effect. Omega-3 fatty acid supplementation significantly reduces the number of APP-positive axons at 30 days postinjury to levels similar to those in uninjured animals. Omega-3 fatty acids are safe, affordable, and readily available worldwide to potentially reduce the burden of traumatic brain injury.

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