Aggression, Fish Oil, and Noradrenergic Activity

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KEY POINTS

• Fish oil reduces aggression in young adults, female schoolchildren, and children with attention-deficit/hyperactivity disorder.
• Attention-related symptoms of attention deficit/hyperactivity disorder are improved by learning but not following docosahexaenoic acid.
• The effects of docosahexaenoic acid could be explained by depression of central noradrenergic activity rather than enhancement of central serotonergic activity.
• Central nonadrenergic activity could explain fish oil’s preventive effects against sudden cardiac death (lethal arrhythmias).

1. INTRODUCTION

Fish oil is known to exert an influence on behavior and mood. We have been studying the effects of fish oil, especially docosahexaenoic acid (DHA), a major active component of fish oil, on aggression in double-blind trials (see below). Cross-national association of economy-related seafood consumption with the incidence of major depression (Hibbeln, 1998) and bipolar disorders (Noaghiul & Hibbeln, 2003) suggest that greater seafood consumption predicts lower lifetime prevalence rates of those psychiatric disorders. Stoll et al. (1999) reported a preliminary interventional trial of patients with bipolar disorder in which symptoms were reduced in the fish oil group. A few double-blind studies (Nemets, Stahl, & Belmaker, 2002; Peet & Horrobin, 2002) aimed at major depression with eicosapentaenoic acid (EPA), another major active fish oil component, were also successful. We recently performed a case-control study of suicide attempt in China and found that EPA and DHA in the red blood cells of suicide attempters (n = 100) were significantly lower than in controls (n = 100) (Huan et al., 2004).

These studies all imply that fish oil may activate the central serotonergic system. However, our other recent studies seem to support a hypothesis that the central noradrenergic system may be depressed by fish oil administration. This chapter discusses the relationship of aggression and fish oil from a new point of view, namely, the central adrenergic system.
2. THE AGGRESSION-CONTROLLING EFFECTS OF FISH OIL

About 10 yr ago we performed a double-blind study using students as subjects. Forty-one students were allocated to either a control (n = 22) or a DHA group (n = 19) in a double-blind manner. Subjects of the DHA group were asked to take 10–12 capsules containing DHA-rich fish oil (1.5–1.8g DHA/d) for 3 mo. Those in the control group took a soybean-based control oil. At the start and end of the study, aggression of the subjects was measured with the Picture-Frustration (PF) Study (Rosenzweig, 1978). This psychological test consisted of 24 pictures illustrating frustration. Subjects were asked to look at pictures and describe their first reactions. Their reactions were regarded as aggression if their comments were against others. The degree of aggression was calculated as 100 × total aggressive comments/24. There was a stressor component at the end of the study. A few days after the second (last) PF Study, either the final or most important term exams started for all the subjects. Therefore, subjects were likely stressed while busy preparing for the exams around the last PF Study. Aggression in the control group increased (from 35 to 45; p < 0.002) because of the presence of the stressor, but it stayed unchanged (at 31) in the DHA group. There were highly significant differences in changes in aggression between the two groups (p < 0.003). This study indicated a possibility that stressor-enhanced aggression might be controlled by prior administration of DHA (Hamazaki et al., 1996). When there was no stressor, DHA supplementation did not decrease aggression, but might even have increased it with marginal significance (Hamazaki et al., 1998).

Several groups of investigators have reported relationships between fish oil and aggression or hostility. Gesch, Hammond, Hampson, Eves, and Crowder (2002) performed a placebo-controlled, double-blind, randomized trial of nutritional supplements (including essential fatty acids) on 231 young adult prisoners for a minimum of 2 wk, and found that, compared with those receiving placebos, those receiving the active capsules committed significantly fewer offenses. The amounts of fatty acids provided to the experimental group were so small—80 mg EPA and 44 mg DHA—that it is difficult to determine if those n-3 fatty acids contributed to reducing the offenses. However, this study is in line with the idea that n-3 fatty acids are able to control aggressive behavior.

Very recently a relationship between DHA and hostility was also found in a large-scale epidemiological study. Iribarren et al. (2004) reported a cross-sectional observational study as part of an ongoing cohort study, the Coronary Artery Risk Development in Young Adults (CARDIA) study. The multivariate odds ratios of scoring in the upper quartile of hostility measure using the Cook-Medley scale were significantly lower by 10% with one standard deviation higher DHA intake.

In one of our recent DHA-supplementation studies, 166 schoolchildren 9–12 yr of age (81 boys and 85 girls) were in a placebo-controlled, double-blind trial (Iomura et al., 2005). Subjects in the DHA group took DHA-fortified foods (3.6 g of DHA + 0.84 g of EPA/wk) for 3 mo. Impulsivity in girls assessed by their parents was significantly decreased in the DHA group compared with the control group. This effect of DHA was not observed in boys. Impulsivity is also related to serotonin function (Krakowski, 2003).

3. DHA, THE SEROTONERGIC SYSTEM, AND AGGRESSION

An inverse relationship between a lifelong aggression history and concentrations of 5-hydroxyindolacetic acid (5-HIAA), the major metabolite of serotonin, in the cerebrospi-