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LETTER TO THE EDITOR

n−3 Fatty acids and the endocannabinoid system

Eiji Oda

Department of Internal Medicine
Niigata Prefectural Yoshida Hospital
Yoshida Daibochou 32-14
Tsubame, Niigata 959-0242
Japan
E-mail: ijie{at}venus.sannet.ne.jp

Dear Sir:

Carpentier et al (1) mentioned in a recent issue of the Journal that the pleiotrophic effects of n−3 polyunsaturated fatty acids (PUFAs) decrease the burden of the metabolic syndrome, which prevails in Western countries and is related to the epidemic of obesity. In large epidemiologic studies, persons who consume higher amounts of fish also consume higher amounts of total calories but are not more obese, although the levels of exercise are similar in both Western countries (2, 3) and in Japan (4). Previously, I speculated that, at least in part, the beneficial effects of fish oil on obesity and obesity-related metabolic risk factors may be related to long-chain monounsaturated fatty acids (5), which may have relatively high ligand activities on peroxisome proliferator–activated receptor delta (6). Recently, Horvath (7) reviewed the effects of the endocannabinoid system on energy homeostasis and pointed out that the initial anorectic effect of the cannabinoid receptor 1 (CB1) antagonist, rimonabant, is diminished after the first weeks, whereas longer lasting weight loss is achieved. These findings indicate that the peripheral metabolic actions of cannabinoids are very important in body weight regulation. It is possible that n−3 PUFAs may act as competitive inhibitors in the peripheral endocannabinoid system, thereby promoting energy metabolism and exerting antiobesity and antiinflammatory effects. Two major CB1 agonists—anandamide (arachidonoyl ethanolamine) and 2-arachidonoyl glycerol—are n−6 PUFA derivatives, whereas n−3 and n−6 PUFAs are competitors as components of cell membrane phospholipids and in many biochemical pathways, such as eicosanoids and leukotrienes. At least in the brain of mice, n−3 PUFA deficiency elevates and n−3 PUFA enrichment reduces 2-arachidonoyl glycerol concentrations (8).

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REFERENCES

1. Carpentier YA, Portois L, Malaisse WJ. n−3 Fatty acids and the metabolic syndrome. Am J Clin Nutr 2006;83 (suppl):S1499–504.[Abstract/Free Full Text]
2. Mozaffarian D, Psaty BM, Rimm EB, et al. Fish intake and risk of incident atrial fibrillation. Circulation 2004;110:368–73.[Abstract/Free Full Text]
3. Frost L, Vestergaard P. n−3 Fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. Am J Clin Nutr 2005;81:50–4.[Abstract/Free Full Text]
4. Iso H, Kobayashi M, Ishihara J, et al. Intake of fish and n−3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-based (JPHC) Study Cohort 1. Circulation 2006;113:195–202. [Abstract/Free Full Text]
5. Oda E, Hatada K, Kimura J, et al. Relationship between serum unsaturated fatty acids and coronary risk factors. Negative relations between nervonic acid and obesity-related risk factors. Int Heart J 2005;46:975–85.

6. Johnson TE, Holloway MK, Vogel R, et al. Structural requirements and cell-type specificity for ligand activation of peroxisome proliferator-activated receptors. J Steroid Biochem Molec Biol 1997;63:1–8.[Medline]
7. Horvath TL. The unfolding cannabinoid story on energy homeostasis: central or peripheral site of action? Int J Obes Relat Metab Disord 2006;30:530–2.
8. Watanabe S, Doshi M, Hamazaki T. n–3 Polyunsaturated fatty acid (PUFA) deficiency elevates and n–3 PUFA enrichment reduces brain 2-arachidonoylglycerol level in mice. Prostaglandins Leukot Essent Fatty Acids 2003;69:51–9.[Medline]