



Editorial

Omega-3 Fatty Acids and Obesity

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Obesity rates continue rise to worldwide. In order to reduce the morbidity and mortality associated with obesity, as well as alleviate the impact on health care expenditures, the need for efficacious treatment strategies are in high demand. One promising approach is to include a diet high in “functional foods” into a weight loss regimen. Such foods provide an alternative to the limited number of FDA-approved pharmacotherapeutics and are a healthy option to the use of unregulated botanical and diet supplements. For instance, a diet high in omega-3 fatty acids (ω -3 FAs) has the potential to aid in the management of obesity and associated metabolic alterations. This concept emerged from the early studies of the Greenland Eskimos, which consumed of 700 mg/day dietary fat from marine fish. These fats were dense in ω -3 FAs and were associated with a significantly lower heart disease risk compared to Eskimos consuming a Western diet [1]. Benefits of omega-3 rich foods like fish, flaxseed, green leafy vegetables and some spices have been widely reported. Organizations such as American Heart and the WHO already recommends the consumption of 200 to 500 mg of ω -3 FAs in the form of eicosapentaenoic and docosahexaenoic acid (EPA and DHA respectively) 1 to 2 times per week for cardiovascular health.

More recently, however, a more scientific approach and the mechanisms behind the benefits of ω -3 FA research have been explored. Hainault et al. [2] demonstrated adipose tissue deposits from animals fed ω -3 FAs have 20 to 30% less subcutaneous and visceral fat, respectively [2]. Additional studies by Belzung et al. [3] suggest that there is a dose response protective effect for ω -3 FAs specifically that the highest dose showed the greatest reduction in epididymal fat mass and a dose dependent attenuation of retroperitoneal fat mass [3]. It has been suggested earlier by Parrish et al. [4] that these protective effects may be a result of reductions in fat deposited in existing adipocytes since their results showed no change in adipocyte number, just size when the animals were put on an ω -3 FAs rich diet [4]. Exploration of the mechanisms behind this change in fat accumulation by Cunnane et al. [5] showed that ω -3 FAs are incorporated in to the liver and adipose tissue deposits. These findings suggest that ω -3 FAs could potentially alter gene expression and change metabolic activity in these tissues [5]. Obesity and the majority of its comorbidities (heart disease, diabetes, cancer) are strongly linked to inflammation; therefore treatments that reduce inflammation are attractive. ω -3 FAs are known to be anti-inflammatory and it was recently reported their effects are receptor mediated [6]. The putative receptor, GPR120, belongs to a group of G-protein coupled receptors, which is one of five possible receptors stimulated by Free Fatty Acids (FFAs) [6].

Long chain FFAs, palmitoleic acid, α -linolenic acid (ALA), and DHA, and all omega-3-type fatty acids, were shown to elicit an increased response in Extracellular signal-Regulated Kinase (ERK) (p44/42) in HEK 293 cells expressing mouse GPR120. In contrast, linolenic acid methyl ester, an omega-6 fatty acid (ω -6 FA), elicited no response. This confirms not only that GPR120 is a fatty acid receptor, but also that it specifically binds ω -3 FAs. An early study [7] did not specify what the response of ω -3 FAs GPR120 binding was, nor if the effect was excitatory or inhibitory. Therefore, Oh et al. [6] utilizing the synthetic agonist GW9508, DHA, and EPA, tested the effect of ω -3 FAs in RAW 264.7 cells, expressing GPR120, of obese WT mice and GPR120 knock-out (KO) mice [6]. When exposed to ω -3 FAs, the WT mice showed a reduction in pro-inflammatory mediators such as TNF- α and TLR4, inhibiting pro-inflammatory pathways associated with NF- κ B, whereas the effect in GPR120 KO mice showed no effect. Through a series of studies this group proposed that the mechanism by which ω -3 FAs was seen to have an anti-inflammatory effect involves β -arrestin2, a protein stimulated by the binding of ligands to GPR120. Oh et al. [6] also established the presence of GPR120 in adipose tissue, pro-inflammatory CD11c+ macrophages, and mature adipocytes. This suggests that ω -3 FAs could exert influence at these cells and tissues to modify the inflammatory response reduce adiposity and reduce incidence of diabetes.

While these studies are exciting and provide insight to the mechanisms of ω -3 FAs and their actions, there is limited work in humans. Observational studies have suggested that there is a relationship between high ω -3 FAs consumption and lower body weight. Both The Women’s Cohort Study [8] and the Health Professionals Follow-Up Study showed that men and women who ate seafood (high in ω -3 FAs) had the lowest body mass index [9] and higher overall health. This is further supported by a few small human trials that suggest incorporation of ω -3 FAs can reduce adiposity [10], attenuate postprandial hunger sensation [11,12] and promote increases in lean tissue mass [13-15]. A recent, double-blind, randomized, controlled trial with two parallel groups on very low calorie diets, one group diet was supplemented with ω -3 FAs (in the form of fish oil) found that the fish oil group showed an improved metabolic profile, however it is hard to distinguish the differences that may have been brought on by a low calorie diet and those by ω -3 FA supplementation [16]. These studies give promise to the influence that incorporation of ω -3 FAs may have an impact on obesity. However, more is needed to investigate the direct impact of ω -3 FAs and obesity outcomes.

As the focus of nutritional concerns in the United States has changed over the past decades, with nutritional deficiencies giving way to health problems associated with nutritional excesses there has been an effort to address diet quality. These recommendations serve to improve health outcomes and reduce morbidity and mortality. Recent reports on the diet quality of Americans finds [17] that there is still a need to choose more nutrient dense foods that are low in saturated fats and added sugars. Whole grains, fruit, dark green and orange vegetables, legumes, and healthy fats, ω -3 FAs, are still among those “foods that need to be encouraged.” Understanding the link between ω -3 FAs, obesity and reduced inflammation leading to improved health outcomes is critical. To date, research in animals

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and some human studies suggest that ω -3 FAs are safe and provide benefits ranging from prevention of weight gain to activating anti-inflammatory pathways. Additional large-scale RCTs are needed to critically assess the efficacy of ω -3 FAs as a benefit from the treatment of obesity and associated metabolic outcomes.

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