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Omega-3 fatty acids and exercise: a review of their combined effects on body composition and physical performance

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Summary

Omega-3 (n-3) fatty acids, and the long-chain n-3 derivatives eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in particular, have been extensively researched for their nutritive effects. Among their many purported benefits, n-3 acids have been implicated as positive mediators of cardiovascular health and body composition. It has therefore been speculated that supplementation may enhance the beneficial effects of physical activity, potentiating greater reductions in body fat and improvements in exercise performance. This paper has three objectives: first, to assess the theoretical basis for a synergistic ef-fect when n-3 supplementation is combined with exercise; second, to review the literature as to specific findings on the subject and third, to make relevant conclusions and recommendations for future research.

Key words: Omega-3 fatty acids – Body composition – Physical performance

Introduction

Omega-3 (n-3) fatty acids, and the long-chain n-3 derivatives eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in particular, have been extensively researched for their nutritive effects. However, despite evidence dating back to the 1930's that n-3 acids are essential for normal growth and dermal function, only in the past several decades have they received just attention for their role as health-promoting agents [32]. Among their many purported benefits, n-3 acids have been implicated as positive mediators of cardiovascular health and body composition.

Initial interest in the cardiovascular benefits of EPA and DHA was aroused by the finding that the Greenland Eskimos and other populations who consume diets rich in these fatty acids have exceedingly low incidences of cardiovascular diseases [20,85]. A large number of both experimental and epidemiological studies have since been conducted to examine the effect of consuming fish oil, which contains high amount of n-3 acids, on cardiovascular health, with a majority showing an inverse correlation on morbidity and mortality [1,33,40,51,63,68]. The cardioprotective effects of n-3 acids are attributed to improvements in various cardiovascular risk factors including a reduction in blood platelet aggregation [45,58], decreased inflammation [29,88], enhanced endothelial function [21], positive changes in blood lipids [9,28,30], and decreased blood pressure [55,60].

The n-3 consumption has also been associated with favourable alterations in body composition. Animal studies have consistently shown a reduced adiposity and an increase in lean tissue growth when dietary n-3 derivatives are substituted for saturated fats [27,50,54], monounsaturated fats [71], and omega-6 (n-6) fatty acids [16, 34,56] on a calorie-for-calorie basis. To date, controlled experiments examining the effect of differing dietary fatty acid compositions on body composition in human subjects are conflicting. Some human trials [15,38,49,78], but not all [22,36], have reported reductions in fat mass with n-3 consumption compared to other oils. Interestingly, DeLany *et al.* [18] found that omega-3s were preferentially metabolised by the body after ingestion in comparison to other fatty acids, noting a high linear relation between oxidation and the number of double bonds.

Given the purported benefits of n-3 on the cardiovascular system and fat metabolism, it has been speculated that supplementation may enhance the beneficial effects of physical activity, potentiating greater reductions in body fat and improvements in exercise performance.

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Thus, the purpose of this paper will be threefold: first, to assess the theoretical basis for a synergistic effect when n-3 supplementation is combined with exercise; second, to review the literature as to specific findings on the subject, and, third, to make relevant conclusions and recommendations for future research.

Theoretical Basis for n-3 Supplementation in Combination with Exercise

Biochemically, n-3 acids are a class of essential polyunsaturated fatty acids that have the first carbon-carbon double bond in the third position from the methyl end of the fatty acid (the n-3 position) and additional double bonds depending on the molecule. Numerous longer chain n-3 fatty acids exist in nature, the most studied of which include the 20 carbon chain EPA with 5 double bonds (known as 20:5) and the 22 carbon chain DHA with 6 double bonds (22:6). EPA and DHA are found in various cold water fish including salmon, mackerel, sardines, and herring. The shortest chain form of n-3 is α-linolenic acid (ALA), which contains 18 carbon atoms and 3 double bonds (18:3). ALA is found in various plant sources such as flaxseeds, soybeans, and walnuts. Human beings can convert ALA into longer chain derivatives through the delta-desaturase enzymatic pathways [47]. However, conversion is largely inefficient, with only 5% of ALA reportedly converted to EPA and less than 0.5% to DHA [59]. This is significant because the longer chain derivatives are purported to have the greatest biological effects in human beings.

With respect to exercise, one potential mechanism whereby n-3 supplementation may enhance benefits is *via* increased lipolysis and β-oxidation. Specifically, n-3 fatty acids are claimed to act as metabolic fuel partitioners [13], upregulating lipid oxidative enzymes and downregulating lipogenic gene expression [35,62]. This is due, at least in part, to the ability of n-3 acids to bind and activate the various peroxisome proliferator-activated receptor (PPAR) isoforms [42,48,67]. PPARs are members of the nuclear receptor superfamily and include PPAR-α, PPAR-γ, and PPAR-δ [24]. The n-3 acids have a particular affinity to act as ligands for the PPAR-α isoform, which is located in the cell nucleus of many body tissues, predominantly those that exhibit high oxidative rates of fatty acids such as the liver, heart, kidney, and muscle [19]. PPAR-α was shown to play an integral role in the management of glucose and fatty acid homeostasis [72], inducing the expression of several gene encoding proteins involved in lipid transport and oxidation including hepatic carnitine acyltransferase, and hepatic and skeletal muscle peroxisomal acyl-CoA oxidase [14]. Hypothetically, increased PPAR-α activity should enable a greater reliance on fat for fuel during exercise while sparing muscle glycogen, and improving both body composition and exercise per-formance. Moreover, n-3 acids may indirectly influence lipid oxidation by suppressing the generation of acetyl-CoA carboxylase [84], which catalyses synthesis of the lipogenic co-enzyme A derivative malonyl-CoA [12]. Malo-nyl-CoA serves as a fatty acid precursor primarily by impairing the activity of the enzyme carnitine palmitoyl-transferase [87], responsible for facilitating the transport of existing fatty acids back into the mitochondrial matrix where they can be oxidised for fuel. By suppressing ma-lonyl CoA, n-3 acids indirectly increase the levels of carnitine palmitoyltransferase, thereby favouring the entry of fatty acids into the mitochondria. This, conceivably, would further enhance the availability of fatty acid substrate for β-oxidation during exercise.

Another mechanism, whereby n-3 acids may confer a positive effect on exercise, is by improving fatty acid delivery to exercising muscles *via* an increased blood flow [31]. Blood flow improvements are believed to be due to an n-3 mediated suppression of n-6 eicosanoid production. Specifically, n-3 and n-6 acids compete for δ-6 desaturase, i.e. for further elongation and desaturation [32]; a high n-6/n-3 ratio can lead to elevated levels of pro-inflammatory prostaglandins and thromboxanes [33,79]. Given that these eicosanoids are pro-aggregatory vasoconstrictors, excessive amounts can lead to reductions in vascular blood flow [64]. Supplementing with n-3 can potentially help to inhibit inflammatory eicosa-noid production, as well as interacting with cyclooxygenase in a manner that reduces platelet aggregation, increases dilation of blood vessels, and improves circulatory response [33,46,80]. Indeed, Walser *et al.* [80] demonstrated that 6 weeks of supplementation with DHA (2.0 g/day) and EPA (3.0 g/day) enhanced exercise-induced increases in brachial artery diameter and blood flow during 90 s of low-intensity handgrip exercise.

Supplementation with n-3 acids may facilitate additional blood flow improvements in exercise by helping to prevent a reduction in red blood cell (RBC) deformability. Exercise has been shown to cause stiffening of erythrocytes [23] which, in turn, can impede circulatory responses [73]. These reductions in RBC deformability have been attributed to an increased peroxidation of lipid membranes resulting from exercise-induced free radical production [74]. A number of studies suggest that n-3 derivatives help to increase the deformability of RBCs [11,76] which would theoretically heighten oxygen and nutrient delivery to exercising muscles and thereby enhance performance.

Table 1. Findings of studies with omega-3 fatty acids ingestion

Effects of omega-3 fatty acids on cardiovascular health	
Low morbidity and mortality	[1,33,40,51,63,67]
Reduction in blood platelet aggregation	[45,58]
Decreased inflammation	[29,88]
Enhanced endothelial function	[21]
Positive changes in blood lipids	[9,28,30]
Increased blood flow	[31,33,46]
Decreased blood pressure	[55,60]
Effects of omega-3 fatty acids on body composition	
Reduced adiposity and increased lean body tissue	[27,38,49,50,53, 54,78]
Decreased appetite	[53]
Effects of omega-3 fatty acids during exercise	
Increased brachial artery diameter	[80]
Loss of body fat	[17,31,81]
Attenuated red blood cell deformability	[26]
Decreased submaximal O_2 uptake and heart rate	[8,57]
Delayed muscle soreness	[75]
Increased exercise-induced protein synthesis	[49,65,70]

Studies Investigating n-3 Acids and Exercise

Despite a wealth of research on the health-related benefits of n-3 acids, studies investigating the effects of combining n-3 supplementation and exercise are limited. The following is a review of the current literature as to studies specifically addressing changes in body composition and exercise performance. To date, only 4 studies could be located that directly evaluated changes in body composition associated with the combined effects of n-3 supplementation and exercise but the results were not uniform.

Warner *et al.* [81] randomly assigned 34 hyperlipidemic subjects to one of 4 groups: fish oil plus exercise, fish oil, corn oil, and control [81]. The exercise group performed aerobic training 3 days a week for 45 – 50 min at 75 – 80% of maximal heart rate. Supplementation amounted to 50 ml of either fish oil or corn oil daily. After 12 weeks, only the fish oil plus exercise group lost a significant amount of body fat. However, the study was limited by the lack of an exercise-only control group, making it difficult to ascertain whether results were due to the combination of fish oil and training *versus* the training protocol alone.

In a controlled study, Brilla and Landerholm [7] assigned healthy, previously sedentary male subjects (19 – 34 years of age; body fat content 15 – 22%) to one of 4 groups: fish, exercise, fish and exercise, and control. The exercising subjects performed three, one-hour aerobic sessions per week. Total omega-3 fatty acid intake in the groups consuming fish was calculated at 4 g/day. After 10 weeks, no significant differences in body composition were noted between any of the groups studied. The fairly low initial body fat levels in participants, however, may have limited the results.

Hill *et al.* [31] assigned 65 overweight (BMI > 25), previously sedentary subjects (24 males, 41 females) with hypertension and/or hyperlipidemia to one of 4 groups: fish oil, fish oil plus exercise, sunflower oil (a source of n-6 fatty acids), or sunflower oil plus exercise. Exercise consisted of walking at 75% of age-predicted maximal heart rate for 45 min three days a week. After 12 weeks, 6 g of fish oil plus exercise resulted in a significantly greater reduction in body fat compared to an equal dose of sunflower oil plus exercise (1.2% and 0.1%, respectively).

Most recently, DeFina *et al.* (2010) conducted a placebo-controlled, randomised trial where 128 overweight and obese subjects (BMI≥26 and <40) were assigned to receive either capsules containing 3.0 g of EPA and 0.6 g of DHA or placebo [17]. Both groups underwent dietary counselling and were provided with calorie-controlled nutritional regimens. In addition, participants received health club memberships and were instructed to perform aerobic exercise at 50 – 85% $\dot{V}O_2$max, 150 min a week, in combination with 20 – 30 min of total-body strength training exercise performed twice weekly. Adherence to the protocol was monitored by the completion of dietary recalls and exercise diaries. After 24 weeks, subjects in both groups lost slightly more than 5% of their body mass with no significant between-group differences reported. The study was limited by self-reported energy intake and expenditure information, which has been shown to be unreliable, particularly in overweight and obese individuals [4,69].

As with the research on body composition, the number of studies directly examining the effects of n-3 supplementation on exercise performance is also limited. Guezennec *et al.* [26] examined the effects of fish oil supplementation on RBC deformability in 14 trained male subjects (19 – 38 years of age) over 6 weeks. Subjects were divided into two groups: a supplement group that consumed 6 g/day of fish oil and a control group that consumed a "standard diet" rich in saturated fats. The participants performed two, one-hour cycling bouts at 70% $\dot{V}O_2max$, pre- and post-study. One test was performed at sea level and the other in a hypobaric chamber at a simulated altitude of 3000 m. The results showed that fish oil supplementation significantly attenuated RBC deformability under hypoxic conditions compared to controls. In contrast to those findings, Oostenbrug et al. [52] recruited 24 trained male cyclists (aged 19 – 42 years) to investigate the effects of 3 weeks of fish oil supplementation (6 g/day) on RBC deformability. At the end of the supplementation period, subjects performed a one-hour bicycle time trial and were evaluated for RBC characteristics. Results showed no significant difference in RBC characteristics nor were any improvements in aerobic endurance performance noted. However, the three-week protocol may not have been long enough to realise an ergogenic effect.

Peoples *et al.* [57] investigated the effect of fish oil supplementation on oxygen consumption during exercise. Using a double-blind, parallel design, 16 well-trained male cyclists were randomly assigned to consume either 8 g/day of fish oil (n = 9; age 23.2 ± 1.2 years) or 8 g/day of olive oil, a source of omega-9 fatty acids (n = 7; age 27.1 ± 2.7 years) for 8 weeks. Subjects were tested on a cycle ergometer for peak oxygen consumption and sustained submaximal exercise at 55% of peak workload both before and after supplementation. At the end of the study, those of the fish oil group had significantly lowered heart rates during incremental workloads to exhaustion as well as displaying lowered steady-state submaximal exercise heart rates, whole-body oxygen consumption, and rate pressure product. However, fish oil supplementation had no significant impact on peak oxygen consumption, a finding consistent with some [52,61] but not all [39] studies.

Yates *et al.* [86] studied lipid profiles and the use of n-3 acids in professional football players. A total of 36 active national football players were randomly assigned to 2 groups: the first group (n = 20) was provided fish oil capsules (2200 mg of mixed DHA, EPA, and 360 mg of other omega-3 acids), and the second group (n = 16) served as controls during a 60-day trial. Serum LDL, HDL, and other subfractions were measured. Compliance, side effects, and seafood consumption data were also collected. Supplementation with n-3 significantly improved the lipid profile of active players randomised to treatment. It was suggested that n-3 supplementation should be considered as a method to improve modifiable cardiovascular risk lipid factors in professional football players.

Finally, Buckley *et al.* [8] evaluated the effects of n-3 on endurance performance and recovery in 25 elite Australian Rules football players. In a double-blind design, subjects were randomly assigned to either 6 g/day of DHA or sunflower oil over the course of a 5-week training period. The subjects performed two separate treadmill trials to exhaustion at a speed equivalent to their average running speed for a 2200-m time-trial, pre- and post-study. The trials were separated by 5-min intermissions. Time to exhaustion (TTE) for Trial 1 was used to assess endurance performance while TTE for Trial 2 was used to assess exercise recovery. Results showed that while heart rate during submaximal exercise was reduced in the fish oil group, no differences were noted between groups in exercise performance or recovery.

Concluding Remarks

At this time, research is largely inconclusive as to the potential synergistic benefits when n-3 is supplemented in conjunction with exercise. There is some evidence that n-3 can modestly enhance lipolysis and β-oxidation during exercise and thereby improve fat loss. There also is modest evidence that n-3 supplementation may help to improve various aspects of exercise performance. However, limitations in study design make it difficult to draw firm conclusions on these topics.

Other areas related to the combined effects of n-3 supplementation and exercise still remain to be explored. For example, given the antagonistic effect of n-3 acids on pro-inflammatory eicosanoids [10], supplementation may help to alleviate exercise-related delayed-onset muscle soreness (DOMS), which can indirectly benefit exercise performance. Positive effects on DOMS may be augmented by the ability of n-3 acids to increase blood flow, thereby aiding in a more rapid nutrient delivery post-exercise. Some studies have shown a beneficial effect [75] while others have not [41]. Further studies are warranted to assess whether n-3 acids may, in fact, produce analgesic effects.

Another area for potential study is the effect of n-3 supplementation on exercise-induced protein metabolism. A number of studies show that n-3 supplementation results in greater accretion of muscle proteins in both animals [3,5,25] and human beings [49,65,70]. Increased protein synthesis may be secondary to n-3 mediated increases in cell membrane fluidity [2]. Cell membranes are vital for regulating the passage of nutrients, hormones and chemical signals into and out of cells. When cell membranes are fluid, they become more permeable, allowing substances and secondary messenger molecules associated with protein synthesis to readily penetrate the cytoplasm [5,25,37]. The n-3 may also enhance mTOR/p70s6k signalling [70], a pathway believed to act as a master network regulating skeletal muscle growth [6,77]. In addition, there is some evidence that n-3 supplementation may decrease proteolysis by downregulating the ubiquitin-proteasome pathway [82,83], which in conjunction with heightened protein synthesis would result in an even greater accretion of muscle proteins. However, none of these studies were carried out in conjunction with physical activity, making it impossible to draw any conclusions to exercising conditions. Further research is needed to examine whether n-3 supplementation may potentiate gains in lean muscle mass when combined with regimented exercise.

Finally, it is possible that n-3 may improve weight loss during exercise by helping to regulate appetite. Parra *et al.* [53] showed that diets rich in n-3 modulate post-prandial satiety in overweight and obese volunteers during weight loss. Given that exercise has been shown to result in better short-term appetite control [43], it would be interesting to assess whether n-3 supplementation might have a synergistic effect on improving post-workout satiety when combined with regimented exercise. If so, this could have significant implications for long-term weight management.

In conclusion, the potential synergism between n-3 supplementation and exercise provides an exciting area for research. Future studies should seek to build on the current body of literature with more stringent controls in study design. Moreover, studies to-date have focused solely on cardiovascular exercise, but it would be interesting to investigate whether n-3 may confer beneficial effects when combined with resistance training. It should be also noted that a high consumption of n-3 can lead to immunosuppression and prolong bleeding time [44,66]. Thus, attempts should be made to establish optimal n-3 dosages to maximise the risk/reward ratio of supplementation.

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