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Effects of exercise training on fatty acid composition under dietary intervention with deficient and adequate levels of n-3 polyunsaturated fatty acids in mice

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ABSTRACT: Omega-3 polyunsaturated fatty acids (n-3 PUFAs), particularly eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), have been widely recognized for their health benefits. While both dietary intake of n-3 PUFAs and exercise training independently influence fatty acid metabolism, their combined effects on tissue-specific fatty acid composition remain unclear. In the present study, we investigated the fatty acid profiles of total lipids in serum, liver, gastrocnemius muscle, heart, kidney and brain to comprehensively evaluate the effects of exercise training under dietary different n-3 PUFAs levels. Results revealed that dietary supplementation with n-3 PUFAs significantly increased EPA and DHA levels and decreased Σn-6/Σn-3 PUFAs ratios in serum, liver, muscle, heart, and kidney. Notably, the exercise-induced changes in n-3 PUFAs were modulated by both dietary n-3 PUFAs levels and exercise duration. Under n-3 PUFAs adequate conditions, short-term exercise preferentially mobilized n-3 PUFAs from peripheral tissues, while long-term exercise promoted DHA redistribution from the circulation to metabolically active tissues. Under n-3 PUFAs deficient conditions, prolonged exercise accelerated tissue n-3 PUFAs depletion, highlighting enhanced utilization and redistribution when dietary supplementation was limited. Notably, exercise training also reduced tissue levels of pro-inflammatory C20:4 and monounsaturated fatty acid C18:1, especially in liver and serum. In contrast, fatty acid composition in the brain remained largely unchanged across interventions. These results highlighted the tissue specific modulation of fatty acid profiles through the interaction of diet and physical activity. This study provided a comprehensive investigation about the changes of fatty acid composition based on exercise training and dietary n-3 PUFAs level *in vivo*, offering a scientific basis for exercise physiology and targeted nutritional supplementation.

Keywords: exercise training; n-3 polyunsaturated fatty acid; dietary; fatty acid composition

1. Introduction

Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are essential nutrients that play a crucial role in maintaining physiological homeostasis and preventing a wide range of chronic diseases[1, 2]. Ample evidence has demonstrated that adequate n-3 PUFAs intake exerts protective effects against cardiovascular disease,

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metabolic syndrome, inflammation, and neurodegenerative disorders[3, 4]. Among these fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are particularly important for cardiovascular and cognitive functions, while alpha-linolenic acid (ALA) serves as their metabolic precursor[5]. International health authorities, such as the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), recommend a daily intake of 250-500 mg of EPA and DHA for adults to maintain optimal health[6]. However, population based dietary surveys consistently reveal that most people fail to meet this recommendation, with especially low n-3 PUFAs consumption observed among physically active individuals and athletes[7]. The high energy demands and specialized dietary practices of athletes often result in an imbalance of dietary fatty acid types, potentially affecting recovery and performance[5].

Previous studies have demonstrated that exercise training can modify fatty acid metabolism and composition in various tissues, thereby influencing lipid oxidation, membrane structure, and energy regulation[8, 9]. Exercise promotes the mobilization and utilization of fatty acids as energy substrates, leading to alterations in both circulation and tissue lipid profiles. In skeletal muscle and liver, exercise-induced adaptations enhance mitochondrial oxidation and remodeling of phospholipid fatty acid composition, which contributes to improved endurance and metabolic flexibility[10, 11]. Similarly, dietary fatty acid profiles, such as the types and ratios of dietary fats, directly determine tissue lipid pools[12]. However, most research in sports nutrition has focused on the effects of protein and carbohydrate intake on energy balance, muscle adaptation, and recovery[13], while the role of dietary fatty acids, particularly n-3 PUFAs, has received far less attention. Recent consensus statements have emphasized that n-3 PUFAs may provide multiple physiological benefits related to exercise. Supplementation with EPA and DHA has been shown to reduce exercise-induced muscle damage and inflammation, improve endothelial function, enhance oxygen delivery, and accelerate post exercise recovery of muscle performance[14]. In addition, n-3 PUFAs may support cardiovascular efficiency, neuromuscular coordination, and adaptive responses to endurance training[15]. Although several studies have investigated the combined effects of dietary intervention and exercise training on fatty acid metabolism in rodents, most have focused on overall lipid oxidation or single tissue such as skeletal muscle[16]. Comprehensive evidence describing how n-3 PUFAs status influences exercise-induced alterations in fatty acid composition across multiple tissues is still limited[17]. In particular, the interactive effects between exercise and varying levels of dietary n-3 PUFAs intake have not yet been systematically examined. Elucidating this relationship is crucial for advancing our understanding of how diet and exercise jointly modulate lipid metabolism and for developing effective nutritional strategies to enhance physiological performance and overall health.

Therefore, the present study aims to investigate the combined effects of exercise training and dietary n-3 PUFAs levels on fatty acid composition in mice. Specifically, we examines how short-term (10 days) and long-term (30 days) exercise interventions under diets containing different n-3 PUFAs concentrations affect the fatty acid profiles of serum, liver, gastrocnemius muscle, heart, kidney, and brain. This study provides new

insights into the metabolic interactions between dietary fatty acids and exercise training, offering a foundation for optimizing nutritional strategies to improve health and performance.

2. Materials and methods

2.1. Animals and diets

All animal procedures were approved by the Ethical Committee for Experimental Animal Care at Ocean University of China (Qingdao, China) (Approval No.: SYXY2019012) and were conducted in accordance with institutional and national guidelines. Five-week-old male ICR mice were obtained from Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China). All mice were acclimated for one week in a specialized room under a 12/12 h light-dark cycle at 23 ± 2℃ with 60 ± 10% relatively humidity and were provided with standard food and water *ad libitum*. After adaption of the environment, the mice were randomly divided into 4 groups (n=8 per group): n-3 PUFAs deficient diet plus sedentary status (DS group), n-3 PUFAs deficient diet plus exercise training (DE group), n-3 PUFAs adequate diet plus sedentary status (AS group), n-3 PUFAs adequate diet plus exercise training (AE group). The n-3 PUFAs deficient diet contained 0.06% Σn-3 PUFAs (as a percentage of total lipids), whereas the n-3 PUFAs adequate diet contained 3.10% Σn-3 PUFAs, primarily derived from purple perilla seed oil. The composition and the percentage of Σn-3 PUFAs in dietary lipids of experimental diets were presented in Table 1.

Table 1. Ingredients and the percentage of Σn-3 PUFAs in total lipids of experimental diets.

	DS and DE	**AS and AE**
Ingredient composition (g/kg)		
Casein	200	200
Sucrose	100	100
Potato starch	397.5	397.5
Maltodextrin	132	132
Cellulose	50	50
Mineral mix	35	35
Vitamin mix	10	10
L-methionine	3	3
Choline bitartrate	2.5	2.5
TBHQ	0.02	0.02
Hydrogenated coconut oil	56.70	52.56
Safflower oil	13.30	12.33
Purple perilla seed oil	-	5.11
Σn-3 PUFAs (% of total lipids)	0.06	3.10

Notes: PUFAs, polyunsaturated fatty acids. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. TBHQ, tertiary butylhydroquinone. -, none added.

2.2. Exercise training

Mice in the DE and AE groups underwent exercise training for 10 and 30 consecutive days. The training protocol alternated daily between treadmill running and swimming. Treadmill intensity was gradually increased from 30 min/day at 15 m/min to 2 h/day at 21 m/min over the first 3 days and maintained thereafter. Swimming duration was similarly increased from 30 min/day to 2 h/day over 3 days, with water temperature maintained at 27 ± 2 °C. Mice in the DS and AS groups were housed under identical conditions but did not

undergo any exercise training intervention. This combined aerobic training model was designed to simulate moderate to high intensity endurance exercise training, while alternating modalities minimized habituation and promoted physiological adaptation. Sedentary groups served as controls to distinguish the independent and combined effects of exercise training and dietary n-3 PUFAs levels on tissue fatty acid composition.

2.3. Blood and tissues collection

After 10- or 30- days of dietary intervention and exercise training, mice were fasted overnight for 12 hours with free access to water and then euthanized by cervical dislocation. Whole blood was collected, and serum was obtained by centrifugation at 7500 × *g* for 15 minutes at 4 °C. The liver, gastrocnemius muscle, heart, kidney, and brain were promptly excised, weighed, snap-frozen in liquid nitrogen, and stored at −80 °C for further analysis.

2.4. Lipid extraction and gas chromatography analysis

The total lipids of serum were extracted according to a published method with minor modifications[18]. Briefly, serum lipids were extracted with chloroform/methanol (1:1, v/v) for three times after incubation in a water bath at 40°C for 30 min. Subsequently, the mixture was then centrifuged at 7500 × *g* for 5 min at 4 °C, and the chloroform phase was collected. For liver, brain, kidney, heart, and gastrocnemius muscle tissues, total lipids were extracted using chloroform/methanol (2:1, v/v) according to a previously classical method[19]. The collected chloroform layers were evaporated to dryness under vacuum and redissolved in petroleum ether. The fatty acid composition of extracted lipids was analyzed by gas chromatography (GC) following methyl esterification.

2.5. Fatty acid composition analysis

Fatty acid composition in tissues was determined by gas chromatography (GC) as fatty acid methyl esters (FAMEs). A known amount of pentadecanoic acid (C15:0, 60 μL per sample) was added as an internal standard for quantification. FAMEs were extracted by adding 1.5 mL of hexane to the tissue sample, followed by vortexing and centrifugation to separate the organic and aqueous layers. One milliliter of the upper hexane layer was collected for GC analysis. The GC analysis was performed using an Agilent 7820A GC system equipped with a flame ionization detector (FID) and an HP-INNOWAX capillary column (30 m × 0.32 mm, 0.25 μm). Sample injection was conducted in split mode (split ratio 20:1), with the injector and detector maintained at 240 °C and 250 °C, respectively. The column oven temperature was programmed from 150 °C to 210 °C at 3 °C/min and held at 210 °C for 20 min. Nitrogen was used as the carrier gas at a flow rate of 1.0 mL/min, and 2 μL of sample was injected. The total analysis time was approximately 48.5 min. Fatty acids were identified by comparing retention times with authentic standards, and the relative contents of individual fatty acids were expressed as a percentage of total identified fatty acids.

For data analysis, fatty acids were categorized as saturated fatty acids (ΣSFAs), monounsaturated fatty acids (ΣMUFAs), and polyunsaturated fatty acids (ΣPUFAs). Quality control was ensured by adding a

known amount of pentadecanoic acid (C15:0) as an internal standard to each sample, allowing accurate calculation of fatty acid contents and monitoring extraction and analysis consistency.

2.6. RNA-Seq transcriptome analysis of the liver

Total RNA was extracted from liver tissues and subjected to library construction and high-throughput sequencing using the Illumina platform (Illumina, San Diego, CA, USA). Clean reads were aligned to the reference mouse genome (Mus musculus, GRCm38/mm10), and gene-level read counts were generated. Normalized expression values were calculated and used for downstream analysis. For visualization, selected lipid metabolism related genes were transformed to Z-scores and subjected to hierarchical clustering based on Euclidean distance. Heat maps were generated using the heatmap package in R.

2.7. Statistical analysis

Statistical analyses were performed using two-way analysis of variance (two-way ANOVA) to evaluate the main effects of diet (n-3 PUFAs deficient vs. adequate) and time (10 days vs. 30 days), as well as their interaction. When significant main effects or interactions were observed, pairwise comparisons were further assessed using Tukey's post hoc test. All data were expressed as mean ± standard error of the mean (SEM), and differences were considered statistically significant at $P < 0.05$.

3. Results

3.1. Effect of exercise training on serum fatty acid composition under dietary intervention with different levels of n-3 polyunsaturated fatty acids

Exercise training in combination with varying levels of dietary n-3 PUFAs may influence the body's fatty acid composition. In the present study, we systematically compared the changes of various kinds of fatty acids in serum after exercise training for 10 and 30 days, including saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs) and PUFAs. As shown in Figure 1A, after 10 days of intervention, no significant changes in serum C14:0, C16:0, or C18:0 were observed between sedentary and exercised groups with either n-3 PUFAs deficient or n-3 PUFAs adequate diets. However, after 30 days of exercise under an n-3 PUFAs adequate diet, the AE group exhibited a significant reduction in C14:0 ($P < 0.05$) and a marked elevation in C18:0 ($P < 0.05$) compared to the sedentary AS group. As shown in Figure 1B, after exercise training for 10 days under the background of n-3 PUFAs deficient diet, the proportion of C18:1 remarkably reduced ($P < 0.05$), meanwhile, no significant difference was observed about C16:1 and C22:1 in comparison with DS group. In addition, prolonged training (30 days) under background of n-3 PUFAs adequate diet, both proportion of C16:1 and C18:1 in AE group significantly decreased when compared with AS group ($P < 0.05$). As depicted in Figure 1C, after 10 days of n-3 PUFAs deficient diet intervention, no significant changes in serum n-6 PUFA levels were observed in the exercise training group compared with the sedentary group. However, after 30 days, the proportion of C20:4 was significantly decreased, while C22:2 was markedly increased in the DE group compared with the DS group. Similarly, under the n-3 PUFAs adequate diet, the percentage of C20:4 was also significantly reduced following 30 days of exercise compared to the sedentary

control. As shown in Figure 1D, a significant decrease in the proportions of ALA, EPA, and DHA was observed in the exercised group after 30 days of intervention with the n-3 PUFAs adequate diet, compared with the sedentary group (all $P < 0.05$). For total fatty acids, the ΣSFAs showed no significant difference between the DS and DE groups following 10- or 30- day interventions. However, after 30 days of exercise training under the n-3 PUFAs adequate diet, a significant increase in ΣSFAs was observed in the AE group compared with the AS group, suggesting that regular exercise may elevate serum ΣSFA levels under conditions of n-3 PUFAs adequate diet. What's more, serum ΣMUFAs significantly reduced after 30 days of exercise under both n-3 PUFAs deficient and adequate diets. Interestingly, ΣPUFAs also exhibited a similar decreasing trend following exercise training as ΣMUFAs (Figure 1E). In aspects of Σn-6 PUFAs in serum after exercise training for 30 days, Σn-6 PUFAs in exercise training group remarkably decreased in comparison with the sedentary group under the background of n-3 PUFAs adequate diet. However, no significant differences in terms of n-6/n-3 PUFAs ratio in serum were observed between sedentary and exercise training groups in both of different levels of n-3 PUFAs diet after intervention irrespective for 10 or 30 days (Figure 1F).

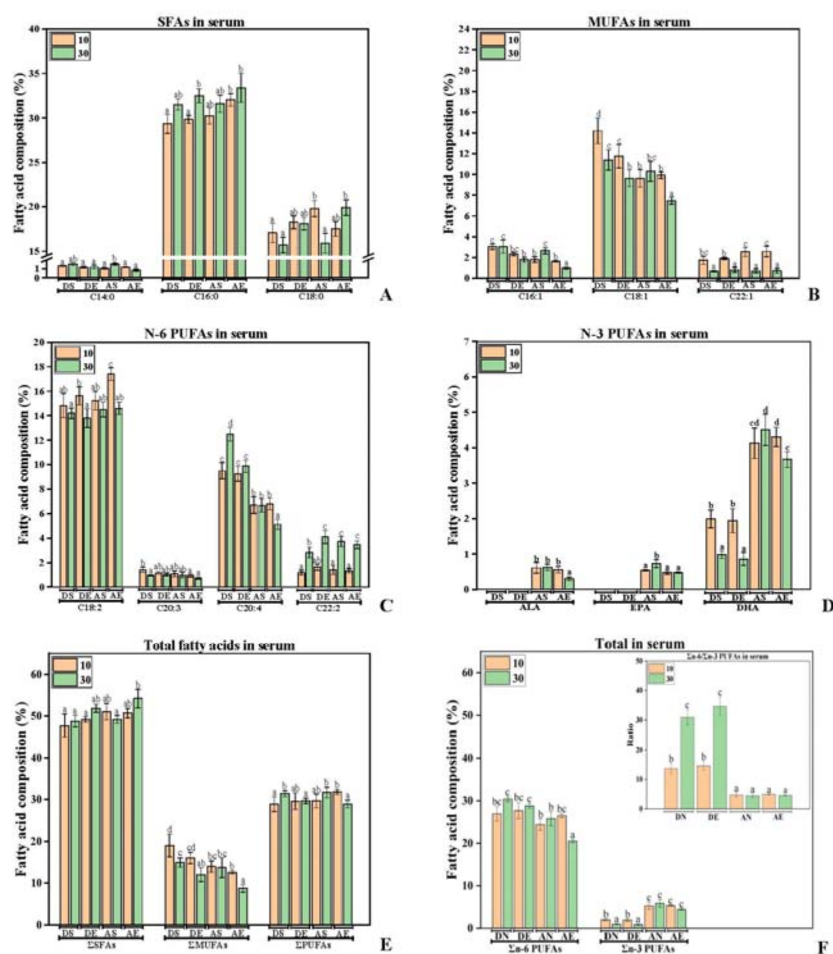


Figure 1. Fatty acid composition (%) in serum after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.2. Effect of exercise training on fatty acid composition in liver under dietary intervention with different levels of n-3 polyunsaturated fatty acids

The liver plays a pivotal role in systemic lipid metabolism, acting as the primary site for fatty acid synthesis, elongation, desaturation, and redistribution[20]. As shown in Figure 2A, after 30 days of intervention under an n-3 PUFAs adequate diet, the contents of SFAs, specifically C16:0 and C18:0, were significantly elevated in the AE group compared to the AS group ($P < 0.05$). Meanwhile, the ratio of C18:0 in both exercise groups (DE and AE group) significantly increased after 10 and 30 days in comparison with the corresponding sedentary groups (DS and AS group). Figure 2B shows that the percentages of C16:1 and C18:1 were markedly reduced in the AE group compared to the AS group after both 10 and 30 days ($P < 0.05$), indicating a possible inhibitory effect of exercise on MUFA synthesis or storage in the liver under sufficient n-3 PUFAs intake. Under the n-3 PUFAs deficient diet, significant difference was only found in the ratio of C16:1 after training for 10 days and the ratio of C18:1 in exercise training group after 30 days. As illustrated in Figure 2C, there were no significant differences in the levels of C18:2 and C20:3 in the liver across all groups. However, C20:4 levels were significantly elevated in exercise groups (DE and AE group) following 10 and 30 days of training compared to their respective sedentary controls ($P < 0.05$), suggesting that physical exercise promotes enrichment of n-6 long-chain PUFAs in the liver. The effects on n-3 PUFAs were shown in Figure 2D. While no significant changes were observed in ALA or EPA. The proportion of DHA in the liver was significantly increased in both DE and AE groups after 30 days of exercise training ($P < 0.05$) in comparison with their respective sedentary control groups (DS and AS group), indicating a favorable effect of exercise on DHA accumulation in the liver under both dietary conditions. As shown in Figure 2E, total fatty acid profiles revealed no significant changes in ΣSFAs, ΣMUFAs, or ΣPUFAs between sedentary and exercised groups after 30 days under the n-3 PUFAs deficient diet. In contrast, under the n-3 PUFAs adequate diet, the AE group exhibited significantly higher proportions of ΣSFAs and ΣPUFAs, and a significantly lower proportion of ΣMUFAs compared to the AS group after 30 days ($P < 0.05$). Figure 2F presents the total contents of n-6 and n-3 PUFAs and their ratio. Under the n-3 PUFAs deficient diet, both Σn-6 and Σn-3 PUFAs were significantly increased in the DE group after 10 days compared with the DS group ($P < 0.05$). Meanwhile, after 30 days, only Σn-6 PUFAs were elevated in the AE group compared to the AS group, but no significant difference was observed in aspects of Σn-3 PUFAs. Importantly, in accordance with the results of serum, there were no significances in the ratio of n-6/n-3 PUFAs ratio between exercised and respective sedentary groups after dietary intervention with different n-3 PUFAs levels. To further elucidate the molecular basis underlying liver fatty acid remodeling, transcriptomic profiling was performed.

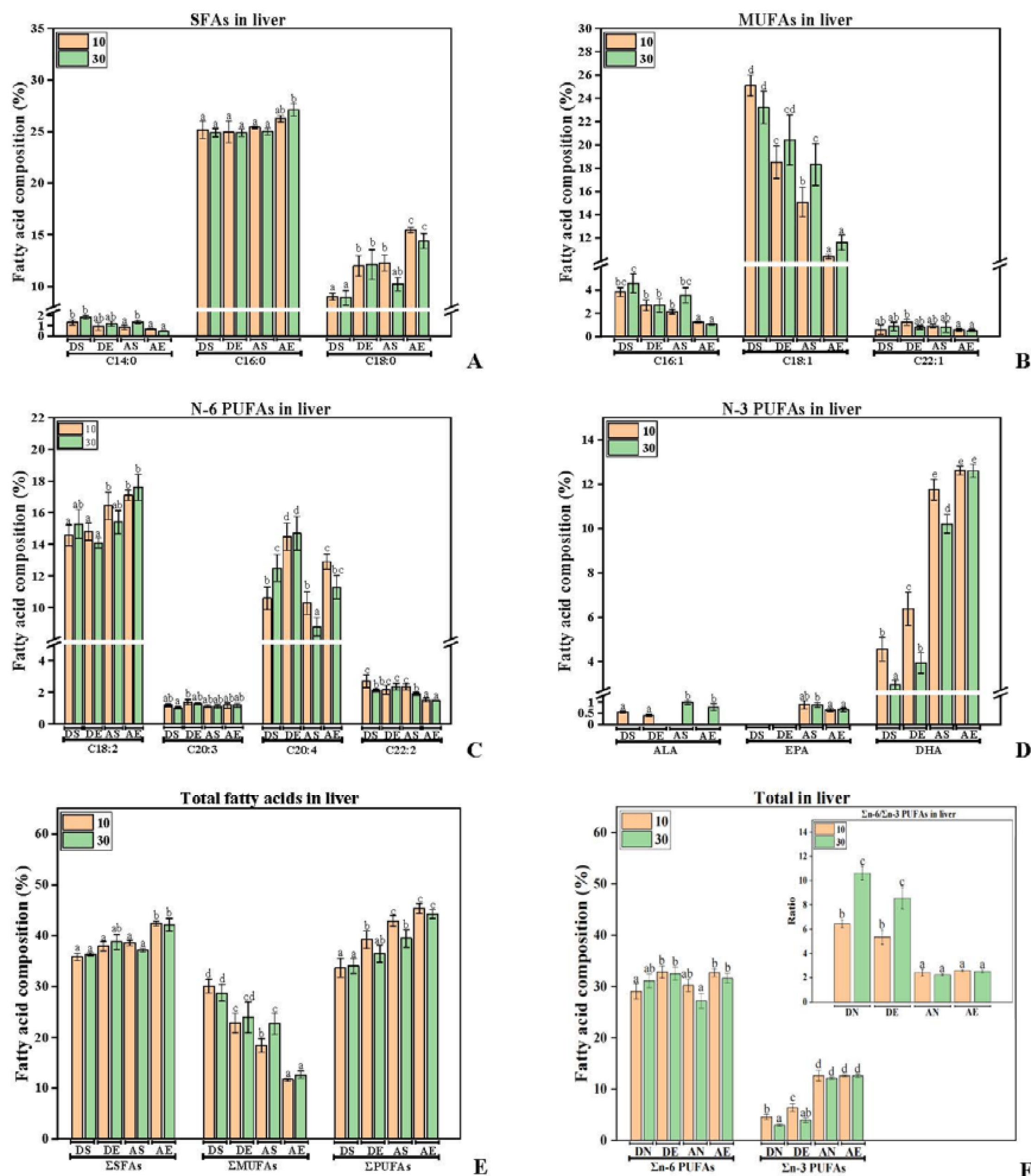
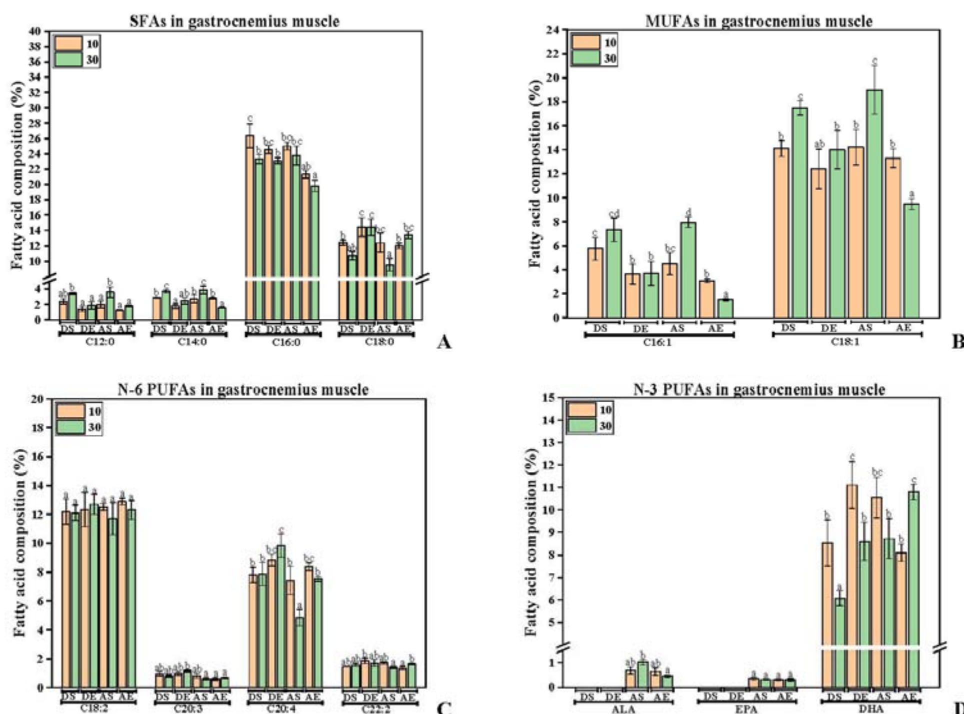


Figure 2. Fatty acid composition (%) in liver after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.3. Effect of exercise training on fatty acid composition in gastrocnemius muscle under dietary intervention with different levels of n-3 polyunsaturated fatty acids

The gastrocnemius muscle is a critical tissue involved in exercise metabolism and is sensitive to both physical activity and dietary lipid composition[21]. In this section, we investigated the effects of exercise training and dietary n-3 PUFAs levels on the fatty acid profile of the gastrocnemius muscle after 10 and 30 days of intervention. As shown in Figure 3A, C16:0, the fatty acid of largest proportion in SFAs, decreased significantly after exercise training for 30 days in comparison with the sedentary group ($P < 0.05$) under n-3

PUFAs adequate background. Meanwhile, the proportion of C18:0 significantly increased in AE group ($P < 0.05$) when compared to that in AS group. No significant changes in C12:0 or C14:0 were detected across groups. As shown in Figure 3B, we found that exercise training groups (DE and AE group) could significantly reduce the ratios of C16:1 and C18:1 compared with their respective sedentary groups (DS and AS group) ($P < 0.05$) regardless of n-3 PUFAs deficient and adequate diet after intervention for 30 days. As illustrated in Figure 3C, there was no significant difference observed about the ratio of C18:2 between exercise training group and respective sedentary group. In addition, the proportion of C20:4 in exercise training groups (DE and AE group) significantly increased when compared with respective sedentary groups (DS and AS group) after 30 days ($P < 0.05$). In aspects of n-3 PUFAs, the percentage of DHA significantly increased in exercise training groups when compared with their sedentary group regardless of n-3 PUFAs deficient and adequate diet after intervention for 30 days (Figure 3D). According to Figure 3E, there was no significant difference about ΣSFAs between exercise training and sedentary groups under the same level of n-3 PUFAs in diet. Interestingly, the proportion of ΣMUFAs significantly decreased and that of ΣPUFAs significantly increased in exercise training groups when compared with respective sedentary groups ($P < 0.05$) after intervention for 30 days regardless of n-3 PUFAs deficient and adequate diet (Figure 3E). As shown in Figure 3F, the percentage of Σn-6 PUFAs significantly increased in exercise training groups (DE and AE group) in comparison with respective sedentary groups (DS and AS group) after intervention for 30 days ($P < 0.05$). The percentage of Σn-3 PUFAs significantly increased in DE group when compared with that in DS group after 10 days ($P < 0.05$). The Σn-6/n-3 PUFAs ratio in gastrocnemius muscle significantly increased in AE compared to AS after 10 days under n-3 PUFAs adequate diet ($P < 0.05$). However, no significant differences were observed under the n-3 PUFAs deficient diet.



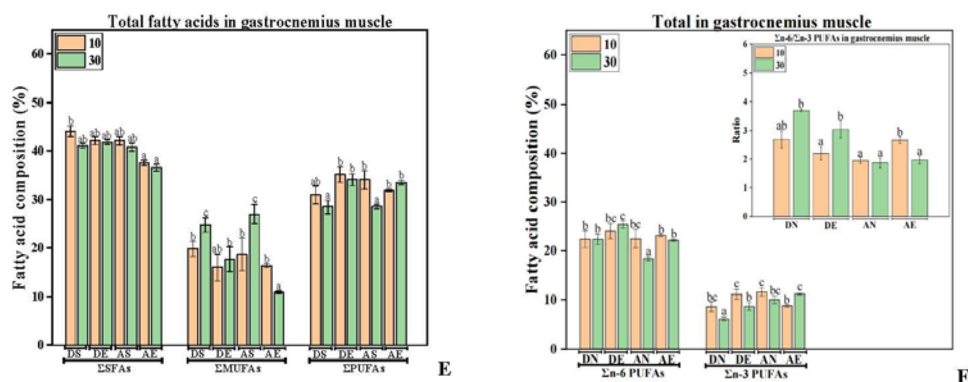


Figure 3. Fatty acid composition (%) in gastrocnemius muscle after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.4. Effect of exercise training on fatty acid composition in heart under dietary intervention with different levels of n-3 polyunsaturated fatty acids

The heart, as a highly oxidative organ, plays a central role during exercise and is sensitive to both physical activity and dietary lipid modulation[22-24]. Figure 4 presented the effects of 10 and 30 days of exercise training under n-3 PUFAs deficient and adequate dietary conditions on cardiac fatty acid composition. As shown in Figure 4A, C16:0 was one of the most predominant SFAs in cardiac tissues, and was significantly reduced in the AE group compared to the AS group after both 10 and 30 days ($P < 0.05$). C18:0 did not display significant change in aspects of percentage between exercise training and sedentary groups regardless of diet or time point. Other SFAs such as C14:0 and C20:0 showed minimal variation and were not significantly affected by intervention. According to Figure 4B, C16:1 significantly decreased in the AE group after 30 days of training compared to the AS group ($P < 0.05$). However, there was no significant difference in the percentage of C18:1 and C20:1 across all groups regardless of 10 and 30 days. As illustrated in Figure 4C, C18:2 levels significantly increased in the AE group after exercise training for 10 and 30 days in comparison with the sedentary AS group ($P < 0.05$) under n-3 PUFAs adequate diet. There were no significant differences observed in the proportion of C20:4 between exercise training and sedentary groups after 10 and 30 days regardless of n-3 PUFAs deficient and adequate diet. Regarding n-3 PUFAs (Figure 4D), DHA was the dominant component in heart tissue. Exercise training under n-3 PUFAs adequate diets (AS and AE group) significantly increased the proportion of DHA, particularly in the AE group after both 10 and 30 days ($P < 0.05$), compared to DS and DE groups. No significant differences were found in the levels of EPA and ALA among groups. As shown in Figure 4E, there were no significant differences about ΣSFAs and ΣPUFAs between exercise training and sedentary groups under the same n-3 PUFAs level in diet, respectively. Interestingly, the proportion of ΣMUFAs significantly decreased in AE group after exercise training for 30 days. In Figure 4F, the percentage of Σn-6 PUFAs significantly increased in AE group after 30 days ($P < 0.05$), and the ratio of n-6/n-3 PUFAs ratio also showed the same change when compared to AS group.

However, no significant changes in the ratio were observed in the n-3 PUFAs deficient groups (DS vs. DE group). While Σn-3 PUFAs increased significantly in AE after 30 days, no significant difference was observed in DE group compared to DS group.

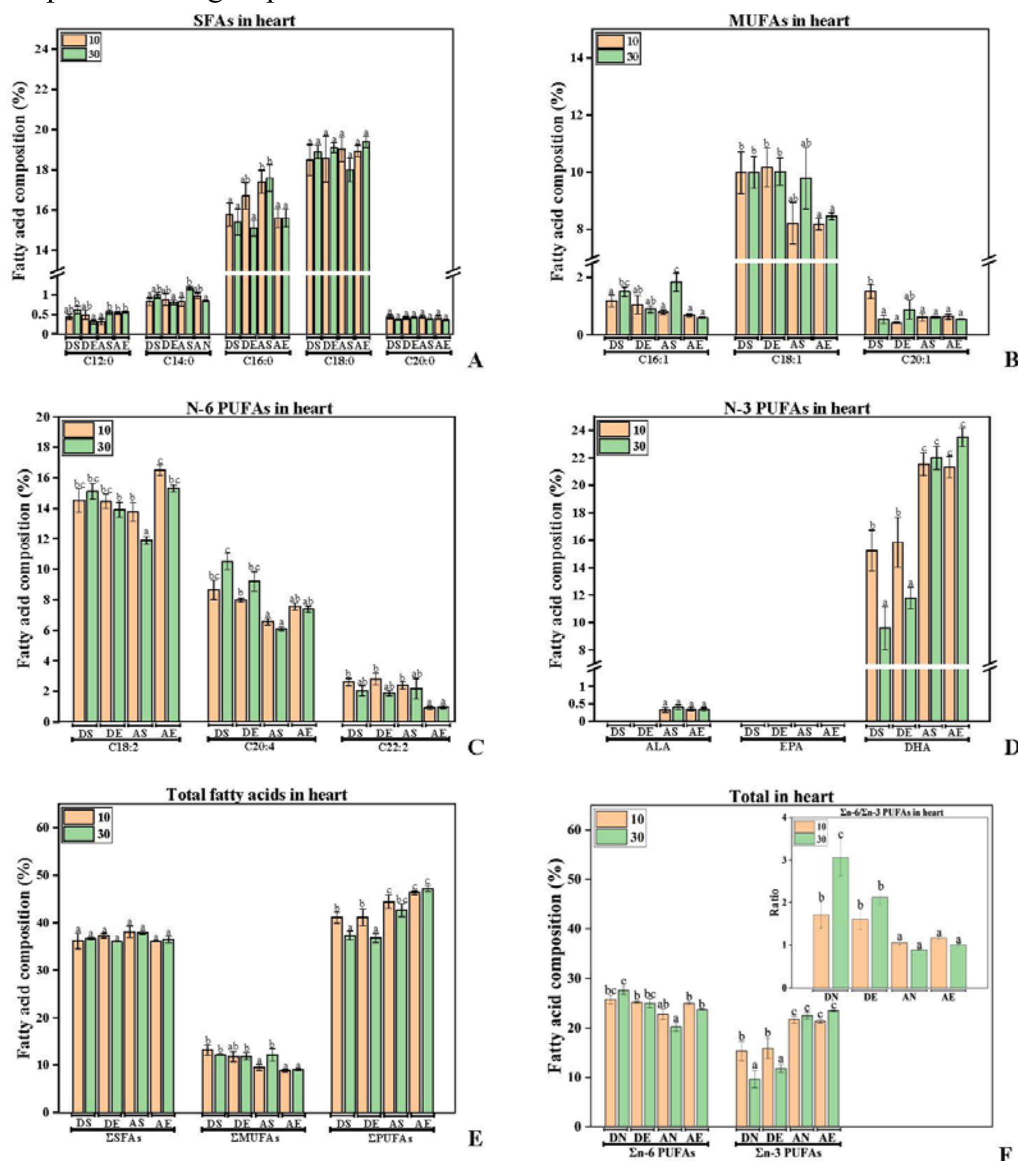
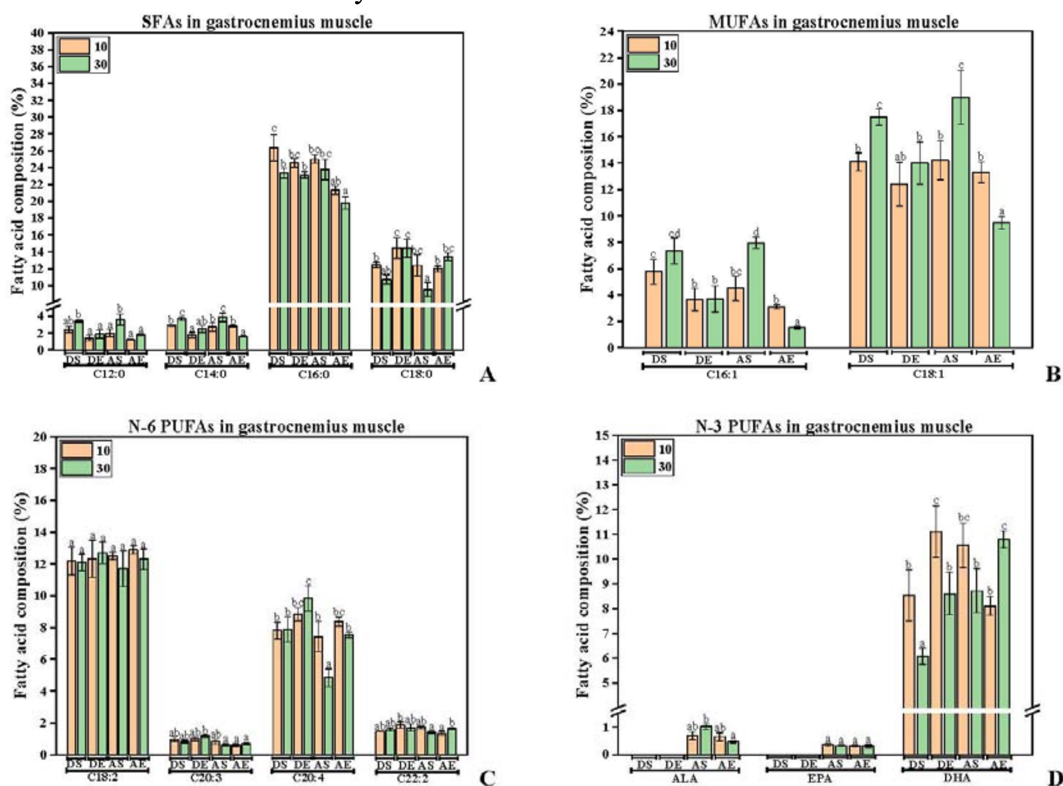


Figure 4. Fatty acid composition (%) in heart after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.5. Effect of exercise training on fatty acid composition in kidney under dietary intervention with different levels of n-3 polyunsaturated fatty acids

Kidney is a vital organ to eliminate metabolic waste products *in vivo*, and the low-intensity physical exercise routinely has no negative impact on renal function to patients with chronic disease[25]. As shown in Figure 5A, there were no significant differences observed about the percentage of C16:0 in kidney between exercise training and sedentary groups, regardless of dietary n-3 PUFAs levels. However, under an n-3 PUFAs adequate diet, the content of C18:0 significantly increased after 30 days of exercise training compared to the

AS group (P < 0.05). In Figure 5B, there were no significant difference observed about the proportion of C18:1 between exercise training and sedentary groups based on the same n-3 PUFAs level in diet. The ratio of C16:1 dramatically reduced after exercise training for 30 days in comparison with the sedentary group under n-3 PUFAs adequate diet, suggesting that prolonged training suppressed the renal accumulation of C16:1 under an n-3 PUFAs adequate diet background. As shown in Figure 5C, under n-3 PUFAs deficient diet, both the proportion of C18:2 and C20:4 did not show significant difference between exercise training and sedentary groups. In contrast, under n-3 PUFAs adequate diet, both the proportion of C18:2 and C20:4 notably increased in exercise training group when compared to their sedentary group. In addition, the proportion of C22:2 significantly reduced in AE group when compared to AS group after intervention irrespective for 10 days or 30 days (P < 0.05). For n-3 PUFAs (Figure 5D), under n-3 PUFAs adequate diet, DHA content in the kidney was significantly elevated in the AE group after 30 days of training compared to the AS group. Although no statistically significant changes were detected in EPA or ALA, an upward trend was observed in the exercise training groups, particularly under n-3 PUFAs adequate conditions. As presented in Figure 5E, there were no significant differences about ΣSFAs and ΣPUFAs between exercise training and sedentary groups, respectively. Interestingly, under n-3 PUFAs adequate diet, the percentage of ΣMUFAs in exercise training group decreased significantly in comparison with sedentary group (P < 0.05). As shown in Figure 5F, no significant changes were found in the total levels of Σn-6 PUFAs or Σn-3 PUFAs between exercise training and sedentary groups, irrespective of dietary background. Likewise, the ratio of Σn-6 to Σn-3 PUFAs in kidney tissue did not differ significantly among the experimental groups. These findings suggested that while exercise training selectively alters specific fatty acid species, it exerted minimal impact on the overall PUFA composition and n-6/n-3 balance in kidney tissue.



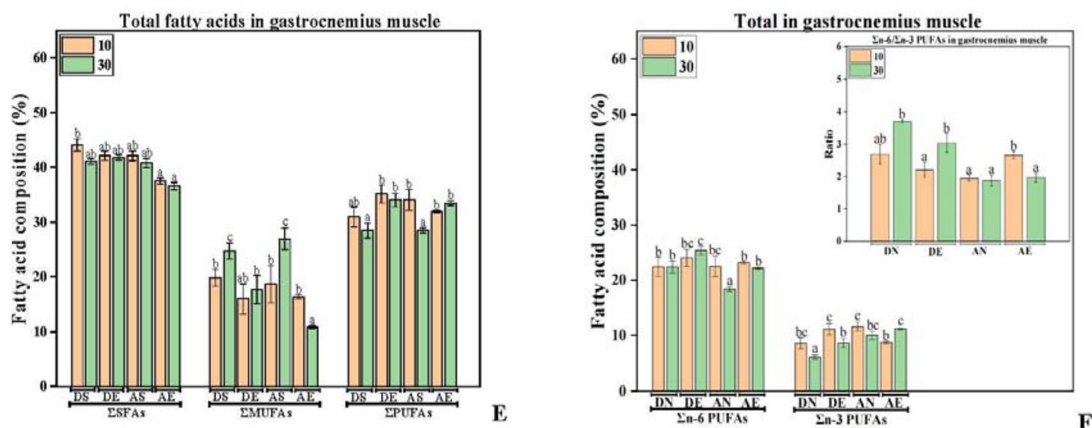
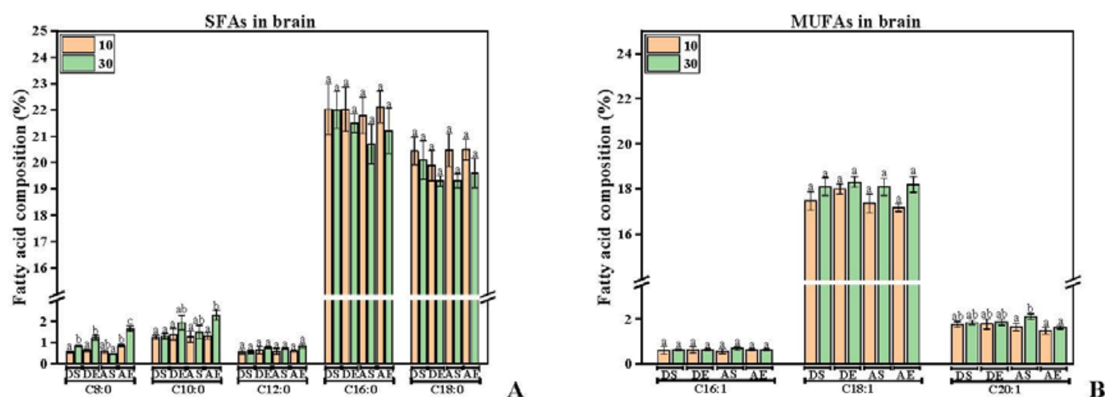


Figure 5. Fatty acid composition (%) in kidney after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs in kidney. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.6. Effect of exercise training on fatty acid composition in brain under dietary intervention with different levels of n-3 polyunsaturated fatty acids

Brain is rich in lipids consisting with glycerophospholipids, sphingolipids, gangliosides and cholesterol[26]. As illustrated in Figure 6A–F, no signific ant differences were observed in the relative abundances of C16:0, C18:0, C18:1, C20:4, and DHA between exercise training and sedentary groups across different dietary n-3 PUFAs levels. Likewise, the total contents of ΣSFAs, ΣMUFAs, and ΣPUFAs showed no significant alterations with exercise intervention. Furthermore, both the Σn-6 PUFAs and Σn-3 PUFAs contents remained unaffected by exercise training. Correspondingly, the ratio of Σn-6 to Σn-3 PUFAs in the brain did not differ significantly between sedentary and exercise training groups under the same dietary conditions. These findings suggested that brain fatty acid composition was relatively resistant to modulation by low-intensity exercise training, even under varying dietary n-3 PUFAs levels.



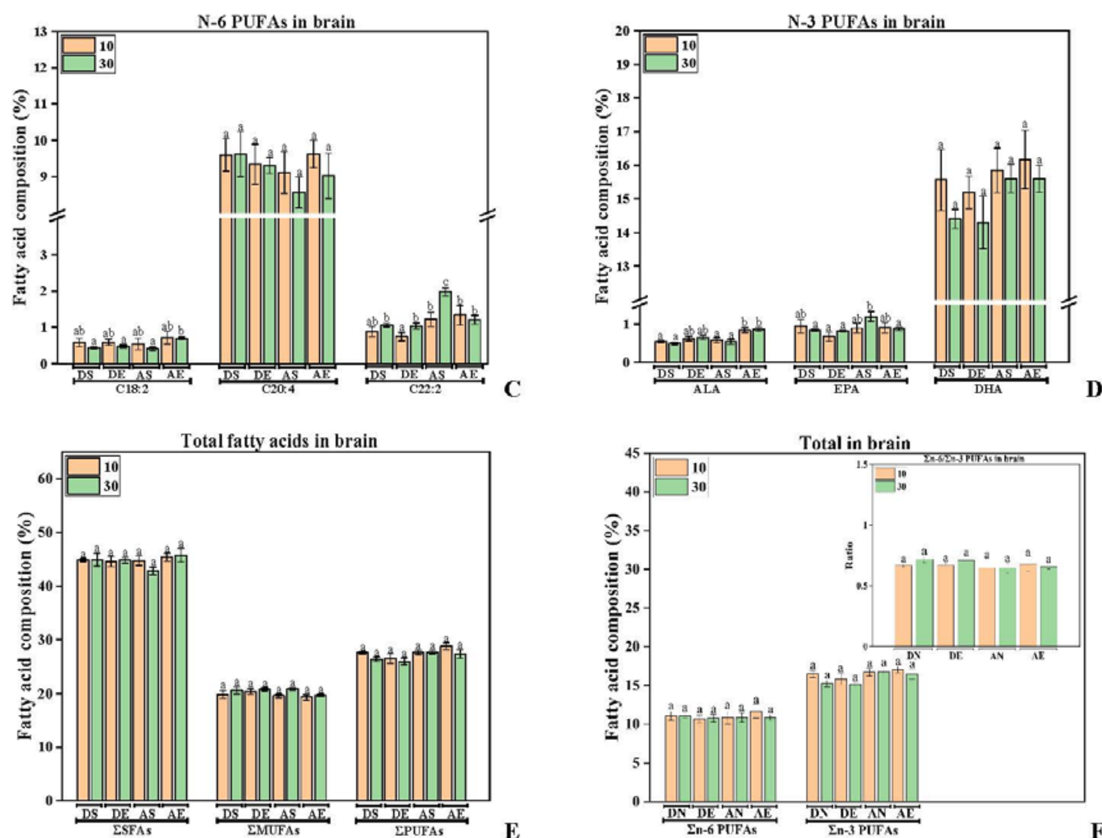


Figure 6. Fatty acid composition (%) in brain after exercise training under dietary intervention with different level of n-3 polyunsaturated fatty acids (PUFAs) for 10 and 30 days. (A) Saturated fatty acids (SFAs). (B) Monounsaturated fatty acids (MUFAs). (C) N-6 PUFAs. (D) N-3 PUFAs. (E) ΣSFAs, ΣMUFAs and ΣPUFAs. (F) Σn-6 PUFAs, Σn-3 PUFAs, and the ratio of Σn-6/Σn-3 PUFAs. DS, n-3 PUFAs-deficient diet plus sedentary status group; DE, n-3 PUFAs-deficient diet plus exercise training group; AS, n-3 PUFAs-abundant diet plus sedentary status group; AE, n-3 PUFAs-abundant diet plus exercise training group. Data were presented as mean ± SEM (n=8 per group). Different letters indicated significant difference at $P < 0.05$ between each group determined by ANOVA.

3.7. Liver transcriptomic signatures underlying PUFAs remodeling

Given the prominent remodeling of liver fatty acid composition, we next explored transcriptomic signatures to gain mechanistic insight into the underlying regulatory processes. As illustrated in Figure 7A, liver transcriptomic analysis revealed a distinct expression pattern for genes involved in endogenous PUFAs elongation and desaturation. Notably, Elovl2, Elovl5, Fads1, and Fads2 exhibited relatively higher expression under n-3 PUFAs deficient conditions compared with adequate dietary groups. This pattern was particularly evident at 30 days, suggesting a compensatory upregulation of endogenous PUFAs biosynthetic machinery when dietary n-3 supply was limited. In contrast, adequate dietary n-3 PUFAs intake was associated with comparatively lower expression of these genes, consistent with reduced reliance on de novo synthesis. As presented in Figure 7B, in contrast, genes involved in mitochondrial and peroxisomal fatty acid β-oxidation, including Cpt1a, Cpt2, Acox1, and related enzymes, did not display a uniform interaction-driven transcriptional activation pattern under combined dietary and exercise intervention. Although modest group-specific variations were observed, no consistent signature of enhanced β-oxidation was detected in the liver transcriptome.

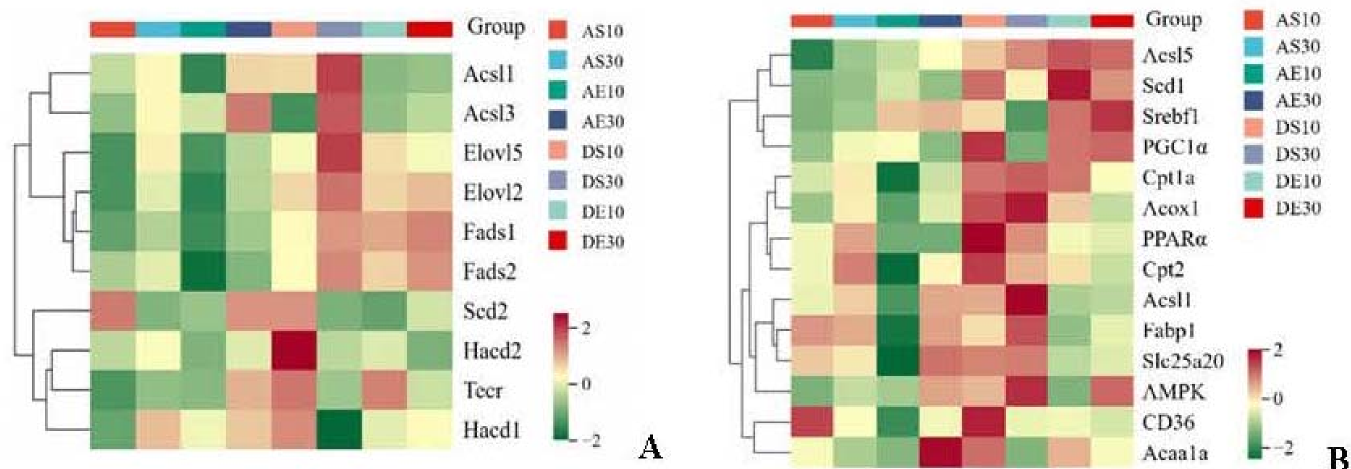


Figure 7. The liver transcriptional signatures associated with PUFA biosynthesis and fatty acid β-oxidation. Heat map of genes involved in PUFAs elongation and desaturation pathways (A), as well as fatty acid β-oxidation and lipid metabolic regulation (B) across experimental groups. The clustering was performed using Euclidean distance. The color bar indicates Z-score transformation of gene expression values calculated from normalized counts, with red representing relatively higher expression and green representing relatively lower expression across groups.

4. Discussion

In recent years, researchers paid more attention on the fatty acid composition in body because of its emerging importance as potential biomarker of several diseases. Meanwhile, the effects of exercise training on fatty acid composition *in vivo* were widely reported. However, the effects of the combined effects of exercise training and n-3 PUFAs level in diet on fatty acid composition in body has never been reported. A 30 days intervention has been shown to be sufficient to induce measurable changes in tissue fatty acid profiles, allowing us to capture relevant alterations within this timeframe. Our study aimed to investigate the effects of 10- or 30-days exercise training under different levels of n-3 PUFAs in diet on fatty acid composition of some tissues (serum, liver, muscle, heart, kidney, and brain) in mice.

N-3 PUFAs, especially EPA and DHA, have been shown to exert multiple physiological activities, including anti-inflammatory, anti-thrombotic, lipid-lowering, and membrane-stabilizing effects [27, 28]. As expected, serum and liver fatty acid profiles were highly responsive to dietary n-3 PUFAs intake, with both EPA and DHA levels markedly increased under n-3 PUFAs adequate conditions. This aligned with previous findings demonstrating rapid incorporation of dietary n-3 PUFAs into circulation and liver lipid pools[29]. The significant elevation of EPA and DHA, accompanied by a marked reduction in the Σn-6/n-3 ratio. These findings are consistent with previous reports demonstrating rapid incorporation of dietary n-3 PUFAs into circulation and liver lipid pools. The liver functions as a central hub for PUFAs metabolism and redistribution, and thus dietary substrate availability was a primary determinant of liver PUFAs homeostasis[30].

Exercise alone exerted modest effects on liver n-3 PUFAs content. However, when combined with adequate dietary supply, exercise was associated with enhanced DHA accumulation in peripheral tissues, including skeletal muscle, heart, and kidney. Notably, skeletal muscle and heart exhibited pronounced DHA enrichment after long-term exercise, consistent with increased membrane remodeling and metabolic adaptation in highly oxidative tissues[31-33], rather than indicating enhanced endogenous elongation or

desaturation in the liver [34]. These findings are more consistent with redistribution and tissue specific incorporation of dietary-derived n-3 PUFAs.

Importantly, liver transcriptomic analysis provided mechanistic insight into these observations. Genes involved in endogenous PUFAs elongation and desaturation, including Elovl2, Elovl5, Fads1, and Fads2, were relatively upregulated under n-3 PUFAs deficient conditions, suggesting compensatory activation of biosynthetic pathways when dietary supply was limited. In contrast, adequate dietary n-3 PUFAs intake was associated with comparatively lower expression of these genes, consistent with negative feedback regulation. Furthermore, canonical regulators of fatty acid β-oxidation did not exhibit coordinated activation in the liver under combined intervention. Collectively, these findings indicate that liver fatty acid remodeling observed in this study is primarily substrate-driven rather than mediated by large-scale transcriptional reprogramming of oxidative pathways.

These findings indicated that while dietary n-3 PUFAs provided essential substrate, exercise was a key driver of tissue specific PUFAs enrichment. Under n-3 PUFAs adequate conditions, short-term exercise preferentially mobilized n-3 PUFAs from peripheral tissues, particularly skeletal muscle, while serum levels remained largely stable, suggesting that early phase utilization of n-3 PUFAs from peripheral tissues could meet increased metabolic demands. Conversely, under adequate dietary supply, prolonged exercise reduced serum DHA concentrations while increasing DHA accumulation in peripheral tissues, indicating a redistribution of dietary derived n-3 PUFAs from serum toward peripheral organs. This duration-dependent redistribution pattern supports a flux-driven remodeling model rather than a transcriptionally driven metabolic reprogramming mechanism.

N-6 PUFAs, including C18:2 and C20:4, were essential for normal physiological functions but could also act as precursors for pro-inflammatory eicosanoids, particularly under conditions of n-3 PUFAs deficiency. Excessive intake or accumulation of n-6 PUFAs without sufficient n-3 balance was associated with inflammation-related diseases[35]. In our study, compared to an n-3 PUFAs adequate, n-3 PUFAs deficient diet combined with exercise increased tissue C20:4 levels, potentially reflecting compensatory elongation and desaturation of n-6 precursors. In contrast, serum lipids primarily reflected redistribution. Thus, the decrease in serum C20:4 may indicate its transfer to metabolically active tissues to support membrane remodeling and energy metabolism. Collectively, these changes do not indicate a uniform stimulation of liver synthesis but rather reflect differences in metabolic flux distribution and tissue-specific utilization capacity.

Moreover, a high Σn-6/Σn-3 PUFAs ratio was linked to elevated risks of carcinogenesis, tumor metastasis, obesity-related inflammation, and insulin resistance, and was proposed as a biomarker of metabolic syndrome and cardiometabolic risk[36, 37]. In our study, the Σn-6/Σn-3 ratio in serum, liver, heart, and kidney was higher in n-3 PUFAs deficient groups compared to adequate groups, suggesting that exercise training may help maintain a lower ratio and support metabolic health under n-3 PUFAs adequate conditions. In addition to n-3 and n-6 PUFAs, monounsaturated fatty acids (MUFA), primarily C18:1, played an important role in lipid metabolism and overall health. We observed a reduction in C18:1 percentages in both

exercise groups after 30 days, particularly in serum and liver, which was consistent with previous reports[31]. Notably, the decrease was more pronounced in the n-3 PUFAs adequate diet group (about 27.5%) than in the deficient group (about 15.5%). Surprisingly, exercise training had minimal impact on fatty acid composition in the brain, including C16:0, C18:0, C18:1, C20:4, DHA, ΣSFAs, ΣMUFAs, ΣPUFAs, and Σn-6/Σn-3 ratios, after 10- or 30- days. This finding was consistent with the restrictive remodeling characteristics of the blood brain barrier [38]. Taken together, the present findings support a framework in which dietary n-3 PUFAs availability serves as the principal determinant of baseline tissue fatty acid composition, whereas exercise training modulates tissue-specific redistribution and incorporation of PUFAs. The observed remodeling patterns appear to be driven predominantly by alterations in substrate flux and lipid pool dynamics, rather than by coordinated transcriptional activation of classical liver lipid metabolic pathways.

Despite these findings, several limitations should be acknowledged. First, this study was designed to compare two distinct dietary conditions, namely n-3 PUFAs deficient and n-3 PUFAs adequate diets, rather than to evaluate graded dose response relationships. Therefore, the observed differences should be interpreted strictly as contrasts between insufficient and sufficient n-3 PUFAs availability, rather than as evidence of a linear or proportional relationship between dietary intake and tissue fatty acid remodeling. The absence of an intermediate dietary n-3 PUFAs level precludes assessment of potential threshold effects, nonlinear responses, or progressive adaptations across increasing intake levels. Consequently, it remains unclear whether moderate or intermediate n-3 PUFAs intake would produce comparable, attenuated, or distinct remodeling patterns. This limitation restricts the extrapolation of the present findings beyond the specific deficient-versus-adequate comparison. Future studies incorporating multiple graded dietary n-3 PUFAs doses will be necessary to determine whether exercise-induced changes in tissue fatty acid composition follow dose-dependent, threshold-dependent, or nonlinear patterns. Second, as sex differences may influence the activity of enzymes involved in fatty acid synthesis and metabolism, future studies should include both male and female subjects to elucidate potential sex-specific responses. Third, although transcriptomic analysis provided pathway-level insight, future studies integrating proteomics, enzyme activity assays, and metabolic flux analysis will be required to clarify whether post-transcriptional regulation or substrate driven dynamics play dominant roles in exercise-induced lipid remodeling. Additionally, longer intervention periods may reveal delayed adaptations that was not captured within the present timeframe.

5. Conclusion

In summary, our study demonstrated that exercise training and dietary n-3 PUFAs levels interacted to modulate tissue specific fatty acid composition in mice. Adequate dietary n-3 PUFAs increased EPA and DHA levels and lowered Σn-6/Σn-3 ratios in serum and peripheral tissues, while exercise further modulated DHA distribution, particularly in skeletal muscle, heart, and kidney. Under n-3 PUFAs adequate conditions, short-term exercise mobilized n-3 PUFAs from peripheral tissues, whereas long-term exercise promoted redistribution of DHA from circulation to metabolically active tissues. Under n-3 PUFAs deficient conditions, prolonged exercise accelerated tissue depletion and redistribution of n-3 PUFAs. Exercise also beneficially

modulated n-6 PUFAs profiles and reduced C18:1 in serum and liver, while brain fatty acid composition remained largely unchanged, which likely reflected homeostatic regulation. Overall, these findings provide insight into the integrated effects of dietary n-3 PUFAs status and exercise on tissue lipid remodeling and support a flux-driven model of fatty acid redistribution rather than extensive transcriptional metabolic reprogramming.

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Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] R. Jäger, J.L. Heileson, S. Abou Sawan, et al., International Society of Sports Nutrition Position Stand: Long-Chain Omega-3 Polyunsaturated Fatty Acids, Journal of the International Society of Sports Nutrition. 22 (2025) 2441775. https://doi.org/10.1080/15502783.2024.2441775.

[2] V. Marchio, G. Augimeri, C. Morelli, et al., Omega-3 fatty acids: molecular weapons against chemoresistance in breast cancer, Cellular & molecular biology letters. 30 (2025) 11. https://doi.org/10.1186/s11658-025-00694-x.

[3] J.J. DiNicolantonio, J.H. O'Keefe, The Importance of Marine Omega-3s for Brain Development and the Prevention and Treatment of Behavior, Mood, and Other Brain Disorders, Nutrients. 12 (2020) https://doi.org/10.3390/nu12082333.

[4] P.R.C. Howe, H.M. Evans, J.C. Kuszewski, et al., Effects of Long Chain Omega-3 Polyunsaturated Fatty Acids on Brain Function in Mildly Hypertensive Older Adults, Nutrients. 10 (2018) https://doi.org/10.3390/nu10101413.

[5] P.A. Nono Nankam, A.E. Mendham, P.J. van Jaarsveld, et al., Exercise Training Alters Red Blood Cell Fatty Acid Desaturase Indices and Adipose Tissue Fatty Acid Profile in African Women with Obesity, Obesity (Silver Spring, Md.). 28 (2020) 1456-1466. https://doi.org/10.1002/oby.22862.

[6] J.P. Schuchardt, P. Beinhorn, X.F. Hu, et al., Omega-3 world map: 2024 update, Progress in lipid research. 95 (2024) 101286. https://doi.org/10.1016/j.plipres.2024.101286.

[7] A. Anzalone, A. Carbuhn, L. Jones, et al., The Omega-3 Index in National Collegiate Athletic Association Division I Collegiate Football Athletes, Journal of athletic training. 54 (2019) 7-11. https://doi.org/10.4085/1062-6050-387-18.

[8] C.J. Gerling, K. Mukai, A. Chabowski, et al., Incorporation of Omega-3 Fatty Acids Into Human Skeletal Muscle Sarcolemmal and Mitochondrial Membranes Following 12 Weeks of Fish Oil Supplementation, Frontiers in physiology. 10 (2019) 348. https://doi.org/10.3389/fphys.2019.00348.

[9] S. Jannas-Vela, A. Espinosa, A.A. Candia, et al., The Role of Omega-3 Polyunsaturated Fatty Acids and Their Lipid Mediators on Skeletal Muscle Regeneration: A Narrative Review, Nutrients. 15 (2023) https://doi.org/10.3390/nu15040871.

[10] P.M. Miotto, C. McGlory, R. Bahniwal, et al., Supplementation with dietary ω-3 mitigates immobilization-induced reductions in skeletal muscle mitochondrial respiration in young women, FASEB journal : official publication of the Federation of American Societies for Experimental Biology. 33 (2019) 8232-8240. https://doi.org/10.1096/fj.201900095R.

[11] M. Tomczyk, Z. Jost, M. Chroboczek, et al., Effects of 12 Wk of Omega-3 Fatty Acid Supplementation in Long-Distance Runners, Medicine and science in sports and exercise. 55 (2023) 216-224. https://doi.org/10.1249/mss.0000000000003038.

[12] X.H. Wang, C.Y. Li, I. Muhammad, et al., Fatty acid composition in serum correlates with that in the liver and non-alcoholic fatty liver disease activity scores in mice fed a high-fat diet, Environmental toxicology and pharmacology. 44 (2016) 140-150. https://doi.org/10.1016/j.etap.2016.04.009.

[13] D.T. Thomas, K.A. Erdman, L.M. Burke, Position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine: Nutrition and Athletic Performance, Journal of the Academy of Nutrition and Dietetics. 116 (2016) 501-528. https://doi.org/10.1016/j.jand.2015.12.006.

[14] M.J. Macartney, L. Hingley, M.A. Brown, et al., Intrinsic heart rate recovery after dynamic exercise is improved with an increased omega-3 index in healthy males, The British journal of nutrition. 112 (2014) 1984-1992. https://doi.org/10.1017/s0007114514003146.

[15] F. Kawabata, M. Neya, K. Hamazaki, et al., Supplementation with eicosapentaenoic acid-rich fish oil improves exercise economy and reduces perceived exertion during submaximal steady-state exercise in normal healthy untrained men, Bioscience, biotechnology, and biochemistry. 78 (2014) 2081-2088. https://doi.org/10.1080/09168451.2014.946392.

[16] T. Li, D.G. Ruan, Z.M. Lin, et al., Endurance Training Counteracts the High-Fat Diet-Induced Profiling Changes of ω-3 Polyunsaturated Fatty Acids in Skeletal Muscle of Middle-Aged Rats, Frontiers in physiology. 10 (2019) 971. https://doi.org/10.3389/fphys.2019.00971.

[17] S.R. Lee, A.V. Khamoui, E. Jo, et al., Effect of conjugated linoleic acids and omega-3 fatty acids with or without resistance training on muscle mass in high-fat diet-fed middle-aged mice, Experimental physiology. 102 (2017) 1500-1512. https://doi.org/10.1113/ep086317.

[18] E.L.G. Bligh, W.J.A. Dyer, A Rapid Method of Total Lipid Extraction And Purification, Canadian journal of biochemistry and physiology. 37 (1959) 911-917. https://doi.org/10.1139/o59-099.

[19] J. Folch, M. Lees, G.H. Sloane Stanley, A simple method for the isolation and purification of total lipides from animal tissues, The Journal of biological chemistry. 226 (1957) 497-509.

[20] G. Fredrickson, F. Barrow, K. Dietsche, et al., Exercise of high intensity ameliorates hepatic inflammation and the progression of NASH, Molecular metabolism. 53 (2021) 101270. https://doi.org/10.1016/j.molmet.2021.101270.

[21] Q. Ouyang, Q. Chen, S. Ke, et al., Rab8a as a mitochondrial receptor for lipid droplets in skeletal muscle, Developmental cell. 58 (2023) 289-305.e286. https://doi.org/10.1016/j.devcel.2023.01.007.

[22] D. Boulghobra, F. Coste, B. Geny, et al., Exercise training protects the heart against ischemia-reperfusion injury: A central role for mitochondria?, Free radical biology & medicine. 152 (2020) 395-410. https://doi.org/10.1016/j.freeradbiomed.2020.04.005.

[23] G. Thompson, G.W. Davison, J. Crawford, et al., Exercise and inflammation in coronary artery disease: A systematic review and meta-analysis of randomised trials, Journal of sports sciences. 38 (2020) 814-826. https://doi.org/10.1080/02640414.2020.1735684.

[24] M.D. Navarro-Hortal, C.L. Ramírez-Tortosa, A. Varela-López, et al., Heart Histopathology and Mitochondrial Ultrastructure in Aged Rats Fed for 24 Months on Different Unsaturated Fats (Virgin Olive Oil, Sunflower Oil or Fish Oil) and Affected by Different Longevity, Nutrients. 11 (2019) https://doi.org/10.3390/nu11102390.

[25] F. Villanego, J. Naranjo, L.A. Vigara, et al., Impact of physical exercise in patients with chronic kidney disease: Sistematic review and meta-analysis, Nefrologia. 40 (2020) 237-252. https://doi.org/10.1016/j.nefro.2020.01.002.

[26] T. Mašek, K. Starčević, Chronic sucrose intake decreases concentrations of n6 fatty acids, but not docosahexaenoic acid in the rat brain phospholipids, Neuroscience letters. 653 (2017) 228-233. https://doi.org/10.1016/j.neulet.2017.05.073.

[27] Z. He, W. Hao, E. Kwek, et al., Fish Oil Is More Potent than Flaxseed Oil in Modulating Gut Microbiota and Reducing Trimethylamine-N-oxide-Exacerbated Atherogenesis, Journal of agricultural and food chemistry. 67 (2019) 13635-13647. https://doi.org/10.1021/acs.jafc.9b06753.

[28] J.E. Singh, Dietary Sources of Omega-3 Fatty Acids Versus Omega-3 Fatty Acid Supplementation Effects on Cognition and Inflammation, Current Nutrition Reports. 9 (2020) 264-277. https://doi.org/10.1007/s13668-020-00329-x.

[29] H. Zhang, Y. He, C. Song, et al., Analysis of fatty acid composition and sensitivity to dietary n-3 PUFA intervention of mouse n-3 PUFA-enriched tissues/organs, Prostaglandins, Leukotrienes and Essential Fatty Acids. 192 (2023) 102568. https://doi.org/https://doi.org/10.1016/j.plefa.2023.102568.

[30] D.B. Jump, Fatty acid regulation of hepatic lipid metabolism, Current Opinion in Clinical Nutrition & Metabolic Care. 14 (2011), https://journals.lww.com/co-clinicalnutrition/fulltext/2011/03000/fatty_acid_regulation_of_hepatic_lipid_metabolism.3.aspx

[31] J.L. Quiles, J.R. Huertas, J.J. Ochoa, et al., Dietary fat (virgin olive oil or sunflower oil) and physical training interactions on blood lipids in the rat, Nutrition. 19 (2003) 363-368. https://doi.org/https://doi.org/10.1016/S0899-9007(02)00949-8.

[32] P.W. Hendrickse, T. Venckunas, J. Platkevicius, et al., Endurance training-induced increase in muscle oxidative capacity without loss of muscle mass in younger and older resistance-trained men, European Journal of Applied Physiology. 121 (2021) 3161-3172. https://doi.org/10.1007/s00421-021-04768-4.

[33] W.S. Harris, M. Miller, A.P. Tighe, et al., Omega-3 fatty acids and coronary heart disease risk: clinical and mechanistic perspectives, Atherosclerosis. 197 (2008) 12-24. https://doi.org/10.1016/j.atherosclerosis.2007.11.008.

[34] D.B. Jump, N-3 polyunsaturated fatty acid regulation of hepatic gene transcription, Current Opinion in Lipidology. 19 (2008), https://journals.lww.com/co-lipidology/fulltext/2008/06000/n_3_polyunsaturated_fatty_acid_regulation_of.5.aspx

[35] G.H. Johnson, K. Fritsche, Effect of Dietary Linoleic Acid on Markers of Inflammation in Healthy Persons: A Systematic Review of Randomized Controlled Trials, Journal of the Academy of Nutrition and Dietetics. 112 (2012) 1029-1041.e1015. https://doi.org/https://doi.org/10.1016/j.jand.2012.03.029.

[36] A.L. Hutchinson, D.M. Liddle, J.M. Monk, et al., n-3 and n-6 Polyunsaturated Fatty Acids Modulate Macrophage–Myocyte Inflammatory Crosstalk and Improve Myocyte Insulin Sensitivity, 16 (2024) 2086. https://www.mdpi.com/2072-6643/16/13/2086

[37] G. Alarcón, J. Roco, A. Medina, et al., Stearoyl-CoA desaturase indexes and n-6/n-3 fatty acids ratio as biomarkers of cardiometabolic risk factors in normal-weight rabbits fed high fat diets, Journal of Biomedical Science. 23 (2016) 13. https://doi.org/10.1186/s12929-016-0235-6.

[38] W. Zhang, R. Chen, T. Yang, et al., Fatty acid transporting proteins: Roles in brain development, aging, and stroke, Prostaglandins, Leukotrienes and Essential Fatty Acids. 136 (2018) 35-45. https://doi.org/https://doi.org/10.1016/j.plefa.2017.04.004.