Abstract Exercise has acute and chronic effects on fat burning. Concerning the acute effect, observed during and after a single exercise session, the enzymes responsible for burning fat increase. Carnitine palmitoyltransferase 1 (CPT1), which regulates the β-oxidation of fatty acids in mitochondria, is believed to play an important role in the acute effect. The activation of AMP-activated protein kinase (AMPK), which detects the energy state of muscles, may contribute to the exercise-induced activation of CPT1. In the chronic effect observed with ongoing exercise training, physiological changes in muscle function are seen. In particular, an increase in the number of mitochondria and enhancement of fatty acid metabolism are observed after endurance training. Peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) plays an important role in adaptive thermogenesis and mitochondrial biogenesis. Exercise enhances the expression of PGC-1α, and the increase in PGC-1α mediates the physiological changes observed in skeletal muscle after endurance training. Recently, several isoforms of PGC-1α were identified. Different signaling pathways regulate the expression of each isoform. In this review, we discuss the regulation of lipid metabolism during physical activity. We also describe the PGC-1α isoforms and the signaling pathways that regulate their expression in relation to the effects of exercise training on skeletal muscle. Finally, we introduce two studies that may explain the systemic effect of endurance training.

Keywords: carnitine palmitoyltransferase 1 (CPT1), AMP-activated protein kinase (AMPK), peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α), β-oxidation, mitochondria, adaptation

Introduction

Nutrients must be metabolized to support life. Most nutrients are used for energy metabolism, namely the synthesis of ATP. The synthesis of ATP uses energy released by the metabolism of organic compounds such as glucose, lipids, and amino acids. Lipids are stored in large quantities in the human body and are used for ATP synthesis during periods of starvation or physical activity. Although fatty acids are used for ATP synthesis from lipids, they must be oxidized within mitochondria and peroxisomes, and they require proteins for delivery because they are insoluble in water. Thus, unlike carbohydrates, lipids cannot be easily used for energy metabolism.

Exercise training prevents obesity, hypertension, diabetes, and hyperlipidemia, which are included in the diagnostic criteria of metabolic syndrome. However, there are many questions about the preventative mechanism of exercise. For example, does exercise prevent hypertension, diabetes, and hyperlipidemia by improving obesity? Although the energy expenditure of skeletal muscle accounts for only 20%–35% of the whole-body basal metabolism in adults (brain, liver, and heart + kidney account for approximately 20% each), the role of skeletal muscle in lipid metabolism is very important because skeletal muscle consumes lipid, rather than sugar, as its main energy substrate, and it is the main source of energy consumption during exercise.
Effect of exercise time and intensity on fatty acid oxidation

Exercise increases blood flow, oxygen consumption, and energy expenditure in the skeletal muscle. The main energy sources for skeletal muscle during exercise are glycogen and triglycerides in the muscle, and glucose and free fatty acids (FFA) in the blood stream. Although the amount of blood glucose absorbed by skeletal muscle increases during exercise, the amount of glucose released from the liver also increases; thus, the blood glucose level during exercise does not change considerably. The FFA concentration in the blood stream increases because the amount of FFA mobilized by fat cells exceeds the amount of FFA taken up by skeletal muscle. Lipolysis, stimulated by catecholamines, glucagon, and glucocorticoids, is believed to mobilize FFAs from fat cells during exercise.

The usage of fatty acids during exercise varies with the time and intensity of exercise. Large increases in the oxidation of FFA and glucose were observed with low-intensity exercise at 30% of maximum oxygen uptake. The proportion of FFA-derived energy production during exercise increased over time: 37%, 50%, and 62% of the energy was produced from FFA oxidation at 90 min, 3 h, and 4 h after the beginning of exercise, respectively (Fig. 1).

The intensity of exercise affects fatty acid usage during exercise. In addition, the origin of FFA varies with the intensity of exercise. As shown in Fig. 2, blood FFA is the main substrate for energy production during exercise at 25% of maximum oxygen uptake (VO2 max), whereas intramuscular triglycerides and blood FFA are used equally at 65% and 85% VO2 max. The amount of energy produced from lipids (blood FFA and intramuscular triglycerides) increases at 65% VO2 max; however, the proportion of energy derived from lipids decreases. During vigorous exercise, such as at 85% VO2 max, the amount and proportion of energy production derived from lipids decreases. Thus, to combat obesity, maintaining low- to moderate-intensity exercise for a long time may be more effective than performing high-intensity exercise for a short time.

The amount of FFA oxidized during exercise differs in trained and untrained people. Usually, FFA oxidation is maximal at an exercise intensity near 50% of maximum oxygen uptake. However, the ability to oxidize FFA increases in people who have improved their heart and lung capacity and muscular strength through exercise training. In these people, the maximum rate of FFA oxidation is observed at an exercise intensity near 60% of maximum oxygen uptake. Fig. 3 compares FFA and carbohydrate oxidation in trained and untrained people exercising at the same intensity. The oxidation of blood FFA mobilized from adipose tissue was higher in the trained people than in the untrained people. Thus, trained people lose weight more easily than untrained people even when they perform the same exercise.

Molecular mechanism of increased FFA oxidation during exercise

Fatty acids derived from the hydrolysis of adipose tissue and skeletal muscle triglycerides are important energy substrates during prolonged moderate-intensity exercise. Hormone-sensitive lipase and adipose triacylglycerol lipase are essential for efficient lipolysis in adipose tissue and skeletal muscle. Both lipases play an important role in the mobilization of FFAs for oxidation during exercise.
lipolytic role during exercise; deletion of these lipases impairs exercise performance in mice. In skeletal muscle, during contraction-induced muscle lipolysis, adipose triacylglycerol lipase and CGI-58 associate, and the lipid droplet-associated proteins work together to regulate lipolysis.

**Mechanism of fat mobilization during exercise.** Exercise is thought to mobilize FFA from adipose tissue through the following pathway: exercise activates the sympathetic nerve, which promotes catecholamine release; catecholamines in turn stimulate β-adrenergic receptors (AR) on adipocytes; β-ARs activate enzymes involved in lipolysis, thus increasing the release of FFA into the bloodstream. However, it is also thought that exercise enhances fat mobilization by stimulation, except for the sympathetic nervous system or the β-AR, because increased fat mobilization during exercise is observed when a β-AR inhibitor is administered before exercise or when all three isoforms of the β-AR are knocked out (unpublished observation by the authors). Atrial natriuretic peptide (ANP), a hormone secreted by the heart, has recently attracted attention. Whereas catecholamines increase cyclic AMP (cAMP) levels in fat cells, ANP and brain natriuretic peptide (BNP) increase cyclic GMP (cGMP) levels. Because the ANP concentration increases in proportion to the intensity of exercise and the amount of cGMP in adipocytes therefore increases as well, ANP may participate in fat mobilization during exercise. However, further studies are required to determine whether ANP administration enhances fat mobilization directly. Furthermore, blood levels of growth hormone, glucagon and glucocorticoid, which increase with exercise, may contribute to fat mobilization.

**Conversion of FFA to ATP in skeletal muscle.** Blood FFA is taken up by skeletal muscle. FFA is converted by β-oxidation into acetyl-coenzyme A (acetyl-CoA), which is used to generate ATP in mitochondria through the TCA cycle and oxidative phosphorylation. As shown in Fig. 4, FFA (denoted LCFA in Fig. 4) binds to albumin in the bloodstream. Because the affinity between FFA and albumin is weak, FFA easily dissociates from albumin and moves into the interstitial space between the gap junctions of capillaries or by fatty acid translocase CD36. Vascular endothelial growth factor-B (VEGF-B) secreted from skeletal muscle contributes to the trans-endothelial transport of circulating FFA into skeletal muscle by enhancing the expression of fatty acid transport proteins (FATPs) in endothelial cells. FFA binds to lipid binding protein (LBP) in the interstitial space. Uptake of FFA into myocytes is then mediated by three different proteins, plasma membrane fatty acid binding protein (FABPpm), CD36, and FATPs. However, these three transporters may channel FFA preferentially to different metabolic fates or pools. For example, FFA transported by FATP1 and CD36 may be used for oxidation and lipid deposition in skeletal muscle, respectively. FFA is thought to enter myocytes via caveolin called as lipid rafts. CoA is added to FFA by acyl-CoA synthetase (ACS) at the plasma membrane. FFA-CoA (acyl-CoA) binds to cytoplasmic fatty acyl-CoA binding protein (ACBP). Some FFA binds to cytoplasmic fatty acid binding protein (FABP) without conversion to acyl-CoA. Part of the acyl-CoA pool is deposited as triglycerides in the cytoplasm, and another part of the acyl-CoA pool is oxidized to produce ATP in mitochondria.

Because acyl-CoA cannot pass through the mitochondrial inner membrane, it must be converted to acylcarnitine by carnitine palmitoyltransferase I (CPT1) at the outer membrane (Fig. 5). Acylcarnitine is transported through the mitochondrial inner membrane by a translocase (CAT) and is converted to acyl-CoA by CPT2 in the inner membrane. FADH₂, NADH+H⁺, and acetyl-CoA are produced from acyl-CoA by β-oxidation, and the TCA
Fig. 4 Schematic representation showing the transport of fatty acids from capillaries to mitochondria\(^{77}\). VLDL, very-low-density lipoprotein; ALB, albumin-bound fatty acid; LPL, lipoprotein lipase; ALB, albumin receptor; LBP, lipid binding protein; FATP, fatty acid transfer protein; ACS, acyl-CoA synthetase; FABP, cytosolic fatty acid binding protein; ACBP, acyl-CoA binding protein; TG, triacylglycerol; LCFA, long-chain fatty acids; CD36, fatty acid translocase; FABP, plasma membrane fatty acid binding protein; CPT1, carnitine palmitoyltransferase 1

Fig. 5 Schematic of the regulation of carnitine palmitoyltransferase 1 (CPT1) activity and malonyl-CoA concentration by acetyl-CoA carboxylase (ACC) and malonyl-CoA decarboxylase (MCD). AMP-activated protein kinase (AMPK), activated during exercise, phosphorylates and inhibits ACC, thereby decreasing the conversion of acetyl-CoA to malonyl-CoA. Consequently, the concentration of malonyl-CoA decreases, inhibition of CPT1 activity diminishes, and CPT1 activity increases. MCD converts malonyl-CoA to acetyl-CoA. SIRT4 deacetylates and inhibits MCD, increasing the concentration of malonyl-CoA and inhibiting CPT1 activity. The relationship between SIRT4 activity and exercise is unknown.
cycle produces additional FADH$_2$ and NADH$+\text{H}^+$ from acetyl-CoA. FADH$_2$ and NADH$+\text{H}^+$ are finally oxidized in the respiratory chain, and ATP is produced by oxidative phosphorylation.

**Exercise-mediated regulation of FFA oxidation in skeletal muscle.** Does exercise stimulate FFA oxidation directly? Alternatively, does exercise enhance FFA oxidation by increasing the supply of FFA in the bloodstream without stimulating any of the steps described above? The rate-limiting step of FFA oxidation during exercise is suggested by the fact that FFA oxidation decreases when exercise intensity increases. During high-intensity exercise, because the rate of fat mobilization from adipose tissue may not be sufficient to match the rate of FFA utilization by muscle, the amount of blood FFA available to skeletal muscle decreases, and the amount of blood glucose available increases. Lipolysis in adipose tissue may be one of the rate limiting steps in FFA oxidation during exercise. In fact, FFA oxidation increased when lipid emulsion was administered intravenously during high-intensity exercise, such as at 85% of maximum oxygen uptake (Fig. 6)\(^4,18\). However, total lipid oxidation was increased by only 1.4-fold, even though the rate of appearance of plasma FFA was increased by 4.7-fold by lipid-heparin infusion. In addition, it has been reported that blood FFA concentration does not decrease during exercise\(^4\). These findings suggest that FFA mobilization from adipose tissue is required to maintain exercise performance, but plasma FFA availability does not limit fat oxidation during exercise.

The transport of FFA into mitochondria by intramuscular CPT1 is considered the rate-limiting step in FFA oxidation. CPT1 activity is inhibited by high concentrations of malonyl-CoA. The concentration of malonyl-CoA is regulated by acetyl-CoA carboxylase (ACC) (Fig. 5). ACC exists in two isoforms: ACC1, which is expressed ubiquitously in many tissues, and ACC2, which is expressed predominantly in skeletal muscle. Phosphorylation of ACC inhibits the generation of malonyl-CoA from acetyl-CoA. ACC2 is believed to localize near the outer mitochondrial membrane, near CPT1. Therefore, when ACC2 is phosphorylated and inactivated, the concentration of malonyl-CoA decreases, thus attenuating inhibition of CPT1. Consistently, activation of CPT1 and prevention of obesity are observed in mice lacking ACC2 in skeletal muscle\(^19\).

How then does exercise regulate ACC2 and CPT1 activity? AMP-activated protein kinase (AMPK) phosphorylates ACC1 at Ser79 and decreases its activity\(^20\) (Fig. 5). Pharmacological activation of AMPK by AICAR phosphorylates Ser79 in ACC1 (equivalent to Ser221 in ACC2) and inhibits its activity\(^21\). In addition, AICAR increases FFA oxidation by phosphorylating ACC and reducing malonyl-CoA\(^22,24\). Activation of skeletal muscle AMPK by overexpression of AMPK$\gamma_3$ also increases FFA oxidation and protects against high-fat diet-induced lipid deposition in skeletal muscle\(^25\). However, decreases in skeletal muscle AMPK in genetically modified mice do not reduce basal FFA oxidation in vivo or in isolated skeletal muscle\(^26-29\). Furthermore, skeletal muscle inhibition of liver kinase B1 (LKB1), the upstream kinase of AMPK, does not decrease basal FFA oxidation despite undetectable AMPKa2 activity and ACC phosphorylation\(^30,31\). AMPK functions as an energy sensor in hypothalamic tissues and in peripheral tissues such as the liver, skeletal muscle, and adipose tissue, and promotes catabolism during energy deprivation\(^32,33\). In skeletal muscle, exercise enhances ATP turnover, leading to rapid, intensity-dependent increases in AMP and ADP levels\(^34\). Because AMPK is also rapidly activated in response to muscle contraction and during exercise\(^35-38\), exercise-induced activation of AMPK is thought to affect FFA oxidation during exercise. In order to determine whether skeletal muscle AMPK alters FFA oxidation during exercise, we measured FFA oxidation in vivo in mice overexpressing a skeletal muscle specific dominant-negative (DN) AMPK\(^26\). Although AMPKa2 activity was inhibited in AMPK-DN mice, an exercise-induced increase in FFA oxidation was observed not only in wild-type littermates, but also in AMPK-DN mice. Using AMPK-DN mice, Dzamko et al. also showed that the activation of AMPK was not required to stimulate fatty acid oxidation in skeletal muscle by either AICAR or muscle contraction\(^27\). In addition, the concentration of malonyl-CoA in skeletal muscle just after exercise does not decrease, and the degree of AMPK activation, ACC phosphorylation, and FFA oxidation, does not correlate with exercise duration or intensity in humans\(^39,41\). For example, during low-intensity exercise, FFA oxidation increases considerably, but AMPK and ACC are only partially phosphorylated\(^42\). Meanwhile, during high-intensity exercise, carbohydrates are preferentially oxidized despite activation of AMPK. Thus, evidence suggests that AMPK-independent kinases are responsible for FFA oxidation, or that residual AMPK activity is sufficient to enhance FFA oxidation in AMPK-

![Image](https://example.com/image.png)

**Fig. 6** The rate of appearance of plasma FFA and the rate of total lipid oxidation by lipid-heparin infusion (lipid infusion) during exercise at 85% of maximal oxygen uptake\(^18\).
Malonyl-CoA decarboxylase (MCD) converts malonyl-CoA to acetyl-CoA (Fig. 5). Recently, SIRT4 was reported to deacetylate and inhibit MCD. Mice lacking SIRT4 (SIRT4 knockout mice) display elevated MCD activity and decreased malonyl-CoA levels in skeletal muscle. Consequently, SIRT4 knockout mice display deregulated lipid metabolism, which leads to increased exercise tolerance. These data suggest that SIRT4 or MCD plays a role in lipid oxidation during exercise.

On the other hand, the malonyl-CoA concentration does not change, or decreases slightly, when FFA oxidation is enhanced following low-intensity exercise. A factor(s) other than malonyl-CoA concentration regulates CPT1 activity or FFA oxidation. For instance, CPT1 activity is regulated by the free carnitine concentration, cytosolic pH, and cytoskeletal network. Further study is required to establish the role of AMPK, ACC, and malonyl-CoA in FFA oxidation. A CPT1-independent mechanism may also exist because CD36 in the mitochondrial membrane reportedly regulates FFA oxidation.

Molecular mechanism of increased FFA oxidation by exercise training (adaptive effect)

The amount of FFA oxidation during exercise differs in those with and without exercise training. Differences in the amount of FFA oxidation are also observed in obese people and elderly people. Because the blood FFA concentration after exercise is similar in trained and untrained people, exercise training does not influence fat mobilization. The difference in FFA oxidation is thought to reflect changes in skeletal muscle function induced by exercise training, a phenomenon known as adaptation. Endurance training changes the muscle fiber type, mitochondrial capacity, and angiogenesis in skeletal muscles. These changes contribute to increased FFA oxidation and improvements in endurance capacity. The transcription co-factor peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) is thought to participate in such changes by regulating gene expression because exercise increases the expression of PGC-1α mRNA and exercise training increases the expression of PGC-1α protein, while also promoting oxidative slow-twitch fiber transformation, mitochondrial biogenesis, and angiogenesis.

Three isoforms of PGC-1α and their exercise-induced expression in skeletal muscle. PGC-1α has two isoforms, PGC-1α-b and PGC-1α-c, in addition to the previously reported isoform, PGC-1α-a. Of 795 amino acids, only the 16 N-terminal amino acids in PGC-1α-a differ from those in PGC-1α-b and PGC-1α-c (Fig. 7A). PGC-1α-b and PGC-1α-c are four and 13 amino acids shorter, respectively, than PGC-1α-a. Comparison of the PGC-1α-b and PGC-1α-c sequences with a murine genomic sequence identified a novel exon. Both PGC-1α-b and PGC-1α-c are transcribed from a novel exon 1 (exon 1b), which is located 13.7 kb upstream of the previously reported exon 1 (exon 1a) in the PGC-1α-a gene (Fig. 7B). The nucleotide sequences downstream of exon 2 are the same in the three transcripts. The nucleotide sequences in PGC-1α-b and PGC-1α-c transcripts derived from exon 1b are different: the nucleotide sequence of PGC-1α-b lacks 50 bp found in the sequence of PGC-1α-c, probably because of alternative splicing within exon 1b.

Several molecular pathways that increase PGC-1α expression after exercise have been reported. AMPK, calcium/calmodulin-dependent protein kinase (CaMK), calcineurin A (CnA), and p38 mitogen-activated protein kinase (MAPK) signaling cascades are well-known upstream regulators of PGC-1α expression in skeletal muscle.

In addition, we have previously shown that β2-AR activation is required for low-intensity exercise-induced PGC-1α expression specifically for that of PGC-1α-b and PGC-1α-c. We also reported that the exercise-induced expression of PGC-1α mRNA isoforms was dependent on the intensity of exercise. A single session of low-intensity exercise increased PGC-1α-b and PGC-1α-c mRNA levels via β2-AR activation, but PGC-1α-a mRNA expression increased only after high-intensity exercise, independent of β2-AR activation. Among the PGC-1α isoforms, PGC-1α-b expression increased the most in response to exercise.

Functions of PGC-1α in skeletal muscle. PGC-1α was identified from a cDNA library prepared from the mRNA of brown adipocytes. PGC-1α was shown to bind peroxisome proliferator-activated receptor (PPAR) γ and to regulate gene expression related to mitochondrial biogenesis and cold-induced thermogenesis. Although PGC-1α itself cannot activate transcription, it can recruit histone acetyltransferases such as CREB response element binding protein-binding protein (CBP)/p300. PGC-1α binds many transcription factors including nuclear respiratory factor (NRF) 1, NRF2, estrogen-related receptor (ERR), PPAR, thyroid hormone receptor (TR), farnesoid X receptor (FXR), liver X receptor (LXR), glucocorticoid receptor (GR), hepatocyte nuclear factor (HNF)-4α, and forkhead box O (FOXO) 1, promotes their transcriptional activity, and thereby activates gene expression related to mitochondrial biogenesis, FFA oxidation, lipoprotein secretion, and gluconeogenesis in various tissues. The transcriptional activation domain in PGC-1α resides in the N-terminal 200 amino acids. This region contains binding sites for the histone acetyltransferases such as CBP/p300 and SRC-1. Only the 16 N-terminal amino acids in PGC-1α-a differ from those in PGC-1α-b or PGC-1α-c. This small difference may affect the binding of the PGC-1α isoforms to putative transcription factors; thus, they may have different roles in metabolism. Functional studies of the PGC-1α isoforms, including mutational analysis...
of amino acids near the N-terminus, are required to substantiate this hypothesis.

Several groups have analyzed the effect of increased muscle PGC-1α on endurance performance. Calvo et al. addressed the effects of PGC-1α-a (A53). Mice with muscle-specific overexpression of PGC-1α-a (MCK-PGC-1α-a) demonstrated an improvement in exercise performance and exhibited ~20% higher maximum oxygen uptake than wild-type mice. However, the MCK-PGC-1α-a mice had elevated PGC-1α-a mRNA levels in the heart, which may have been sufficient to elicit the observed effects on maximum oxygen uptake. In contrast, Wende et al. reported that conditional expression of PGC-1α-a in skeletal muscle (not in heart) for 3–4 weeks increased mitochondrial biogenesis, the capacity for mitochondrial fatty acid oxidation, and muscle glycogen stores. Exercise performance was not different between control and conditional PGC-1α-a mice under a low-intensity exercise protocol. However, conditional PGC-1α-a mice could not tolerate a high-intensity exercise protocol, possibly because they were unable to use muscle glycogen during exercise (A58).

We created mice that overexpressed PGC-1α-b in skeletal muscle, but not in the heart. The alterations in the phenotype of our transgenic mice were comparable to those induced by exercise training in rats and humans. Citrate synthase activity increased 3-fold in our transgenic mice. By comparison, rats showed a 2-fold increase in mitochondrial enzymes and in the capacity of skeletal muscle to oxidize pyruvate after 12 weeks of treadmill exercise training (A59). The 20% increase in maximum oxygen uptake in our transgenic mice was comparable to the 9% - 19% increase in maximum oxygen uptake observed after exercise training in humans (A50). Our data indicated that alterations in skeletal muscle metabolism (increased mitochondrial biogenesis, angiogenesis, and fatty acid transport) caused by PGC-1α-b overexpression also contributed to whole-body maximum oxygen uptake and exercise capacity (Fig. 8), as well as to the pump capacity of the heart. Furthermore, across a broad range of absolute exercise intensities or relative exercise intensities, lipid oxidation was always higher in the transgenic mice than in wild-type littermates, suggesting that lipid was the predominant fuel source during exercise in the transgenic mice. These data suggest that adaptation to exercise training is partly due to the induction and activation of PGC-1α-b. Thus, increasing PGC-1α-b protein expression or activity might be a useful strategy to help sedentary people exercise efficiently, which may help prevent metabolic syndrome and increase lifespan.

**PGC-1α and myokines.** Recently, Boström et al. reported that exercise-induced upregulation of PGC-1α expression in skeletal muscle stimulates the production and excretion of a newly identified peptide hormone, irisin (A71). Irisin triggers precursor cells present within white adipose tissue to differentiate into cells with brown adipocyte characteristics, such as a high abundance of uncoupling protein-1, multilocular fat droplets, and mitochondria. Thus, signals other than sympathetic activation might promote brown adipocyte thermogenesis, and irisin-mediated thermogenesis may be one reason for the anti-obesity effect of exercise training. Furthermore, the study showed that
exercise-induced increases in PGC-1α expression affected not only skeletal muscle, but also the function of other tissues. The systemic effect of exercise training may be caused by a myokine, a hormone secreted from skeletal muscle. Non-adrenergic signals to induce thermogenesis may contribute to the development of new strategies to prevent or treat obesity. In addition, induction of irisin may offer a new way to promote weight loss and improve insulin resistance in patients who cannot exercise. Irisin might also be involved in exercise-induced improvements in cognitive function, which have been linked to the increased expression of brain-derived neurotrophic factor (BDNF)\(^7\)\(^2\). Fibronectin type III domain-containing protein 5 (FNDC5), a muscle protein induced during exercise and cleaved and secreted as irisin, was elevated by endurance exercise in the hippocampus of mice. FNDC5 positively regulates the expression of BDNF. In addition, peripheral delivery of FNDC5 to the liver via adenoviral vectors, resulting in elevated levels of blood irisin, induced the expression of BDNF and other neuroprotective genes in the hippocampus. These data suggest that the beneficial effects of exercise on brain health might derive from the increase in BDNF expression that results from upregulation of FNDC5, the precursor of irisin.

Lipid metabolism plays a major role in endurance performance and body composition. As well as lipid metabolism in skeletal muscle, functional changes in other tissues induced by skeletal muscle-derived myokine may be important factors that will help explain the beneficial effects of exercise in future studies.

References


